FOOD AND DRUG ADMINISTRATION
OFFICE OF DRUG EVALUATION II

TO: Ms. Lorna Wilson

Phone Number: 919-483-5121

Fax Number: 919-315-0033

FROM: Ladan Jafari, Project Manager

DIVISION OF PULMONARY AND ALLERGY DRUG PRODUCTS

CDER Pulmonary Group (HFD-570), 5600 Fishers Lane
Rockville, Maryland 20857

PHONE: (301) 827-1050 FAX: (301) 827-1271

Total number of pages, including cover sheet:4 Date: February 27, 2002

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-077/S-002

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

Attention: Joy E. Ferrell
Director, Regulatory Affairs

Dear Ms. Ferrell:

Please refer to your supplemental new drug application dated April 27, 2001, received April 30, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advair Diskus (fluticasone propionate and salmeterol xinafoate inhalation powder).

We acknowledge receipt of your submissions dated June 6 and 29, and August 31, 2001.

This supplemental new drug application provides for the revision in the DOSAGE AND ADMINISTRATION section to provide specific guidance on the recommendations for the starting dose of Advair for patients with uncontrolled asthma who are currently on short-acting beta-agonist therapy alone.

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

We do not believe that you have provided sufficient evidence of efficacy to support this broadened indication for Advair Diskus. Notably, clinical trial SAS30017 failed to demonstrate the superiority of the combination product Advair Diskus to the single component fluticasone using the protocol-specified analysis. In addition, this supplement did not provide adequate assurance of the relative safety of the combination product compared to the single component fluticasone for the proposed population. Withdrawals due to asthma exacerbation and withdrawals due to worsening asthma (clinical and stability-specified) were higher among subjects treated with the combination product compared to the single component fluticasone. In order for this application to be approved, you must provide substantive efficacy and safety data supporting that this specific population uniquely benefits from the combination product in comparison to its individual moieties and that this benefit is not outweighed by any additional risks.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, call Ms. Ladan Jafari, Regulatory Project Manager, at (301) 827-5584.

Sincerely,

(See appended electronic signature page)

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

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/s/

Robert Meyer
2/27/02 01:20:01 PM

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