DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Office of the Ombudsman
5600 Fishers Lane (HF-7)
Room 14B-03
Rockville, MD 20857

Food and Drug Administration
Rockville MD 20857

February 20, 2001

Jennifer Dudinak
Project Manager
Drug Regulatory Affairs
Hoffmann-La Roche, Inc.
340 Kingsland Street
Nutley, NJ 07110

Re: Request for Designation (21 CFR Part 3)
PEGASYS® (pegylated interferon alfa-2a) with
COPEGUS (ribavirin)
Our File: RFD 2000.023

Dear Ms. Dudinak:

The Food and Drug Administration has completed its review of your request for designation, received and filed by this office on December 4, 2000. By mutual agreement, the deadline for the Agency's response was extended to allow for full consideration of the issues.

The request by Hoffmann-La Roche (HLR) concerns the use of PEGASYS® (pegylated interferon alfa-2a) in combination with COPEGUS (ribavirin) to treat chronic hepatitis C infection. PEGASYS®, which is the subject of a pending biologics license application (BLA) for treatment of hepatitis C, is under review in the Center for Biologics Evaluation and Research (CBER). COPEGUS is the subject of [ ] [ ]; that are under review in both CBER and the Center for Drug Evaluation and Research (CDER). (HLR has provisionally adopted the COPEGUS brand name for ribavirin, but has not yet formally discussed its proposal with FDA.)

The request for designation seeks clarification of the assignment of review responsibility for the combination treatment. The request for designation recommended that primary review responsibility for the combination be assigned to CBER, suggesting that a CBER lead would be appropriate given CBER's experience with both the combination treatment and with PEGASYS® as a monotherapy.

We have carefully considered your request, reviewed the pertinent provisions of the CDER – CBER Intercenter Agreement ("Intercenter Agreement"), and consulted with appropriate officials in CBER and CDER. Because the product is a combination product within the meaning of section 503(g) of the Federal Food, Drug and Cosmetic Act (21

U.S.C. § 353 (g)), assignment of review responsibility is based on a determination of the product's "primary mode of action." In this case, we conclude that the primary mode of action of the combination is attributable to the biologic component, PEGASYS®, with COPEGUS enhancing the biologic's effectiveness. Therefore, we are assigning CBER primary responsibility for the premarket review of the combination. The assignment to CBER is consistent with section III.D.1.c. of the Intercenter Agreement, which assigns CBER primary responsibility for combination products that "consist of a drug component and a biological component where the drug product enhances the efficacy or ameliorates the toxicity of the biological product."

The Division of Application Review and Policy, Office of Therapeutics Research and Review, CBER will be the principal contact point during the course of the review. CBER will conduct its review of the combination treatment in collaboration with CDER review staff from the Division of Antiviral Drug Products. The collaboration will focus on review of the clinical data and labeling for the combination product, and may be extended to other aspects of the review, as appropriate.

Clearance of the combination treatment will be conditioned on approval of both an NDA for COPEGUS and a BLA or supplemental BLA for PEGASYS®. The Agency's review of companion NDA and BLA submissions will present an administrative challenge. Hoffmann-La Roche is encouraged to discuss this challenge with the CBER-CDER collaborative review team as soon as possible. In particular, HLR is encouraged to seek guidance on the format, content, and administrative handling of the companion marketing submissions. Given that a common clinical data base will support marketing approval of the two components of the combination treatment, HLR may want to discuss with FDA the possibility of physically consolidating some or all of its data into a single submission.

For further information about how the agency will organize and conduct its review, contact Wendy Aaronson, Chief, Application Administration Branch, Division of Application Review and Policy, Office of Therapeutics Research and Review, CBER, at 301-827-5101.

If you have any questions about this letter, please contact Tracey Forfa, of this office, at 301-827-3390.

Sincerely yours,

Steven H. Unger
Acting Ombudsman

cc: Wendy Aaronson (HFM-588)
Anthony DeCicco (HFD-530)