DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-164/S-015

Rhone-Poulenc Rorer Pharmaceuticals Inc.
Attention: Mr. Robert W. Babilon
500 Arcola Road
P.O. Box 5096
Collegeville, PA 19426-0800

DEC 31 1998

Dear Mr. Babilon:

Please refer to your supplemental new drug application dated February 28, 1997, received February 28, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lovenox® (enoxaparin sodium) Injection.

We acknowledge receipt of your submissions dated February 28, March 5, 14, and 26, May 7 and 16, June 17 and 18, July 10, and October 8 and 23, 1997, and February 10, May 19 and 28, June 12 and 23, July 6, September 24, and October 8, 1998.

This supplemental new drug application provides for the use of Lovenox® (enoxaparin sodium) Injection for: (1) the inpatient treatment of acute deep vein thrombosis with and without pulmonary embolism, when administered in conjunction with warfarin sodium; and (2) the outpatient treatment of acute deep vein thrombosis without pulmonary embolism when administered in conjunction with warfarin sodium.

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 enclosed 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 enclosed labeling (text for the package insert) and submitted draft labeling (immediate container and carton labels submitted May 19, 1998). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 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. Since there are currently two approved package inserts for Lovenox Injection (printed in Mason Alfort and Dagenham), please submit the appropriate number of copies of each of the package inserts. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-164/S-015." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your facsimile dated December 29, 1998. These commitments, along with any completion dates agreed upon, are listed below.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" 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

Please submit one market package of the drug product when it is available.

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, contact Karen Oliver, Regulatory Health Project Manager, at (301) 827-7310.

Sincerely,

Lilia Talarico, M.D., Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: package insert labeling text