DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-950

Dey Laboratories, L.P.
2751 Napa Valley Corporate Drive
Napa, CA 94558

Attention: Peggy J. Berry
Director
Regulatory Affairs

Dear Ms. Berry:

Please refer to your new drug application (NDA) dated May 28, 1998, received May 29, 1998, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for DuoNeb (3.0 mg albuterol sulfate and 0.5 mg ipratropium bromide per 3 mL) Inhalation Solution.

We acknowledge receipt of your submissions dated July 2 and August 26, 1998, and February 11, March 15 and 26, and November 29, 1999, and January 20, September 19, October 23, November 10, and December 6 and 12, 2000, and February 14, 15, 22, 23, 27, and 28, and March 1, 6, 7, 8, 9, 13, 15, 16, and 19, 2001. Your submission of September 19, 2000, constituted a complete response to our June 2, 2000, action letter.

This new drug application provides for the use of DuoNeb (3.0 mg albuterol sulfate and 0.5 mg ipratropium bromide per 3 mL) Inhalation Solution for the treatment of bronchospasm associated with COPD for patients who require more than one bronchodilator.

We have completed the review of this application, as amended, and it is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted March 16, 2001, vial labeling submitted March 9, 2001, protective foil overwrap label submitted March 16, 2001, and carton labels submitted March 16, 2001). 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 the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-950." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your agreement to monitor leachable compounds through the expiry period of the product for the first three commercial batches to be placed in your long-term stability program. If you are not able to correlate the leachable compounds profile to the existing extractable compounds profile after analysis of the first three commercial batches, further monitoring may be necessary.

We remind you of your postmarketing study commitments in your submission dated March 9, 2001. These commitments are listed below.

1. Conduct a 90-day inhalation toxicology study in one rodent and one non-rodent species to qualify the bis-ether albuterol impurity.

   Final Report Submission: Within 12 months of the date of this letter

2. Conduct a study to identify and quantitate foreign particulates through the shelf-life of the drug product. Submit a prior approval supplement to tighten (as appropriate) the proposed acceptance criteria based on these data.

   Final Report Submission: Within 12 months of the date of this letter

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 Final Report" or "Postmarketing Study Correspondence."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We are waiving the pediatric study requirement for the use of DuoNeb (3.0 mg albuterol sulfate and 0.5 mg ipratropium bromide per 3 mL) Inhalation Solution for the treatment of bronchospasm associated with COPD for patients who require more than one bronchodilator, because this disease does not substantially affect pediatric populations.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Mr. David Hilfiker, Regulatory Project Manager, at (301) 827-1084.

Sincerely yours,

S

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