DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-433

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

Attention: Dawn Watson
Director, U.S. Regulatory Affairs, Respiratory

Dear Ms. Watson:

Please refer to your new drug application (NDA) dated February 26, 2002, received February 27, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Flovent HFA (fluticasone propionate HFA) Inhalation Aerosol.

We acknowledge receipt of your submissions dated April 5, and 16, May 21, and 31, June 24, and 28, July 9, and 24, September 5, and 19, October 3, and December 13, 2002, August 11, and November 13, 2003, and April 2, 16, 20, 26, and 29, and May 7, 11, 12, and 13, 2004.

The November 13, 2003, submission constituted a complete response to our December 27, 2002, action letter.

This new drug application provides for the use of Flovent HFA (fluticasone propionate HFA) Inhalation Aerosol for maintenance treatment of asthma as prophylactic therapy in adults and adolescent patients 12 years of age and older.

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

The final printed labeling (FPL) must be identical to the submitted labeling [text for the package insert (copy enclosed) and Patient Instructions for Use (copy enclosed) submitted on May 13, 2004, and carton and container labeling submitted on May 12, 2004]. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-433**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of the following agreements.

1. (b)(4)----------issues will be addressed for fluticasone propionate and fluticasone ---------- through NDA 20-121/S-027 for FLONASE® (fluticasone propionate) Nasal Spra----------Refer to July 8, 2003, meeting minutes.)

2. Implementation of a modified cascade impactor assay, with a reduced number of actuations per assay, will occur within 18 months of product launch. (Note: the to-be-proposed method is not limited to (b)(4)--------per assay, but it should not include changes in acceptance criteria for (b)(4)---------- ----------

3. The phenomenon of atypically high results at the end of inhaler use for manual sample collection after automated discharge of waste actuations, will continue to be investigated. Any necessary changes resulting from this investigation will be appropriately submitted within 12 months of approval.

4. You will continue to re-evaluate the acceptance criteria for the concentration of the drug substance in the suspension. Any necessary changes resulting from this investigation will be appropriately submitted within 12 months of approval.

5. The robustness of the (b)(4)-- ---------- will continue to be investigated. Appropriate regulator---------- ----------onths of approval if any additional change in the method is required.

6. You will investigate the apparent drug interference with quantification of the (b)(4)---------- in the drug product compared with placebo, and then propose suitable drug pr---------- criteria for(b)(4)---------- which are based on the findings of the investigations. These will ---------- within 6 months of approval.

7. You commit to working with your supplier(b)(4)----------to re-evaluate the methodology used to measure ---------- ----------get date for the completion of this commitmen---------- --------ency's recent letter, i.e. March 2005.

8. A final specification for valve actuation force will be submitted within 6 months after approval of this NDA.

9. Submit the(b)(4)---------- during the ----------

10. Within 4 weeks of the date of approval, you will propose additional controls for (b)(4)--------- (b)(4)----------as part of the system suitability. This is an ----------lance (below) is approved. This proposal will include a detailed, tiered approach for addressing mass balance failures outside the range of (b)(4)------ of label claim.

11. You will submit a prior approval supplement to implement final acceptance criteria for quantitative mass balance within 3 months of product launch. This pertains to the specification for (b)(4using the cascade impactor.

12. (b)(4)----------

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. We are waiving the pediatric study requirement for ages 0 months to less than 6 months and deferring pediatric studies for ages 6 months to less than 12 years for this application.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the treatment of asthma in pediatric patients ages 6 months to 11 years of age.

   Final Report Submission: May 14, 2007.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**."

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 Drug Products, 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, MD 20857

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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Ms. Ladan Jafari, Regulatory Project Manager, at (301) 827-1084.

Sincerely,

{See appended electronic signature page}

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

Enclosure (Package insert & Patient Instructions for Use)

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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