DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

NDA 50-705/S-005

Aventis Pharmaceuticals, Inc.
Attention: Mr. Jay Kraker
Specialist, Regulatory Affairs
200 Crossing Boulevard
P.O. Box 6890
Bridgewater, NJ 08807-0890

Dear Mr. Kraker:

Please refer to your supplemental new drug application dated October 29, 2004, received November 1, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rifater® (rifampin, isoniazid and pyrazinamide) Tablets, 120 mg/50 mg/300 mg.

We acknowledge receipt of your submission dated April 18, 2005.

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the package insert (additions are double underlined and deletions are struck out):

1. In the **ADVERSE REACTIONS** section, **Adverse Reactions Reported for Individual Components** subsection, the following revisions were made:

   Rifampin:
   Hematologic: Thrombocytopenia has occurred primarily with high dose intermittent therapy, but has also been noted after resumption of interrupted treatment. It rarely occurs during well-supervised daily therapy. This effect is reversible if the drug is discontinued as soon as purpura occurs. Cerebral hemorrhage and fatalities have been reported when rifampin administration has been continued or resumed after the appearance of purpura.
   ~~Transient~~ Lleukopenia, hemolytic anemia, and decreased hemoglobin have been observed. Agranulocytosis has been reported rarely.

   Pyrazinamide:
   Other: Mild arthralgia and myalgia have been reported frequently. Hypersensitivity reactions including rashes, urticaria, and pruritus have been reported. Angioedema has been reported rarely. Fever, acne, photosensitivity, porphyria, dysuria, and interstitial nephritis have been reported rarely.

2. "µg/mL" was changed to "mcg/mL" throughout the label.

3. The company's signature was revised and website information was added to read:

   ~~Prescribing Information as of March 2000~~

   ~~Merrell Pharmaceuticals Inc.~~

   ~~Subsidiary of Hoechst Marion Roussel, Inc.~~

   ~~Kansas City, MO 64137 USA~~
   ~~Rifater Tablets are manufactured by:~~
   ~~GRUPPO LEPETIT S.p.A.~~
   ~~20020 Lainate, Italy~~

Rev. April 2005

Rx only

`Manufactured by:
GRUPPO LEPETIT S.p.A.
20020 Lainate, Italy
MADE IN ITALY

Manufactured for:
Aventis Pharmaceuticals Inc.
Kansas City, MO 64137 USA

www.aventis-us.com

We have completed the review of this supplemental new drug application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text (enclosed). Accordingly, this supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (text for the package insert submitted April 18, 2005).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submission 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 as "**FPL for approved supplement NDA 50-705/S-005."** Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Robin Anderson, R.N., M.B.A., Labeling Reviewer, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Renata Albrecht

4/28/05 03:22:03 PM