CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

002255Orig1s000

OTHER ACTION LETTER(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-255

COMPLETE RESPONSE

Schwarz Biosciences, Inc.
Attention: Alan Blumberg
Senior Director, US Regulatory Affairs
P.O. Box 110167
Research Triangle Park, NC 27709

Dear Mr. Blumberg:

Please refer to your new drug application (NDA) dated September 28, 2007, received September 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Vimpat (lacosamide) Oral Solution (b) (4).

We acknowledge receipt of your additional submissions dated:

November 26, 2007	March 20, 2008	April 30, 2008	July 17, 2008	September 4, 2008
December 13, 2007	April 3, 2008	May 9, 2008	July 30, 2008	September 23, 2008
January 23, 2008	April 9, 2008	May 27, 2008	August 1, 2008	October 15, 2008
February 13, 2008	April 14, 2008	June 11, 2008	August 14, 2008	October 21, 2008
February 22, 2008	April 18, 2008	July 11, 2008 (2)	August 27, 2008	

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. Before this application may be approved, we ask that you address the following issues.

CLINICAL

As discussed with you during a teleconference with the Agency on April 23, 2008, we have concluded that the solution concentration (b) (4) may lead to significant dosing errors. Specifically, we are concerned that the recommended or prescribed doses (in milligrams) can not be measured accurately with this concentration (b) (4) of solution. The Agency's Division of Medication Error and Prevention Analysis (DMEPA) notes that most liquids are prescribed and measured in milliliters, and that postmarketing experience has shown that demarcation in milligrams instead of milliliters is associated with numerous medication errors.

In addition, [redacted] (b) (4) we have concerns regarding the accuracy of the measured dose if, for example, a small dose is prescribed [redacted] (b) (4).

We note your recognition of these issues in an email from Ms. Misty D'Ottavio of your firm sent to Dr. Ware of this Agency on April 28, 2008 as follow-up to the teleconference with you on April 23, 2008. In that email Ms. D'Ottavio states the following:

> "Schwarz will evaluate other concentrations of lacosamide oral syrup [*sic*] to alleviate the Agency's concern with prescribing and dosing errors and to eliminate the need for a special dosing device. A previous formulation of lacosamide oral syrup [*sic*] utilized a 10 mg/mL concentration, and therefore, Schwarz may first look at that concentration with some minor optimization to expedite development efforts. The revised formulation/concentration, along with all appropriate data, will be provided to the Agency as soon as available."

LABELING

1. We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html.

2. Please submit draft carton and container labeling revised as follows:

   - We ask that you revise the precautionary warning statement for phenylketonurics [redacted] (b) (4)

   - Add the following bolded statement or appropriate alternative to the carton and container labels per 21 CFR 208.24(d): "**ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide**".

OTHER

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a

meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (http://www.fda.gov/cder/guidance/2125fnl.htm).

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Supervisory Regulatory Project Manager, at (301) 796-1160.

Sincerely,

{See appended electronic signature page}

Ellis F. Unger, M.D.
Deputy Director (Acting)
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/

Ellis Unger
10/28/2008 07:36:11 PM