DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-164

Aventis Pharmaceuticals, Inc.
Attention: Joseph A. Carrado, M.Sc., R.Ph.,
Director and Regulatory Liaison
Global Drug Regulatory Affairs
200 Crossing Blvd., P.O. Box 6800
Bridgewater, NJ 08807-0800

Dear Mr. Carrado:

Please refer to your supplemental new drug application dated May 15, 2001, received May 16, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lovenox (enoxaparin sodium) Injection, 300 mg/3.0 mL.

We acknowledge receipt of your submissions dated September 20, 2002 and January 17, 2003.

Your submission of September 20, 2002 constituted a complete response to our August 30, 2002, action letter.

This supplemental new drug application provides for a multiple-dose vial presentation of Lovenox Injection (300 mg/3 mL) at a concentration of 100 mg/mL and preserved with benzyl alcohol at 1.5% (m/v) level; a new contract manufacturing site, (b)(4)----------
(b)(4)----------
(b)(4)----------

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revision listed below.

In the **WARNINGS** section, **Pregnancy, Miscellaneous** subsection**,** in the first paragraph, third sentence, that reads, "Because benzyl alcohol may cross the placenta, Lovenox multiple-dose vials, preserved with benzyl alcohol, should be used with caution in pregnant women only if clearly needed (see **PRECAUTIONS**, **Pregnancy**)." insert the word "and" before the word "only" so that the sentence reads as follows:

> "Because benzyl alcohol may cross the placenta, Lovenox multiple-dose vials, preserved with benzyl alcohol, should be used with caution in pregnant women and only if clearly needed (see **PRECAUTIONS**, **Pregnancy**)."

The final printed labeling (FPL) must be identical, and include the minor editorial revision indicated, to the submitted labeling (package insert submitted September 20, 2002 and immediate container and carton labels submitted September 20, 2002). This revision is a term of the approval of this application.

In addition, we recommend that you include multiple instructions for use in each multiple vial package.

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 20-164/S-043." Approval of this submission by FDA is not required before the labeling is used.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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, call Diane Moore, Regulatory Project Manager, at (301) 827-7476.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Gastrointestinal & Coagulation Drug Products
Office of Drug Evaluation III
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/

Joyce Korvick
1/23/03 05:26:58 PM
for Dr.Robert Justice