DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-515/S-010/S-018

GlaxoSmithKline
Attention: Mary E. Martinson
Senior Director, Psychiatry, US Regulatory Affairs
Five Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Dear Ms. Martinson:

Please refer to your supplemental new drug application (NDA 21-515/S-010) dated November 23, 2004, received November 24, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Wellbutrin XL (bupropion hydrochloride) Extended-Release Tablets.

We acknowledge receipt of your submissions dated December 13, 2005, April 19, 1006, April 27, 2006, and May 22, 2006.

Your submission of December 13, 2005 constituted a complete response to our May 20, 2005 action letter.

We additionally acknowledge receipt of your supplemental application (NDA 21-515/S-018) dated May 16, 2006.

These supplemental new drug applications provide for the following changes:

NDA 21-515/S-010
For the use of Wellbutrin XL in the prevention of seasonal major depressive episodes in patients with seasonal affective disorder.

NDA 21-515/S-018
Revision of pregnancy category from a Category B to a Category C.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and medguide).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15

of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplements NDA 21-515/S-010/S-018**." Approval of this submission by FDA is not required before the labeling is used.

Pediatric Research Equity Act (PREA) Requirements-Studies Deferred
All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for ages 0 to 12 (neonates, infants, and children) years and deferring pediatric studies for ages 13 to 17 years (adolescents) for this application.

Pediatric Exclusivity
Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity, you should submit a "Proposed Pediatric Study Request" ***in addition to*** your plans for pediatric drug development described above. Please note that satisfaction of the requirements in Section 2 of PREA alone may not qualify you for pediatric exclusivity.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of such postmarketing commitments shall be reported annually according to 21 CFR 314.81. The associated commitment is listed below.

Phase 4 Commitments

We remind you of your postmarketing commitments agreed upon in a communication dated May 31, 2006. These commitments are listed below.

1. Deferred Pediatric Studies under PREA

Your deferred pediatric study required under Section 2 of the Pediatric Research Equity Act (PREA) is considered a required postmarketing study commitment. The status of such postmarketing commitments shall be reported annually according to 21 CFR 314.81. The associated commitment is listed below.

You are required to assess the safety and effectiveness of Wellbutrin XL Extended-Release tablets for the prevention of seasonal major depressive episodes in patients with seasonal affective disorder in pediatric patients ages 13 to 17 (adolescents). There should be a reasonable distribution of both sexes in these age strata.

Final Report Submission: 3 years from the date of this letter

Please submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment, whether submitted to the IND or the NDA, must be clearly designated **"Required Pediatric Study Commitments."**

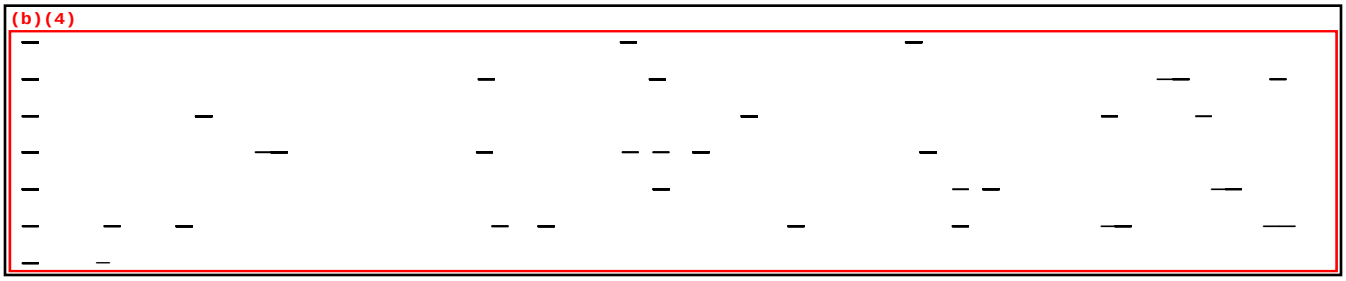
2. Clinical

An adequately powered and designed short-term trial to evaluate the effects of bupropion on intraocular pressure in normal volunteers.

Draft Protocol to Agency: 3 months from the date of this letter.
Final Report Submission: 18 months from the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

(b)(4)



Please submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the 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 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Renmeet Gujral, Pharm.D., Regulatory Project Manager, at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure : Package Insert & MedGuide