DEPARTMENT OF HEALTH & HUMAN SERVICES

HFD-104
Murphy

Food and Drug Administration
Rockville MD 20857

NDA 21-014

FEB 28 2000

Novartis Pharmaceuticals Corporation
Attention: Michael J. Macalush
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Mr. Macalush:

Reference is made to your Proposed Pediatric Study Request submitted on February 22, 1999 for Trileptal ™ (oxcarbazepine) Tablets to IND (b) (4)

To obtain needed pediatric information on oxcarbazepine, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit information from the following studies:

Types of Studies
Study 1: Pediatric Efficacy and Safety Study (1 month to 4 years)
Study 2: Pediatric Efficacy and Safety Study (1 month to 16 years)
Study 3: Pediatric Safety Study (1 month to 4 years)
Study 4: Pharmacokinetic Study (1 month to 16 years)

Indications to be studied
Study 1: To establish efficacy and short-term safety of oxcarbazepine as adjunctive therapy in the treatment of partial seizures in pediatric patients ages 1 month to 4 years.

Study 2: To establish efficacy and short-term safety of oxcarbazepine as monotherapy in the treatment of partial seizures in pediatric patients ages 1 month to 16 years.

Study 3: To determine the long-term safety (duration of a minimum of 6 months) of oxcarbazepine as monotherapy or adjunctive therapy in the treatment of partial seizures in pediatric patients ages 1 month to 4 years.

Study 4: To determine the steady-state pharmacokinetics in pediatric subjects ages 1 month to 16 years.

Age group in which studies will be performed:
Study 1: 1 month to 4 years
Study 2: 1 month to 16 years
Study 3: 1 month to 4 years
Study 4: 1 month to 16 years

Study Endpoints:
Study 1 and 2: A single standard measure of seizure frequency should be chosen as the primary outcome measure, and standard measures of safety (clinical-including signs and symptoms-and laboratory).

Study 3: Appropriately frequent standard measures of safety (clinical-including signs and symptoms-and laboratory).

Study 4: Pharmacokinetic measurements as appropriate.

Drug Information:

Dosage Form: Oral tablet and other formulation as appropriate for younger patients.
Route of Administration: Oral
Regimen: To be determined by the development plan

Drug specific safety concerns:
Hepatic, hematologic and skin hypersensitivity reactions, and hyponatremia.

Statistical information, including power of study and statistical assessments:
Study 1: Assessment of the between group difference on a standard measure of partial seizure frequency by a statistical methodology appropriate to the data generated and descriptive analysis of safety data. A sufficient number of pediatric patients to be able to detect a statistically significant difference between treatment and control should be included.

Study 2: Analyses appropriate to the design of the study.

Study 3: Descriptive analysis of the safety.

Study 4 : Descriptive assessment of the effect of age on pharmacokinetic parameters.

***Labeling that may result from the studies*:** Appropriate sections of the label may be changed to incorporate the findings of the studies.

***Format of reports to be submitted*:** Full study reports not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation.

Timeframe for submitting reports of the studies: Reports of the above studies must be submitted to the Agency on or before January 14, 2005. Please remember that pediatric exclusivity extends only existing patent protection or exclusivity that has not expired or been previously extended at the time you submit your reports of studies in response to this Written Request.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written

agreement by submitting a proposed written agreement. Clearly mark your submission **"PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as **a new drug application or as a supplement to your approved NDA** with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, call Melina Malandrucco, R.Ph, Regulatory Project Manager, at (301) 594-5526.

Sincerely yours,

RB for RT 2/28/00

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Archival NDA 21-014 and IND (b) (4)
HFD-120/Division file
HFD-120/Malandrucco
HFD-120/Katz/Hershkowitz/Burkhart/Boehm/Glass
HFD-101/Office Director
HFD-600/Office of Generic Drugs
HFD-2/M.Lumpkin
HFD-104/D.Murphy
HFD-002/T.Crescenzi

PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION