DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018936/S-091/S-093/S-095
NDA 021235/S-015/S-016/S-017

SUPPLEMENT APPROVAL

Eli Lilly & Company
Attention: Kevin C. Sheehan, MS, Pharm.D.
Manager, Global Regulatory Affairs - US
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Sheehan:

Please refer to your Supplemental New Drug Applications (sNDA) dated and received May 21, 2009 (018936/S-091 and 021235/S-015), November 6, 2009 (018936/S-093 and 021235/S-016), and April 14, 2010 (018936/S-095 and 021235/S-017), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prozac (fluoxetine hydrochloride) 10 mg, 20 mg, and 40 mg capsules and Prozac Weekly (fluoxetine hydrochloride) 90 mg delayed-release capsules.

We acknowledge receipt of your amendments dated November 12, 2009, September 13, 2010, October 22, 2010, March 23, 2011, and March 25, 2011.

Your October 22, 2010, submission constituted a complete response to our September 24, 2010, action letter for applications 018936/S-095 and 021235/S-017.

We also refer to your March 22, 2011, email correspondence providing changes to FDA's March 15, 2011 proposed labeling which resulted in mutual labeling agreement.

Please note that this letter corrects our letter dated April 4, 2011, in which text was inadvertently added to the letter. This letter serves as the official document, retaining the approval date of April 4, 2011.

These supplemental applications provide for the following revisions to product labeling:

018936/S-091 & 021235/S-015, submitted as "Prior Approval" supplements:

1. Revisions to Section 6.2 (Other Reactions)
   - Addition of 4 new Medical Dictionary of Regulatory Activities (MedDRA) adverse reaction terms (i.e. Balance Disorder, Bruxism, Gynecological Bleeding, and Hypotension)

- Reinstatement of 3 Adverse Reaction terms (i.e. Alopecia, Dysuria, and Micturition Disorder)
- Inclusion of the adverse event term depersonalization

2. The following minor additional changes:
   - Deletion of "have not been established" at the end of Section 2.6
   - Revisions to Description Data Source in Sections 5.3, 5.4, 5.5, and 6.1
   - Minor editorial changes

018936/S-093 & 021235/S-016, submitted as "Changes Being Effected" supplements:

1. Revision to Section 8.1 (Pregnancy) to add a statement to the Pregnancy section of the Prozac (fluoxetine) label that states a potential risk of cardiovascular defects in infants of women who were exposed to fluoxetine during the first trimester of pregnancy.
2. Deletion of label language from Prozac USPI and Medication Guide related to the discontinued Prozac Oral Solution.

018936/S-095 & 021235/S-017, submitted as "Prior Approval" supplements:

- These supplements provide for a comprehensive Medication Guide as requested in Agency correspondence dated March 15, 2010.

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to, except with the revisions indicated, the enclosed labeling (text for the package insert and Medication Guide) with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes with the revisions approved in this supplemental application, as well as annual reportable changes, and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

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, contact CDR Kofi Ansah, Senior Regulatory Project Manager, at (301)796-4158.

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: Content of Labeling

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

/s/

THOMAS P LAUGHREN
04/04/2011