

Food and Drug Administration
Rockville MD 20857

IND 28,705

AUG 20 1999

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

Dear Dr. Brophy:

Please refer to your Investigational New Drug Application (IND) for olanzapine.

We also refer to your amendments of May 7, 1999, providing the new protocol F1D-MC-HGHL, entitled, "Olanzapine Versus Placebo in the Prevention of Relapse in Bipolar Disorder."

We have completed the review of your submission and an issue of concern is the population initially treated. Since there are short-term data suggestive of an acute antimanic effect of olanzapine, logically the patients recruited for this trial should be those same patients, i.e., patients with either acute mania or a mixed state. However, you intend to include patients with acute depression as well, and to randomize any "responders" along with those manic and mixed patients who are "responders." The difficulty is that there are no data addressing the short-term antidepressant efficacy of olanzapine. Consequently, it would be misleading to describe the outcome of the initial phase of this study, since it would imply that olanzapine has an antidepressant effect, when in fact, this has not been established. We request that you limit enrollment to patients with acute mania or mixed states as the index episode for entry into this trial.

If you have any questions, contact Steven D. Hardeman, R.Ph., Regulatory Project Manager, at (301)-594-5533.

Sincerely yours,

Russell Katz, M.D.
Acting Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ZY 654 710

RECEIVED AUG 25 1999