DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-903/S-030

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 applications dated March 26, 2003, received March 28, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for REBETOL® (ribavirin) capsules for use in combination with the approved biologic products Intron®A (interferon alfa 2b) (Rebetron Combination Therapy™), and PEG- Intron® (peg-interferon alfa 2b) powder for injection.

We acknowledge receipt of your submission dated June 20, 2003.

This supplemental new drug application provides for the inclusion of precautionary information to the REBETOL® (ribavirin) and REBETRON COMBINATION THERAPY™ package inserts regarding information about the co-administration of Rebetol® (ribavirin) and stavudine or zidovudine to patients co-infected with HIV and Hepatitis C virus (HCV), as follows:

Label Revisions: Package Insert

1. Insertion of a new first sentence in the **CLINICAL PHARMACOLOGY, Drug Interactions** section, as follows:

   Ribavirin has been shown *in vitro* to inhibit phosphorylation of zidovudine and stavudine which could lead to decreased antiretroviral activity.

2. Insertion of a new subsection in the **PRECAUTIONS, Drug Interactions** section, as follows:

   Stavudine and Zidovudine: Ribavirin may antagonize the in vitro antiviral activity of stavudine and zidovudine against HIV. Therefore, concomitant use of ribavirin with either of these drugs should be used with caution (see **CLINICAL PHARMACOLOGY: Drug Interactions**).

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effect for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application 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 June 20, 2003).

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-030." 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 call Destry Sillivan, 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

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

/s/

Jeffrey Murray
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