DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 76-345

FEB 18 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 January 9, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Glyburide and Metformin Hydrochloride Tablets, 1.25 mg/250 mg, 2.5 mg/500 mg, and 5 mg/500 mg.

Reference is also made to your amendments dated April 25, 2002; May 16, November 21, and November 21, 2003; and January 14, 2004. We also acknowledge receipt of your correspondence dated November 7, 2003, and January 14, 2004, addressing the patent issue noted below.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Glyburide and Metformin Hydrochloride Tablets, 1.25 mg/250 mg, 2.5 mg/500 mg, and 5 mg/500 mg, to be bioequivalent and therefore, therapeutically equivalent to the listed drug, Glucovance® Tablets 1.25 mg/250 mg, 2.5 mg/500 mg, and 5 mg/500 mg, respectively, of Bristol Myers Squibb. 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, Glucovance® Tablets of Bristol Myers Squibb, 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 No. 6,303,146 (the '146 patent) is scheduled to expire on January 14, 2020. Your application contains a patent certification to

the '146 patent under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '146 patent is invalid and will not be infringed by your manufacture, use, or sale of Glyburide and Metformin Hydrochloride Tablets, 1.25 mg/250 mg, 2.5 mg/500 mg, and 5 mg/500 mg. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action is brought against IVAX Pharmaceuticals, Inc. (IVAX) for infringement of the '146 patent. This action must be brought against IVAX prior to the expiration of forty-five days from the date the notice you provided under paragraph (2)(B)(i) was received by the NDA/patent holder(s). You have notified the agency that IVAX complied with the requirements of Section 505(j)(2)(B) of the Act, and that no action for infringement of the '146 patent was brought against IVAX within the statutory forty-five day period.

With respect to 180-day generic drug exclusivity, we note that IVAX was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the '146 patent. Therefore, with this approval, IVAX is eligible for 180-days of marketing exclusivity for Glyburide and Metformin Hydrochloride Tablets 1.25 mg/250 mg, 2.5 mg/500 mg, and 5 mg/500 mg. This exclusivity will begin to run from the date IVAX begins commercial marketing of the drug product.

With respect to the "first commercial marketing" trigger for the commencement of exclusivity, please refer to 21 CFR 314.107(c)(4). The Agency expects that you will begin commercial marketing of this drug product in a prompt manner. Please submit correspondence to your application stating the date you commence commercial marketing of this product.

If you have any questions concerning the effective date of approval of an abbreviated new drug application and the Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

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.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

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 (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours

(b)(6)

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