DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-903/S-033

Schering Corporation
Attention: Mary Jane Nehring
Senior Director, Marketed Products, Support and Training
Worldwide Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Ms Nehring:

Please refer to your supplemental new drug application dated December 05, 2003, received December 08, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rebetron™ Combination Therapy.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below/indicated in the enclosed labeling.

The information related to pediatric use of Rebetol Capsules and Oral Solution into the Rebetron Combination Therapy label is acceptable and consistent with the information in the Rebetol label.

However, during the review of this supplement, an oversight related to the population for which Rebetol Capsules and Oral Solution are approved was noted. Currently the label reads:

> REBETOL (ribavirin, USP) Capsules and Oral Solution are indicated in combination with INTRON A (interferon alfa-2b, recombinant) Injection for the treatment of chronic hepatitis C in patients 3 years of age and older with compensated liver disease previously untreated with alpha interferon or in patients 18 years of age and older who have relapsed following alpha interferon therapy.

However, patients <5 years of age did not receive Rebetol Capsules in the pediatric trials.

The Indications and Usage states in the Rebetol Capsules and Oral Solution label will be revised to describe the approved uses of each formation in the adult and pediatric populations as follows:

> **INDICATIONS AND USAGE**
>
> **Adult Use**
> REBETOL (ribavirin, USP) Capsules and Oral Solution are indicated in combination with INTRON A (interferon alfa-2b, recombinant) Injection for the treatment of chronic hepatitis C in patients 18 years of age and older with compensated liver disease previously untreated with

alpha interferon and in patients 18 years of age and older who have relapsed following alpha interferon therapy.

REBETOL Capsules are indicated in combination with PEG-INTRON (peginterferon alfa-2b, recombinant) Injection for the treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alpha and are at least 18 years of age.

The safety and efficacy of REBETOL Capsules or Oral Solution with interferons other than INTRON A or PEG-INTRON products have not been established.

Pediatric Use
REBETOL (ribavirin, USP) Capsules are indicated in combination with INTRON A (interferon alfa-2b, recombinant) Injection for the treatment of chronic hepatitis C in patients 5 years of age and older with compensated liver disease previously untreated with alpha interferon and in patients who have relapsed following alpha interferon therapy.

REBETOL (ribavirin, USP) Oral Solution is indicated in combination with INTRON A (interferon alfa-2b, recombinant) Injection for the treatment of chronic hepatitis C in patients 3 years of age and older with compensated liver disease previously untreated with alpha interferon and in patients who have relapsed following alpha interferon therapy. Evidence of disease progression, such as hepatic inflammation and fibrosis, as well as prognostic factors for response, HCV genotype and viral load, should be considered when deciding to treat a pediatric patient. The benefits of treatment should be weighed against the safety findings observed (see **PRECAUTIONS Pediatric Use**) for pediatric subjects in the clinical trials.

Please submit the FPL electronically 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, in no case 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 supplement NDA 20-903/S-033." 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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please contact Tanima Sinha, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Jeffrey Murray, M.D.
Deputy Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure: approved draft labeling

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

/s/

Debra Birnkrant
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NDA 20-903