**DEPARTMENT OF HEALTH & HUMAN SERVICES** **Public Health Service**

**Food and Drug Administration**
**Rockville MD 20857**

NDA 21-411

Eli Lilly and Company
Attention: Gregory Brophy, Ph.D.
Director, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, Indiana 46285

Dear Dr. Brophy:

Please refer to your new drug application (NDA) dated October 11, 2001, received October 12, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Strattera® (atomoxetine hydrochloride) Capsules.

We acknowledge receipt of your submissions dated September 26, October 10, 18, 23 and 31; November 11, 12 and 20, 2002.

The September 26, 2002, submission constituted a complete response to our August 12, 2002 action letter.

This new drug application provides for the use of Strattera® (atomoxetine hydrochloride) Capsules for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD) for children and adolescents ages 6 - 18 and adults.

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 application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the agreed upon enclosed labeling (text for the package insert and patient 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 the copies of 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 available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-411." Approval of this submission by FDA is not required before the labeling is used.

Post Marketing Commitments

We remind you of your post marketing study commitments in your submission of November 20, 2002. These commitments are listed below.

1. 75-day Repeated Dose Toxicity Study in Young Rats to qualify i(b)----------

   Study Start: April 14, 2003
   Final Report: November 15, 2003

2. Ames Test to qualify (b)----------

   Study Start: Estimated start date January 15, 2003
   Final Report: Estimated report date April 4, 2003

3. In vitro chromosomal aberration study to qualify i(b)----------

   Study Start: Estimated start date January 15, 2003
   Final Report: Estimated report date April 30, 2003

We also acknowledge your November 26, 2002, telephone commitment to conduct post marketing studies to assess long-term efficacy and effects on growth. We would like to promptly schedule a meeting with you to discuss the specific details of these studies and the timelines for their completion.

Please submit all clinical protocols to your IND for this product; and, all non-clinical and chemistry protocols and all final study reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), please include a status summary of each commitment in your annual report to this NDA. This status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, the number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled, 'Postmarketing Study Protocol', 'Postmarketing Study Final Report', or 'Postmarketing Study Correspondence'.

Chemistry Issues

1. A 24 month expiry is granted for drug product in commercial packages (30 count in 75 mL WHDPE bottles and 2000 count in 1500 mL WHDPE bottles) and physician sample packs (14 and 24 counts in 50 mL WHDPE bottles and 4, 10, 14 and 24 counts in blisters). A 12 month expiry is granted for the drug product physician sample packs of 4 and 10 counts in 50 mL WHDPE bottles based on the stability data provided.

2. We have not completed validation of the regulatory methods. However, we expect to continue to work with you to resolve any problems that may be identified.

Biopharmaceutics Issues

1. The following agreed upon dissolution method and specification has been approved for all strengths of atomoxetine HCl capsules (5,10, 18, 25, 40 and 60 mg) capsules:

| | |
|---|---|
| Apparatus: | USP apparatus II (paddle) at 50 rpm |
| Medium: | 1000 ml of 0.1 N HCL at 37°C |
| Specification: | Q = (b)--at 30 minutes. |

2. Please note that we still do not consider atomoxetine hydrochloride to be a BCS class 1 drug since it fails to meet the criterion for dissolution.

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

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81. In addition, we request that you report any post-marketing cases of appendicitis or diabetes mellitus/hyperglycemia as 15-day reports.

If you should have any questions, please call Ms. Anna Marie H. Weikel, R.Ph., Regulatory Affairs Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Director
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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Robert Temple

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