DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

APPROVAL LETTER

NDA 21-520/S-008, S-010

Eli Lilly & Company
Attention: Gregory T. Brophy, Ph.D.
Director, US Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Brophy:

Please refer to your June 22, 2006 supplemental new drug application (S-010) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SYMBYAX (olanzapine and fluoxetine HCl) Capsules. We also acknowledge receipt of your amendments to this supplemental application dated October 9, 2006, February 2, 2007, and March 26, 2007.

Please also refer to your March 16, 2006 supplemental new drug application (S-008) for this same drug product.

S-008 provides for modifications to the labeling for SYMBYAX to revise language in the CLINICAL PHARMACOLOGY, *Pharmacodynamics* and CLINICAL PHARMACOLOGY, *Special Populations, Race* subsections and the PRECAUTIONS, *Nursing Mothers* subsection.

S-010 provides for the addition of a 3 mg / 25 mg (olanzapine / fluoxetine) dosage strength, with appropriate modifications to the DESCRIPTION, DOSAGE AND ADMINISTRATION, and HOW SUPPLIED sections of labeling; this strength had been previously included in your initial NDA submission, but was withdrawn prior to approval of the NDA.

We have completed our review of these applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed labeling text (package insert and immediate container label).

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and to the submitted labeling (immediate container label submitted October 9, 2006.). 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 21-520/S-008, S-010**." Approval of this submission by FDA is not required before the labeling is used.

Postmarketing Commitment: PREA
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 requirements for this application, for children aged 0 to 9 years [the condition is difficult to diagnose and treat in this age group]. We are deferring submission of your pediatric studies for ages 10 to 17 years until May 30, 2012. Please note that the required studies should be considered to apply to the full range of approved dosage strengths for SYMBAX, as deemed appropriate for the pediatric age group, and not only to the 3 mg / 25 mg dosage strength. Your proposed clinical protocol should address dosage selection.

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

1. Pediatric safety and efficacy study under PREA for the treatment of major depressive episodes associated with bipolar disorder in pediatric patients ages 10 to 17.
Final Report Submission: On or before **May 30, 2012.**

For the above Phase 4 Commitment, submit the clinical protocol (s) to your IND for this indication. Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitment**".

Dissolution Specification and Expiration Date
Please adopt the following dissolution method and specifications for the 3 mg/ 25 mg strength of olanzapine/fluoxetine hydrochloride capsules:

Apparatus:	USP Apparatus 2 (Paddle) at 50 RPM
Medium:	900 mL of 0.1N hydrochloric acid at 37±0.5°C
Specifications:	------ **of both fluoxetine and olanzapine dissolved at 30 minutes.**

A 36 month expiration date, as requested, is granted based upon the available stability data.

Request for Advertising / Promotional Materials
We request that you submit four copies of the introductory promotional materials 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

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/s/

Thomas Laughren
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