DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-936/S-067

Eli Lilly and Company, Inc.
Attention: Greg Brophy, Ph.D.
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Brophy:

Please refer to your supplemental new drug application dated March 21, 2001, received March 23, 2001, submitted under section 505 (b) of the Federal Food, Drug, and Cosmetic Act for Sarafem® (fluoxetine hydrochloride) capsules (NDA 18-936/ S-067). The supplemental application provides for the use of Sarafem in the treatment of premenstrual dysphoric disorder (PMDD), using an intermittent dosing regimen, as an alternative to the currently approved continuous dosing regimen.

Please also refer to our approvable action letter for this supplemental application, issued January 17, 2002. Your subsequent amendment to the supplemental application, which was submitted to FDA on Febtuary 4, 2002, and received on February 5, 2002, constituted a complete response to our action letter.

We have completed the review of this application as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the supplemental application is approved effective on the date of this letter (see electronic signature page for date).

The final printed labeling (FPL) must be identical to the enclosed labeling text (text for the package insert with PPI). For your convenience, we have appended both a marked-up and a clean copy of the agreed-upon FPL to this letter. Please note that marketing this product with FPL that is not identical to the approved labeling text may render the product misbranded, and an unapproved new drug.

Please submit the copies of the final printed labeling (FPL), electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is abailable, but no more than 30 days after it is printed. If you choose to submit paper copies, please individually mount 10 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated “FPL for approved Supplemental NDA 18-936 / S-067”. Approval of this submission by FDA is not required before the labeling is used.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Pediatric Final Rule
You have previously been advised that as of April 1, 1999, the Pediatric Final Rule (63 FR 66632) requires that 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 note your submission of a pilot pediatric study protocol outline to this Division on January 22, 2001. As indicated in our letter of August 8, 2001, we consider this an acceptable pilot study, but it will not meet the requirements of the Pediatric Rule. We also note your confirmation as of May 28, 2002 that the pilot study is in progress, and we are aware that questions of diagnostic reliability and validity remain to be settled. We therefore remain in agreement, as noted in our January 17, 2002 approvable letter, that you may submit either a request for a waiver or detailed protocols for definitive pediatric studies, based on the outcome of your pilot study. We reiterate our request that you submit this information within 120 days of submitting the final report for the pilot pediatric study to this Division.

Financial Disclosure Rule
Also, as you know, on February 2, 1999, the Financial Disclosure Rule, published in the Federal Register of February 2, 1998, became effective. We note that you have satisfactorily addressed the requirements of this rule in this supplemental application as amended. Please note that this requirement will apply to pediatric studies conducted in accordance with the Pediatric Final Rule. For further information about this requirement, you may contact Ms. Lee Ripper, Associate Director, Regulatory Affairs, Office of Drug Evaluation II, at 301-827-5921.

Promotional Materials
We note your prior submission of introductory promotional materials that you propose to use for these products, submitted and received on April 29, 2002. This information has been forwarded to the Division of Drug Marketing, Advertising, and Communications.

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, please call Doris J. Bates, Ph.D., Regulatory Project Manager, at 301-594-2850.

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

Enclosure (Revised Final Labeling, clean copy and marked up version)

[Please note that the electronic signature page will be the last page of the document, following the enclosed labeling.]

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

/s/

Russell Katz

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