DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-409

Merck Research Laboratories,
Division of Merck & Co., Inc.
RY 33-720
P.O. Box 2000
Rahway, NJ 07065

Attention: David Altarac, M.D., MPA
Director, Regulatory Affairs

Dear Dr. Altarac:

Please refer to your new drug application (NDA) dated September 28, 2001, received September 28, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Singulair (montelukast sodium) Oral Granules.

We acknowledge receipt of your submissions dated January 25 and 28, February 22, March 27, April 23, May 3, 7, 21, and 23, June 4, 7, and 10, July 15, 18, 22, 23 and 25, 2002.

This new drug application provides for the use of Singulair (montelukast sodium) Oral Granules in treatment of asthma as the primary formulation for patients 12 months to less than 2 years of age, and as an alternate formulation for ages 2 to 5 years.

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 and patient package insert submitted July 25, 2002, immediate container and carton labels with agreed upon revisions submitted July 25, 2002). 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 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 ten of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission, "**FPL for approved NDA 21-409**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your agreement stated in the July 15, 2002, submission (Attachment 2, page 8), to provide the study results demonstrating the effectiveness of additional implemented controls on fluidization times and atmospheric ozone on sulfoxides in the drug product by March 31, 2003. In addition to the above report, you agreed to provide the Certificates of Analysis from the validation

granulation batches and packaged formulation used in the above study, as well as an updated master batch record with the above mentioned changes. Accordingly, the study results should be submitted to the Agency in the form of a prior approval supplement before product launch.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

Based on the information submitted, we conclude the following:

For use of montelukast sodium in the treatment of asthma,

- We are waiving the pediatric study requirement for this action for this application for patients less than 6 months of age.

- You have fulfilled the pediatric study requirement at this time for patients 6 months of age and older.

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 and Allergy Drug Products and two copies of both the promotional materials, the mock-up form of the complimentary carton, and the package inserts 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. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. 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).

(b)(4)----------

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. 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.

If you have any questions, call Christine Yu, R.Ph., Regulatory Project Manager, at (301) 827-1051.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert, Patient Package Insert

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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