DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-427/S-015/S-017

Eli Lilly and Company
Attention: Bryan Boggs, Pharm.D.
Manager, U.S. Regulatory Affairs
Eli Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Boggs:

Please refer to your supplemental new drug applications dated October 31, 2006 (S-015), and May 17, 2007 (S-017), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cymbalta (duloxetine hydrochloride) Delayed-Release 20mg, 30mg and 60mg capsules.

We acknowledge receipt of your submissions to S-015 dated September 28, 2007, and October 29, 2007. Your submission dated September 28, 2007, constituted a complete response to our action letter dated August 28, 2007.

Reference is also made to Agency letters dated May 18, 2007, and July 30, 2007, requesting information on overdose as well as revisions to the labeling pertaining to serious skin reactions and hyponatremia. We also acknowledge your responses dated August 17, 2007 and November 27, 2007.

The above supplemental applications provide for the following changes to product labeling:

**S-015**

- Revisions throughout labeling to provide for the results of your maintenance data in adult patients with Major Depressive Disorder.

**S-017**

- Revisions to the Precautions-Discontinuation of Treatment with Cymbalta and Adverse Reactions-Postmarketing Spontaneous Reports sections.

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

**Request for Safety Data and Follow-Up Monitoring**

1. We are requesting that you conduct an analysis of serious skin reactions in the placebo-controlled clinical trials database.
2. We are requesting an enhanced pharmacovigilance program by submitting to the Agency of 15-days expedited reports for any serious skin or hypersensitivity reaction with the expectation that these reports would have better collection of information and follow up of these cases.

We are waiving the requirements of 21 CFR 201.157(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

The final printed labeling (FPL) must be identical to the enclosed labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission **"SPL for approved supplements NDA 21-427/S-015 and S-017"**.

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 children aged 0 to 17 years for this application since it is often difficult to perform long term studies within this age group.

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) 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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

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

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

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 CDR Bill Bender, Regulatory Project Manager, at (301) 796-2145.

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

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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Thomas Laughren

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