NDA 20-234

MAR 25 1996

Ciba Pharmaceuticals
Ciba-Geigy Corporation
Attention: Adrian L. Birch
556 Morris Avenue
Summit, NJ 07901

Dear Mr. Birch:

Please refer to your new drug application of October 31, 1991, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tegretol®-XR (carbamazepine extended release tablets) 100 mg, 200 mg, and 400 mg tablets.

We acknowledge receipt of the following amendments:

December 28, 1995	January 29, 1996	January 20, 1996
February 6, 1996	February 8, 1996	February 9, 1996
March 15, 1996		

We have completed the review of this application and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the final printed labeling submitted on February 6, 1996. Accordingly, the application is approved effective on the date of this letter.

As you were notified in the telephone conversation of February 21, 1996, between Steven D. Hardeman, of this Division and Ms. Mara Stiles of your firm, the Office of Clinical Pharmacology and Biopharmaceutics has established revised Q values for the interim dissolution specifications. The revised values are:

3 hours
6 hours
12 hours
24 hours

Please note that we have incorporated the wider ranges that you have requested with the exception of the lower limit of the 12-hour point and the upper limit of the 6-hour point. We believe that it is necessary to maintain the lower limit of the 12-hour point at 65% to ensure that patients receive the expected total dose. (If the tablet is not sufficiently dissolved at 12 hours, it is possible that it could be eliminated before the full dose is released). It should be noted that with these revised specifications, none of the 20 production batches and none of the 11 developmental lots for which you have submitted data would potentially fail based on having

mean values outside of the proposed specifications. In addition, only six of the production batches would require testing to the S2 or S3 level.

Once you have generated the requested data on 12 tablets of each strength from three consecutive production batches, please forward the result to the Agency so that final specifications can be established.

We note that you have committed to conduct and complete a revalidation for each of the three strengths of Tegretol®-XR, processed at target conditions, including granulation, compression, coating, laser drilling and drying operations.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. We note your commitment to continued cooperation in this matter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Steven D. Hardeman, R.Ph., Regulatory Management Officer, at (301) 594-2777.

Sincerely yours,

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