DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 77-415

DEC 15 2006

IMPAX Laboratories, Inc.
Attention: Mark C. Shaw
Vice President,
Regulatory Affairs and Compliance
30831 Huntwood Avenue
Hayward, CA 94544

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 30, 2004, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Bupropion Hydrochloride Extended-release Tablets USP, (XL) 150 mg and 300 mg (Once Daily Dosing).

Reference is also made to your amendments dated June 21 and 29, August 5, September 28, and November 9, 2005; June 5, July 12, July 26, August 4, August 8, August 16, August 18, November 2, and December 14, 2006.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your Bupropion Hydrochloride Extended-release Tablets USP, 150 mg, at this time because of the patent issue noted below. Therefore, only your Bupropion Hydrochloride Extended-release Tablets USP, 300 mg, is **approved.** Your Bupropion Hydrochloride Extended-release Tablets USP, (XL) 150 mg is **tentatively approved.**

The reference listed drug (RLD) upon which you have based your ANDA, Wellbutrin XL Extended-release Tablets, 150 mg and 300 mg of GlaxoSmithKline (GSK), is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos. 6,096,341 (the '341 patent) and 6,143,327 (the '327 patent) are both scheduled to expire on October 30, 2018.

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Bupropion Hydrochloride Extended-release Tablets USP, (XL) 150 mg and 300 mg, under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately unless action is brought against IMPAX Laboratories, Inc. (IMPAX) for infringement of one or more of the patents that were the subjects of paragraph IV certifications. This action must be brought against IMPAX prior to the expiration of 45 days from the date the notice you provided under section 505(j)(2)(B) was received by the NDA/patent holder(s). You notified the agency that litigation was initiated against IMPAX for infringement of the '341 patent in the United States District Court for the Eastern District of Pennsylvania [Bovail Laboratories, Inc. v. Impax Laboratories, Inc., Civil Action No. 05-cv-1085]. This litigation was initiated within the statutory 45-day period with respect to the 150 mg strength; however, it was initiated outside the 45-day period with respect to the 300 mg strength.

## I. Approval of Bupropion Hydrochloride Extended-release Tablets USP, 300 mg

The Division of Bioequivalence has determined your Bupropion Hydrochloride Extended-release Tablets USP, (XL) 300 mg to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Wellbutrin XL Extended-release Tablets of GlaxoSmithKline. Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution specifications are as follows:

The dissolution testing should be conducted in 900 mL of 0.1 N HCl at 37°C, using USP Apparatus I (basket) at 75 rpm.

The test product should meet the following specifications:

1 hr: [redacted]
2 hrs:
4 hrs:
8 hrs:
12 hrs

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data for the first three production size batches. Data should be submitted as a Special Supplement - Changes Being Effected when there are no revisions to the "interim" specifications or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

With respect to 180-day generic drug exclusivity, we note that Anchen Pharmaceuticals, Inc. (Anchen) was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the '341 and '327 patents. Therefore, Anchen is entitled to the 180-day exclusivity for the 150 mg and 300 mg strengths following the final approval of its ANDA. However, we note that IMPAX and its marketing partner, TEVA Pharmaceuticals, have entered into an agreement with Anchen regarding the relinquishment or selective waiver of exclusivity for the 300 mg strength.

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.

Postmarketing 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 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 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
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 all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

## II. Tentative Approval of Bupropion Hydrochloride Extended-release Tablets USP, 150 mg

As noted above, we are unable to grant final approval to your Bupropion Hydrochloride Extended-release Tablets USP, (XL) 150 mg, at this time because of the litigation initiated against IMPAX for infringement of the '341 patent. Your Bupropion Hydrochloride Extended-release Tablets USP, (XL) 150 mg, is therefore **tentatively approved.** This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practices of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii)

   b. the date the court decides[1] that the '341 patent is invalid or not infringed. See sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act, or,

   c. the '341 patent has expired, and

2. The agency is assured there is no new information that would affect whether final approval should be granted.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT - FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as

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[1] This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.

appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a MINOR AMENDMENT - FINAL APPROVAL REQUESTED.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in 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 application 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. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 501 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

For further information on the status of this application, or prior to submitting additional amendments, please contact Lisa Kwok, Project Manager, at 301-827-9275.

Sincerely yours,

Robert Lee Sest / for

12/15/2006

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