HFD-104
D. Murphy

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-963

Alcon Laboratories
Attention: Susan H. Caballa
Director, Regulatory Affairs
6201 South Freeway, R7-18
Fort Worth, TX 76134-2099

OCT 15 1999

Dear Ms. Caballa:

Reference is made to your approved new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Timolol Maleate (timolol maleate ophthalmic gel forming solution) Ophthalmic Gel Forming Solution, 0.25% and 0.5%.

To obtain needed pediatric information on timolol maleate for the treatment of elevated intraocular pressure, the Food and Drug Administration (FDA) is hereby issuing to you an official Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act. FDA requests that you submit information from the following study:

Type of Study:
The study should be a randomized, double-masked, parallel dose comparison trial. The study should be of at least 12 weeks duration and should include a minimum of four evaluations including baseline and end of treatment.

Indication/Objective:
The primary objective of the study should be to evaluate the safety and the clinical response on elevated intraocular pressure among treatment groups. Enrolled patients should include male and female pediatric patients with a clinical diagnosis of glaucoma or elevated intraocular pressure.

Age Groups:
Pediatric patients should be less than 6 years of age. There should be at least 5 pediatric patients per arm per strata. The strata should consist of approximately 1 year intervals (i.e., between 1 week and 1 year, between 1 year and 2 years, between 2 years and 3 years, etc.).

Drug Information:
Timolol maleate ophthalmic gel forming solution, 0.25% and 0.5% should be compared to an appropriate control treatment.

Drug Specific Safety Concerns:
In addition to monitoring adverse events, vital signs, intraocular pressure, visual acuity, dilated ophthalmoscopy, and corneal diameter should be performed at baseline and end of therapy. Particular attention should be made to evaluate the drug product's effects on safety evaluations of pulse, blood pressure, and alertness.

Statistical Analysis:
At least 30 patients per arm should be enrolled.

Labeling:
Appropriate sections of the label may be changed to incorporate the finding(s) of the study.

Format of Reports To Be Submitted:
A full study report providing the analyses outlined in this request should be provided at the completion of this study. The report, which has not previously been submitted to the Agency, should include the complete analysis, assessment, and interpretation of the study.

Timeframe:
The report of the above study must be submitted to the Agency on or before August 1, 2001. Please keep in mind that pediatric exclusivity only extends existing patent protection or exclusivity that has not expired at the time you submit your reports of the studies in response to this Written Request.

Please submit the protocol for the above study 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.

The report of this study should be submitted as a supplement to your approved NDA, with the proposed labeling you believe would be warranted based on the data derived from this study. When submitting the report, 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 mail/messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, Maryland 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 applications. Submissions of proposed changes to this request should be clearly marked **"PROPOSED CHANGES IN 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 to the pediatric population.

If you have any questions, please contact Joanne Holmes, M.B.A., Clinical Reviewer, at (301) 827-2090.

Sincerely,

Robert J DeLap 15 October 1999

Robert DeLap, M.D., Ph.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
IND 52,197
NDA 20-963
HFD-550 Div Files
HFD-550/Dep Dir/Chambers WRC 10/5/99 JH 8/20/99
HFD-550/Clin Rev/Holmes
HFD-550/SCSO/Zeccola
HFD-550/Proj Mgr/Gorski 8/24/99
HFD-550/Proj Mgr/Rodriguez
HFD-105/ADRA/Walling
HFD-600/Office of Generic Drugs
HF-2/Lumpkin
HFD-104/DMurphy
HFD-002/T.Crescenzi

Drafted by: jh/August 18, 1999
Filename: 20963pedrequest.doc

PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)