DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103780/5052

DEC 17 2004

Serono, Incorporated
Attention: Pamela Williamson Joyce
Vice President, Regulatory Affairs and Quality Assurance
One Technology Place
Rockland, MA 02370

Dear Ms. Williamson Joyce:

Your request to supplement your biologics license application for Interferon beta-1a to add Laboratories Serono S.A. (LSA), Aubonne, Switzerland as an additional manufacturing site for the formulation, fill, bulk packaging and release testing for prefilled syringes; to add an alternate test to verify the integrity of the sterile filters prior to filtration; and, to add an 8.8 mcg presentation of Rebif for use in a new patient titration pack has been approved.

Results of ongoing stability studies should be submitted throughout the dating period, as they become available, including the results of stability studies from the nine qualification lots.

We have approved the stability protocols in your supplement for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

We acknowledge your written commitments to conduct postmarketing studies as described in your letter of (b)(4) as outlined below:

Postmarketing Studies not subject to reporting requirements of 21 CFR 601.70.

1. To analyze historical data on file by (b)(4) (b)(4)

We request that you submit protocols and all study final reports to your BLA STN BL 103780. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

Please submit final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy as well as original paper copies (ten for circulars and five for other labels).

Please refer to http://www.fda.gov/cder/biologics/default.htm for important information regarding therapeutic biological products, including the addresses for submissions. Effective October 4, 2004, the new address for all submissions to this application is:

CDER Therapeutic Biological Products Document Room
Center for Drug Evaluation and Research
Food and Drug Administration
12229 Wilkins Avenue
Rockville, Maryland 20852

This information will be included in your biologics license application file.

Sincerely,

(b)(6)

Amy S. Rosenberg, M.D.
Director
Division of Therapeutic Proteins
Office of Biotechnology Products
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

CONCURRENCE PAGE

Letter Type: LETTER: Approval (AP)

Summary Text: Manuf. Supplmt. Other
REVIEW COMPLETION REQUIRED BY: RIS

SS Data Check:
- **Place copy of Approval Ltr. with original signature concurrence page in Archival package behind the "Approval Materials" Tab after LAR (Licensing Action Recommendation).**

RIS Data Check:
- **Verify short summary - Ltr. & Submission screen should match.**
- **Check Letter for PMCs (if PMCs - add "PMCs - Approved With" special characteristic code.)**
- **Perform Review Completion Process**
- **Milestone: Confirm Approved Status**

cc: Attached label (if any) is sent to everyone
HFD-122/A. Rosenberg
HFD-122/B. Cherney
HFD-122/S. Kirshner
HFD-106/K. Weiss
HFD-108/M. Walton
HFD-108/E. Unger
HFD-108/J. Hyde
HFD-108/S. Comfort
HFD-109/K. Needleman
HFD-109/C. O'Leary
HFD-328/C. Renshaw
HFD-328/J. Li
HFD-106/G. Jones
HFD-240/OTCOM/ B. Poole (if labeling changes)
HFD-013/FOI D.Taub (if labeling changes)
HFD-013/FOI H. Brubaker (if labeling changes)
HFD-322/IPCB E. Rivera-Martinez
HFD-328/TFRB Blue File/Mike Smedley
HFM-110/RIMS R. Eastep
DRMP BLA file (hard copy)

History: K. Needleman: 12.14.04

File Name: S:\Needleman\BLA\Interferon beta-1a\103780_5052\BL103780_5052_ap.doc

(b)(6)

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