DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-247

Forest Laboratories, Inc.
Harborside Financial Center
Plaza III, Suite 602
Jersey City, NJ 07311

Attention: Michael K. Olchaskey, Pharm.D.
Associate Director, Regulatory Affairs

Dear Dr. Olchaskey:

Please refer to your new drug application (NDA) dated April 27, 2000, received April 27, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aerospan (flunisolide HFA, 80 mcg) Inhalation Aerosol.

We acknowledge receipt of your submissions dated May 31, June 2, 13, and 16, August 28, September 21, 22, and 27, October 2, and 19, November 9, and December 26, 2000, and January 3, February 14, March 7, and 29, June 29, August 28, October 11, and 24, and December 7, 2001, and July 24, October 4, and 22, 2002, and February 5, and 21, May 8, June 5, 10, and July 1, August 20, October 20, December 12, 17, and 19, 2003, January 12, and 14, March 31, May 3, July 6 and 26, August 6, and 25, 2004, and July 26, August 11, September 27, November 4, and 22, December 7, 21, and 28, 2005 , and January 6, 20, 25, 26, and 27, 2006.

The July 25, 2005, submission constituted a complete response to our April 20, 2004, action letter.

This new drug application provides for the use of Aerospan (flunisolide HFA, 80 mcg) Inhalation Aerosol for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients 6 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 enclosed labeling (text for the package insert, and Patient Information Leaflet, submitted January 27, 2006, immediate container and carton labels submitted on January 26, 2006). Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and (an) unapproved new drugs.

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 21-247**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of the following agreements as listed in your submission dated January 25, 2006.

1. Submit the test results for all flunisolide hemihydrate containers stored in the (b)(4) facility in (b)(4) as correspondence to the NDA.

2. Perform acceptance testing of drug substance batches no more than 90 days prior to its use in the formulation.

3. Reevaluate the (b)(4) levels and revise the acceptance criteria based upon the results obtained from analysis of the first three post-approval production-scale batches. Submit a prior approval supplement for this change.

4. Adopt the proposed acceptance criteria for related substances in the drug substance on an interim basis until the (b)(4) site is approved for use in this application. You will file a post-approval supplement to support the use of the new drug substance from the (b)(4) site prior to its use in the manufacturing of the drug product (provided that (b)(4) also submits a new DMF for the drug substance). For the flunisolide hemihydrate from (b)(4) you will amend the NDA to include revised acceptance specifications wherein you commit to adopt the (b)(4) specifications. After you have manufactured three full-scale batches at the (b)(4) site, you and (b)(4) must submit test results for review and reevaluation of the acceptance criteria.

5. Repeat the tests provided by (b)(4) on the Certificate of Compliance for the first three lots intended for commercialization. Thereafter, you agree to test every (b)(4) lot manufactured by (b)(4) annually. In addition, you agree to testing the first three commercial lots for extractables using Forest test procedure (b)(4) and for product performance measured by (b)(4), and medication delivery/through life (test methods (b)(4) or (b)(4).

6. Review the fill weight data with 3M after one year of production and revise these specifications if appropriate.

7. Institute changes in your manufacturing process to minimize oxidation of flunisolide hemihydrate drug substance. (Refer to your meeting with the Division dated November 20, 2002).

8. Provide a (b)(4) actuation indicator.

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 to less than 6 months of age and deferring pediatric studies for greater than 6 months of age to less than 6 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 greater than 6 months to less than 6 years.

   Final Report Submission: January 2008.

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**".

We remind you of your postmarketing study commitments in your submission dated January 27, 2006. These commitments are listed below.

1. Conduct a study to comprehensively address device durability and reliability.

Protocol Submission:	by June 2006
Study Start:	by August 2007
Final Report Submission:	by January 2009

2. Conduct a labeling comprehension study to ensure that patients are able to read and use the device in the manner specified in the labeling.

Protocol Submission:	By June 2006
Study Start:	By May 2007
Final Report Submission:	By January 2008

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

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 the Division of Pulmonary & Allergy Products and two copies of both the promotional materials and the package inserts 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 also have the following additional comments:

1. Submit 3 copies of the methods validation package as well as make available samples for the FDA analytical laboratory.

2. Submit the results of a growth study to the NDA (21-247) as a supplement.

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) 796-1231.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package insert & carton/container labeling