DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-254/S-004

GlaxoSmithKline
P. O. Box 13398
Five Moore Drive
Research Triangle Park, NC 27709-3398

Attention: Purnima Narang
Senior Project Manager

Dear Ms. Narang:

Please refer to your supplemental new drug application dated November 30, 2007, received November 30, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advair HFA (fluticasone propionate and salmeterol xinafoate inhalation powder) Inhalation Aerosol.

We acknowledge receipt of your submissions dated April 8, and July 8, 11, 15, 18, 22, and 29, 2008.

This supplemental new drug application provides for revisions to the package insert and medication guide to provide for the addition of a dose counter to Advair HFA Inhalation Aerosol.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

## REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable. Your supplemental new drug application (NDA) dated November 30, 2007, is not an application for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Therefore, there are no pediatric assessments required in conjunction with this supplemental NDA.

## RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a REMS for an approved drug if the FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(2)). This provision took effect on March 25, 2008.

Since Advair HFA was approved in 2006 for the long-term, twice-daily maintenance treatment of asthma in patients 12 years of age or older, FDA has become aware of new safety information about a

similar product (Advair Diskus) that shows that there is an increased incidence of pneumonia in COPD patients who take ADVAIR DISKUS. The safety information is from 2 one-year treatment studies and 1 three-year treatment study with ADVAIR DISKUS. Advair HFA contains the same active ingredients in relative strengths (salmeterol and fluticasone propionate) as Advair Diskus but in an inhalation aerosol formulation. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. FDA previously approved a Medication Guide required for distribution with Advair HFA in accordance with 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Advair HFA poses a serious and significant public health concern requiring distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Advair HFA. FDA has determined that Advair HFA is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Advair HFA. This includes the new safety information regarding the increased risk of pneumonia identified above. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Advair HFA.

Your proposed REMS, submitted on July 29, 2008, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your July 29, 2008, submission.

Information needed for assessment of the REMS may include but may not be limited to:

a. A survey of patients' understanding of the serious risks of Advair HFA.
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

Use the following designator to prominently label all submissions, including supplements, relating to this REMS:

**NDA 21-254 REMS ASSESSMENT**
**NDA 21-254 PROPOSED REMS MODIFICATION**

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert, Medication Guide) and submitted on July 18, 2008. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-254/S-004".

**PROMOTIONAL MATERIALS**

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of Pulmonary and Allergy Products and two copies of both the promotional materials and the package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ladan Jafari, Regulatory Project Manager, at (301) 796-1231.

Sincerely,

*{See appended electronic signature page}*

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Package Insert, Medication Guide, REMS

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

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/s/

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Badrul Chowdhury

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