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RESEARCH**

*APPLICATION NUMBER:*

**19-839/S-044**

**20-990/S-010**

**APPROVABLE LETTER**



NDA 19-839/S-044  
NDA 20-990/S-010

Pfizer Inc.  
Attention: Alan J. Dunbar  
Director, Worldwide Regulatory Strategy  
235 E. 42nd Street  
NY, NY 10017

Dear Mr. Dunbar:

Please refer to your supplemental new drug applications dated December 14, 2001, received December 17, 2001, submitted under section 505(b) pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Zoloft (sertraline hydrochloride) 25 mg, 50 mg, and 100 mg tablets (19-839) and 20 mg/ml oral concentrate (20-990).

We additionally reference an Agency action letter dated September 30, 2002.

We acknowledge receipt of your submission dated December 19, 2002. Your submission of December 19, 2002 constituted a complete response to our September 30, 2002 action letter.

These "Prior Approval" supplemental new drug applications provide for additional safety data in the pediatric population.

We have completed the review of these applications, as amended, and they are approvable. Before these applications may be approved, however, it will be necessary for you to submit the following information and respond to the following issues:

### **Labeling**

Accompanying this letter (Enclosure) is the Agency's counterproposal to the labeling submitted in your December 19, 2002 amendment. We have accepted many of your proposed changes, however, we are requesting additional data to justify your proposed alternative language in the **Pediatric Use** section. We have included bracketed comments to denote our explanation for revisions to the labeling. Additionally, please note that the labeling may need to be subsequently revised based upon our receipt and further review of the pediatric growth data requested later in this letter.

### **Pediatric Growth Data**

We are concerned about the summary statement proposed for labeling in regard to weight change during the long term (6-month) open label extension on sertraline treatment. While the summary statement suggests no weight change, it is our impression, looking at the data on change in weight percentile, that a preponderance of patients in the group who had placebo during the controlled phase and sertraline during the open extension moved to lower weight percentiles during that 6 month period. Thus, we request additional analyses for these data to clarify this finding. In the meantime, we have deleted this statement from labeling.

Investigators have used growth curve data to assess growth in open label studies, in some cases by using z-scores. A z-score is the number of standard deviations that one is from their gender/age standardized mean. Investigators determine each subject's z-score at the beginning and then at the end of the observation period. If the mean change in the z-score is negative, then the group did not grow as expected based on normal population data.

Please provide an electronic data set for the long-term open-label study as well as the two placebo-controlled studies that includes one row for each patient and includes the study number, indication, age, gender, baseline weight and z-scores (prior to the controlled trial and baseline for the open-label phase), end of the open-label phase weight and z-scores, treatment and assigned dose.

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

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to file amendments, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the applications. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, call 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

Enclosure

36 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

X § 552(b)(4) Draft Labeling

\_\_\_\_\_ § 552(b)(5) Deliberative Process