DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-936/S-068/S-069
NDA 20-101/S-030/S-031
NDA 20-974/S-003/S-004
NDA 21-235/S-001/S-002

Eli Lilly and Company
Attention: Gregory T. Brophy, Ph.D.
Lilly Corporate Center
Indianapolis, IN 46285-2643

Dear Dr. Brophy:

We acknowledge receipt of your supplemental new drug applications dated July 8, received July 9, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prozac (fluoxetine hydrochloride) pulvules (NDA 18-936/S-069), Prozac solution (NDA 20-101/S-031), Prozac tablets (NDA 20-974/S-004), and Prozac Delayed-Release Capsules (NDA 21-235/S-002).

Reference is also made to Agency communications dated January 9, March 19, and April 19, 2004, requesting revisions to product labeling in order to incorporate class labeling revisions.

The above supplemental applications, submitted under "Changes Being Effected", provide for the following revisions to product labeling:

1. The addition of a new subsection under **WARNINGS** entitled **Clinical Worsening and Suicide Risk**.
2. Revisions to the **PRECAUTIONS-Information for Patients** section regarding clinical worsening.
3. Deletion of the section in **PRECAUTIONS-General** entitled "Suicide".
4. Add a reference to the **WARNINGS** section at the end of the **PRECAUTIONS- Pediatric Use** section, i.e., (see **WARNINGS-Clinical Worsening and Suicide Risk**).
5. The addition of a new subsection entitled **Discontinuation of Treatment with Prozac** in the **PRECAUTIONS-General** section.
6. The addition of a new subsection entitled **Abnormal Bleeding** in the **PRECAUTIONS-General** section.
7. The relocation of the **Hyponatremia** subsection from the end of the **PRECAUTIONS** section to the **PRECAUTIONS-General** section.
8. The addition of an abnormal bleeding paragraph in the **PRECAUTIONS-Information for Patients** section.
9. The addition of a new subsection entitled **Drugs That Interfere With Hemostasis (Non-selective NSAIDs, Aspirin, Warfarin, etc.)** in the **PRECAUTIONS-Drug Interactions** section.
10. The addition of a new subsection entitled **Pregnancy-Nonteratogenic Effects** in the **PRECAUTIONS-Pregnancy** section.
11. The addition of a new subsection entitled **Treatment of Pregnant Women During the Third Trimester** in the **DOSAGE AND ADMINISTRATION-Special Populations** section.

12. The addition of a new subsection entitled **Discontinuation of Treatment with Prozac** in the **DOSAGE AND ADMINISTRATION** section.

We have completed our review of supplemental applications 18-936/S-069, 20-101/S-031, 20-974/S-004, and 21-235/S-002, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the submitted final printed labeling (package insert submitted July 8, 2004), which incorporates all of the revisions made in the above supplements. Accordingly, these supplemental applications are approved effective on the date of this letter.

Additionally, since supplemental applications 18-936/S-068, 20-101/S-030, 20-974/S-003, and 21-235/S-001 are superceded by the approval of 18-936/S-069, 20-101/S-031, 20-974/S-004, and 21-235/S-002, these supplemental applications will be retained in our files.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Mr. Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

Sincerely,

*{See appended electronic signature page}*

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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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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Russell Katz
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