DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-267/S-001 **SUPPLEMENT APPROVAL**

Abbott Laboratories
Attention: Lee Muraoka
Director, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Mr. Muraoka:

Please refer to your supplemental new drug application dated and received on December 16, 2008, submitted under section 505(b)of the Federal Food, Drug, and Cosmetic Act (FDCA) for Depakote (divalproex sodium) Extended Release 250 and 500 mg tablets.

We acknowledge receipt of your submissions dated December 16, 2008, March 19, 2009, and May 15, 2009.

This "Prior Approval" supplemental new drug application provides for the following labeling changes:

Section 1: Indications and Usage, subsection 1.1 Mania, paragraph three

"The ~~***safety and***~~ effectiveness of valproate for long-term use in mania, i.e., more than 3 weeks, has not been ~~***systematically evaluated***~~ **demonstrated** in controlled clinical trials. Therefore, physicians who elect to use Depakote ER for extended periods should continually reevaluate the long-term risk-benefits of the drug for the individual patient."

Section 2: Dosage and Administration, subsection 2.1 Mania, paragraph two

"There is no body of evidence available from controlled trials to guide a clinician in the longer term management of a patient who improves during Depakote ER treatment of an acute manic episode. While it is generally agreed that pharmacological treatment beyond an acute response in mania is desirable, both for maintenance of the initial response and for prevention of new manic episodes, there are no ~~***systematically obtained***~~ data to support the benefits of Depakote ER in such longer-term treatment (i.e., beyond 3 weeks)."

Section 6: Adverse Reactions, subsection 6.1 Mania, paragraph one

"The incidence of treatment-emergent events has been ascertained based on combined data from two **three week** placebo-controlled clinical trials of Depakote ER in the treatment of manic episodes associated with bipolar disorder."

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text.

LABELING

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert).

Within 14 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission **"SPL for approved supplement NDA 22-267/S-001."**

We note that you have fulfilled the pediatric study requirement for all relevant ages for this application.

POSTMARKETING COMMITMENTS

We acknowledge your written commitment to conduct the following postmarketing study as described in your email dated October 8, 2009 and as outlined below:

PMC1552-1
Conduct an adequate and well-controlled drug-drug interaction study to systematically evaluate whether an interaction occurs between olanzapine and Depakote ER when they are co-administered.

Final Protocol Submission:	by January 16, 2010
Study Completion Date:	by July 16, 2011
Final Report Submission:	by October 16, 2011

Submit the protocol to your IND for this product, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA, referencing PMC 1552-1. Use the following designators to prominently label all submissions, including supplements, relating to this postmarketing study commitment, as appropriate:

- **POSTMARKETING STUDY COMMITMENT PROTOCOL**
- **POSTMARKETING STUDY COMMITMENT FINAL REPORT**
- **POSTMARKETING STUDY COMMITMENT CORRESPONDENCE**

In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The 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, number of patients entered into each study.

REPORTING REQUIREMENTS

All 15-day alert reports, periodic (including quarterly) adverse drug experience reports, field alerts, annual reports, supplements, and other submissions should be addressed to the original NDA 21-168 for this product, not to this NDA. In the future, do not make submissions to this NDA except for the final printed labeling requested above.

If you have any questions, call Terry Harrison, Regulatory Project Manager, at (301) 796-2770.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: agreed-upon labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22267	SUPPL-1	ABBOTT LABORATORIES	DEPAKOTE ER

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

THOMAS P LAUGHREN
10/15/2009