DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-077/S-029

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

Attention: Mary V. Sides
Assistant Director, Regulatory Affairs

Dear Ms. Sides:

Please refer to your supplemental new drug application dated October 6, 2006, received October 10, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advair Diskus (fluticasone propionate and salmeterol xinafoate inhalation powder) 250/50 mcg.

We acknowledge receipt of your submissions dated October 25, November 16, and December 11 and 15, 2006, January 19, and 23, February 26, June 8, and 25, July 5, and October 31, 2007, and January 16, February 20, March 12, and 31, and April 11, 14 16, 17, 22, and 23, 2008.

Your submission of October 31, 2007, constituted a complete response to our August 7, 2007, action letter.

This supplemental new drug application provides for the use of Advair Diskus 250/50 mcg for the maintenance treatment of airflow obstruction and reducing exacerbations in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

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.

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 April 22, 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 21-077/S-029".**

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 routes of administration, and new dosing regimens 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.

We are waiving the pediatric study requirement for ages 0 to 18 because necessary studies are impossible or highly impracticable. COPD does not exist in children.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENT

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 Secretary 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 Diskus was approved, FDA has become aware of new safety information. Three controlled clinical trials have identified an increased risk of pneumonia in patients with COPD treated with Advair Diskus. 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 Diskus in accordance with 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Advair Diskus 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 Diskus. FDA has determined that Advair Diskus 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 Diskus. 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 Diskus.

The proposed REMS you submitted on April 23, 2008, 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 April 23, 2008, submission. The timetable you submitted is as follows:

1st FDAAA assessment:	October 2009 (18 months from approval)
2nd FDAAA assessment:	April 2011 (3 years from approval)
3rd FDAAA assessment:	April 2015 (7 years from approval)

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

a. Survey of patients' understanding of the serious risks of Advair Diskus.
b. Report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24

c. Report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

For administrative purposes, all submissions related to this REMS must be clearly designated as a **"REMS Submission"**.

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 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 (Labeling)

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

/s/

Badrul Chowdhury

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