DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 51,709
NDA 20-625
NDA 20-786
NDA 20-872

Aventis Pharmaceuticals Inc.
Route 202-206
Bridgewater, NJ 08807-0800

WRITTEN REQUEST #2
AMENDMENT #1

Attention: Susan Witham
Director, Drug Regulatory Affairs

Dear Ms. Witham:

Reference is made to your submission (#059) to IND 51,709 dated July 26, 2001, requesting changes to FDA's April 23, 2001, Written Request #2 for pediatric studies for fexofenadine.

We have reviewed your proposed changes and are amending the below-listed section of Written Request #2. All other terms stated in our Written Request #2 issued on April 23, 2001, remain the same. The changes are noted in italics.

Clinical Endpoints

Study 1: Determine the plasma concentration of fexofenadine using the same validated assay method employed previously or using an adequately cross-validated assay method. Safety endpoints must include adverse events, vital signs, physical examinations, and ECGs. *Adverse events must be recorded.* Vital signs and physical examinations must be performed at screening or baseline and at the end of the study. If a single-dose study is performed, a twelve-lead ECG should be performed at the estimated T_{max}. If a multiple-dose study is performed, clinical chemistries, and hematology profiles must be performed at screening or baseline, and at steady-state, and ECGs should be performed at baseline or screening, at the time of estimated T_{max} after the initial dose, and at the time of estimated T_{max} after steady-state is achieved.

Reports of the studies that meet the terms of Written Request #2 dated April 23, 2001, as amended by this letter must be submitted to the Agency on or before January 31, 2003, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

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. Please 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 supplement to each of your approved NDAs, 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 #2 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, contact Ms. Christine Yu, Regulatory Project Manager, at 301-827-1051.

Sincerely,

{See appended electronic signature page}

John K. Jenkins, M.D.
Director
Office of Drug Evaluation II
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/

John Jenkins

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