NDA 18-936/S-058

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

Dear Dr. Brophy:

Please refer to your resubmitted supplemental new drug application (S-058) dated January 21, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SARAFEM™ (fluoxetine hydrochloride) Pulvules. This submission constituted a complete response to our December 22, 1999 action letter. We also acknowledge receipt of your submissions dated:

February 25, 2000	March 8, 2000	April 6, 2000
April 21, 2000	April 24, 2000	May 5, 2000
May 16, 2000	May 24, 2000	May 25, 2000
May 30, 2000	June 5, 2000 (2)	June 6, 2000
June 28, 2000	June 29, 2000	

In addition, we note discussions which have taken place between representatives of your firm and this Agency on April 11, 2000; May 26, 2000; June 6, 2000; June 22, 2000; and June 27, 2000.

Supplemental application S-058 proposes the use of fluoxetine in the treatment of PMDD (premenstrual dysphoric disorder). We have completed the review of this resubmitted supplemental 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 labeling text (please refer to the enclosed physician and patient package insert text). Accordingly, supplemental application S-058 is approved, effective on the date of this letter.

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

Please submit 20 copies of the FPL, as soon as it is available, in no case more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated “FPL for approved sNDA number 18-936/S-058”. Approval of this submission by FDA is not required before the labeling is used.

Please also submit one market package of the drug product when it is available. This

may be the smallest available package size of the lowest dosage strength you propose to market.

We note that both your container labeling and your package insert contain the storage instruction, “Protect from Light”. This is intended to protect the drug product from light-induced discoloration in the approved blister packaging. We note your commitment, as discussed with representatives of this Division on June 27, 2000, to monitor the drug product in photostability studies, to submit the results of such studies within six months of the date of issuance of this letter, and to remove the light protection instruction from labeling via a CBE-30 labeling supplement if the stability studies demonstrate that light protection is not necessary.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product in the newly approved indication. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Neuropharmacological Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a “Dear Health Care Practitioner” letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this supplemental NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We note that adverse reaction reports associated with either PROZAC® or SARAFEM™ should be submitted to NDA 18-936.

You have previously been advised that 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 April 24, 2000 submission of a proposal for a pilot study of PMDD in adolescents, to estimate its prevalence and

evaluate its response to treatment with fluoxetine. Further correspondence on this proposal has been forwarded to you under separate cover on June 19, 2000.

Also, as you know, on February 2, 1999, the financial disclosure rule, published in the Federal Register of February 2, 1998, became effective. Although your supplemental NDA was submitted (and all clinical studies in the NDA were completed) before this rule was in effect, for any covered clinical studies submitted after February 2, 1999 which relate to this indication, the regulations require financial information on clinical investigators conducting those trials. Please note that this requirement also applies to pediatric studies conducted in accordance with the Pediatric Final Rule. For further information about this requirement, you may contact Ms. Linda Carter, Associate Director, Regulatory Affairs, Office of Drug Evaluation I at 301.594.6758.

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 concerning this supplemental NDA, please contact Doris J. Bates, Ph.D., Regulatory Project Manager, at (301) 594-5536.

Sincerely yours,

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

Attachment (agreed-upon package insert text)