DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-822/S-016
NDA 21-046/S-002

Forest Laboratories, Inc.
Attention: Tracey Varner
Senior Manager, Regulatory Affairs
Harborside Financial Center
Plaza Three, Suite 602
Jersey City, NJ 07311

Dear Ms. Varner:

Please refer to your supplemental new drug applications dated April 18, received April 19, 2002, submitted under section 505(b) pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Celexa (citalopram hydrobromide) 10 mg, 20 mg and 40 mg Tablets (20-822) and 10 mg/5 ml Oral Solution (21-046).

These "Prior Approval" supplemental new drug applications propose the use of Celexa (citalopram hydrobromide) tablets and oral solution to treat pediatric major depressive disorder (MDD).

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b)(5). The deficiencies may be summarized as follows:

Specifically, the results from one of your two studies, Study 94-404, failed to demonstrate the efficacy of Celexa in pediatric patients with MDD. While we consider the second study, Study CIT-MD-18, to be positive, a single positive study is not sufficient, in our view, to support this new claim in pediatric MDD. We made this point in our April 28, 1999 written request, i.e., that the history of predominantly negative placebo-controlled trials in pediatric MDD argues against the extrapolation of the MDD claim from adults to pediatric patients on the basis of the adult data alone, or even on the basis of one positive study in pediatric patients, along with positive adult data.

Given the fact that negative trials are frequently seen, even for antidepressant drugs that we know are effective, we also do not feel that it would be useful to describe the one positive and the one negative trial in labeling, since this may be misinterpreted as evidence that Celexa either does work in this population, or does not. Rather, we feel that these two studies, by themselves, are essentially uninterpretable, since we know that, in adults, studies in MDD, even if fully

adequate on face and for drugs that we know to be effective, fail to discriminate the active drug from placebo about half the time.

Thus, in the absence of sufficient evidence to support this new claim, we feel that the existing language, suggesting simply that efficacy has not been established in this population, is still most appropriate. Regarding the PK and safety data, we feel that it is not useful to add these data, given the fact that efficacy has not been established.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action, FDA may proceed to withdraw the supplemental application. 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 products may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this changes prior to approval of this supplemental application.

If you have any questions, call Paul David, Senior Regulatory Health 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

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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