NDA 20-929

AstraZeneca LP
725 Chesterbrook Blvd
Wayne, PA 19087-5677

Attention: Eric Couture, Ph.D.
Director, Regulatory Affairs

Dear Dr. Couture:

Please refer to your new drug application (NDA) dated November 18, 1997, received November 20, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pulmicort Respules (budesonide inhalation suspension).

We acknowledge receipt of your submissions dated January 7, 15, and 30, February 5 and 6, March 5, 6, and 12, May 12, August 7 and 20, and November 30, 1998, April 9, and May 6, 1999, February 9, June 2 and 9, July 10 (2 submissions) and 25 (2 submissions), August 1, 3, 4, and 7, 2000. Your submission of February 9, 2000, constituted a complete response to our February 11, 1999, action letter.

This new drug application provides for the use of Pulmicort Respules (budesonide inhalation suspension) for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted August 4, 2000, patient instructions for use, immediate container and carton labels submitted August 3, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug. As committed to in your August 3, 2000, submission, within 4 months of launch (February 1, 2001) you will utilize only the immediate container and carton labels containing the revised statement “Do NOT use in an ultrasonic nebulizer.”

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after

it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for

industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-929." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated August 3, 2000. These commitments, along with any completion dates agreed upon, are listed below.

1. Study and report by October 1, 2003, the effects of maintenance therapy with Pulmicort Respules at recommended doses in the indicated population ($\geq$1 year of age) on the immunogenicity of a live virus vaccine (e.g., varicella).

2. Continue on-going studies to further refine the [ ]assays, and provide the data from these assessments along with resulting proposed specifications on or before October 12, 2000 (as committed to in attachment 4 of the August 3, 2000, submission).

3. Develop and validate an appropriate test method and propose a finished product specification for [ ] by December 1, 2000.

4. Reevaluate and tighten the content uniformity specification based on data collected from post approval production batches by October 12, 2000, or at least 20 batches, whichever comes first.

5. Monitor for [ ] and establish final specifications based on data collected by December 31, 2000, or approximately 50 lots, whichever comes first.

Submit commitments 2 – 5 as individual prior approval supplements.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

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. Nevertheless, we expect

your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until July 31, 2002.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

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, call Mrs. Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely,

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research