DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-929

AstraZeneca Pharmaceuticals, L.P.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Attention: Christopher Blango
Director, Regulatory Affairs

WRITTEN REQUEST
Amendment #5

Dear Mr. Blango:

Reference is made to the FDA's December 14, 1998, Written Request for pediatric studies for budesonide, and to the FDA's December 22, 1999, May 22, 2000, June 6, 2001, and July 31, 2002, amended Written Requests for pediatric studies.

Reference is also made to the teleconference between representatives of AstraZeneca and the Division of Pulmonary and Allergy Drug Products on August 8, 2002, regarding changes to FDA's December 14, 1998, Written Request for pediatric studies for budesonide as amended.

As a result of the August 8, 2002, teleconference, we are amending the below-listed section of the Written Request. All other terms related to Study 1 stated in our amendment issued on July 31, 2002, remain the same. All terms relating to Study 2 stated in our Written Request issued on December 14, 1998, and the amendments dated December 22, 1999, and May 22, 2000, remain the same.

Study evaluation:

Study 1: The efficacy evaluations may include parent or caregiver ratings of patient asthma symptom scores, use of rescue medications, asthma episodes, and subject discontinuations due to treatment failures. These should be assessed at least every 4 weeks. Safety measures should include recording of adverse events, physical examination, oropharyngeal and nasal fungal cultures, and assessment of linear growth. These should be performed before treatment and at least every 4 weeks. Serum chemistry and hematology should be performed before treatment, and at the end of the study. Assessment of adrenal function must be performed before treatment, and at the completion of the study. Adrenal function must be assessed by an appropriate test for the study population, such as by an ACTH stimulation test of HPA-axis, or by measurement of timed urinary free cortisol excretion. A single measurement of A.M. cortisol level will not be adequate. The assessment of adrenal function must be performed in at least 72 subjects who complete the study, at least two-thirds of whom must have received active treatment (at least 24 patients total receiving active treatment must be <9 months old at enrollment). For convenience and standardization of the procedure, the assessment of adrenal function may be performed at a limited number of study centers provided the selected study centers enroll a sufficient number of study

subjects who complete the study to achieve the required minimum number of subjects assessed.

Reports of these studies that meet the terms of the Written Request dated December 14, 1998, as amended on December 22, 1999, May 22, 2000, June 6, 2001, and July 31, 2002, and by this letter must be submitted to the Agency on or before September 3, 2002, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

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. 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.

Submit reports of the studies as a supplement to an approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, 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. In addition, 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, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

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, call Colette Jackson, Project Manager, at 301-827-5580.

Sincerely,

{See appended electronic signature page}

Robert Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:

HFD-570/division file
HFD-570/Jackson
HFD-570/Barnes
HFD-570/Purucker
HFD-570/Meyer
HFD-570/Jenkins
HFD-600/Office of Generic Drugs

Drafted by: Purucker/Jackson/August 9, 2002
Initialed by: Purucker/August 9, 2002
Chowdhury/August 9, 2002
Barnes/August 9, 2002
Ripper/August 9, 2002
Meyer/August 12, 2002

Finalized by: CCJ/August 13, 2002
filename: N:/MY DCOUMENTS/N20929WR.DOC
PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert Meyer

8/13/02 10:55:23 AM