DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-592

Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, New Jersey 07936-1080

Attention: Ann Shea
Senior Associate Director, Regulatory Affairs

Dear Ms. Shea:

Please refer to your new drug application (NDA) dated December 17, 2002, received December 18, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Foradil Certihaler (formoterol fumarate) Inhalation Powder.

We acknowledge receipt of your submissions dated March 17, April 3, 14, 15, and 30, June 6, July 15, August 29, September 3, and 30, October 23, November 6, and December 1, and 3, 2003, January 21, 24, and 27, October 4, November 22, and 23, and December 7, 2004, March 1, April 8, and October 10 2005, and March 1, 29, and 30, April 12, and 13, June 15, August 18, October 20, November 28, and December 7, 2006.

The June 15, 2006, submission constituted a complete response to our April 11, 2006, action letter.

This new drug application provides for the use of Foradil Certihaler (formoterol fumarate) Inhalation Powder for long-term, twice-daily (morning and evening) administration in the maintenance treatment of asthma and in the prevention of bronchospasm in adults and children 5 years of age and older with reversible obstructive airway disease.

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 (package insert submitted December 13, 2006**,** Medication Guide submitted December 13, 2006 (copy enclosed), immediate container and carton labels submitted December 13, 2006). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit either an electronic version or 20 paper copies of the FPL as soon as it is available (no more than 30 days after it is printed). If paper copies are submitted, individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-592**." Approval of this submission by FDA is not required before the labeling is used.

Submit an updated version of 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. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

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 and two copies of both the promotional materials and the package insert directly to:

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

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

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

We remind you of your agreement listed in your amendments dated October 4, 2004, August 18, and November 20, 2006, to complete following:

1. Submit a prior approval supplement post-approval to revise, if feasible, the acceptance criteria for the aerodynamic particle size distribution (APSD) by (b)(4) once (b)(4) consecutive production scale drug product batches are manufactured with well-controlled lactose and tested with the optimized procedures (i.e., suitable absolute and vacuum ramp profile, environmental controls, optimized device equilibration and handling). Avoid proposing permissive acceptance criteria to encompass all data for all (b)(4) ge groupings for all batches produced thus far, since this will not be in the best interest of quality control. Establish the "linkage" of production scale batch APSD to that for the clinical/primary stability batches focusing on the groups expected to be most clinically relevant (e.g., S2-S4).

2. Continue to investigate what measured parameters of the lactose can be used to detect changes that will impact on the resultant aerodynamic particle size distribution of the drug product. Once identified, these can be implemented as controls for acceptance of incoming lactose.

3. Continue to monitor the levels of amorphous content of the lactose excipient and consider the introduction of a mandatory storage period prior to use in formulation and/or a tightening of the specification acceptance criterion.

4. Finalize the impurities acceptance criteria for the lactose once (b)(4)) lactose batches are manufactured using [redacted] final process to produce lactose for your drug product.

5. Establish final acceptance criteria for the routine extractables for the critical components of the drug product device once the extractables results from (b)(4) batches are obtained.

6. The following agreements pertain to the control of foreign particulates in the drug

product components and subcomponents.

a. Reevaluate the acceptance criteria applied at release for foreign particulates in filled reservoirs of the drug product and tighten these, if appropriate, to reflect the data from the first (b)(4) consecutive production batches.

b. Reevaluate the acceptance criteria applied for acceptance of the levels of foreign particulates in the lactose excipient and the empty reservoirs and tighten these, if appropriate, to reflect the data from the first (b)(4) consecutive batches, respectively, received for production batches of the drug product.

c. Undertake every reasonable effort to decrease the levels of foreign particulates that may emanate from the drug product during patient usage, and agree that the final acceptance criteria for drug product components (i.e., empty reservoirs, lactose) and subcomponents (i.e., formulation-filled reservoirs) will not be widened from the interim levels proposed in the June 24, 2004, amendment.

7. Provide the updated Mg stearate testing monograph including the revision tightening the specific surface area specification to (b)(4).

8. Provide a methods validation package as outlined in comment 6j of the October 17, 2003, letter within 3 months following the approval of the application.

9. Provide web-based instructions for use similar to those developed for Foradil Aerolizer.

If you have any questions, call Ms. Akilah Green, Senior Regulatory Management Officer, at (301) 796-1219.

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

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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