DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-903/S-015

Schering Corporation
Attention: Joseph F. Lamendola
Senior Director, Marketed Products, Support and Training
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Lamendola,

Please refer to your supplemental new drug application dated April 24, 2001, received April 24, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act REBETOL® (ribavirin) capsules for use in combination with the approved biologic product Intron®A (interferon alfa 2b) (Rebetron Combination Therapy™).

We acknowledge receipt of your submissions dated May 25, 2001, and October 30, 2001.

This "Changes Being Effected" supplemental new drug application provides for the inclusion of a new subsection of the **PRECAUTIONS, Drug Interactions** section in the REBETRON COMBINATION THERAPY™ label. This subsection describes the possibility of lactic acidosis occurring in patients treated with ribavirin and purine nucleosides, as follows:

> **Drug Interactions**
> **Nucleoside Analogs:** Administration of nucleoside analogues has resulted in fatal and nonfatal lactic acidosis. Coadministration of ribavirin and nucleoside analogues should be undertaken with caution and only if the potential benefit outweighs the potential risks.

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 effective 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 October 30, 2001).

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 supplement NDA 20-903/S-015." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, 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 Destry M. Sillivan, M.S., Regulatory Project Manager, at (301) 827-2335.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
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/

Debra Birnkrant
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