

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: 020164/S010**

**MICROBIOLOGY REVIEW(S)**

**REVIEW FOR HFD-180  
OFFICE OF NEW DRUG CHEMISTRY  
MICROBIOLOGY STAFF HFD-805**

*Oliver*

**Microbiologist's Review # 1 of NDA 20-164: S-008, S-010, S-011, S-012  
September 16, 1996**



**A. 1. APPLICATION NUMBER:**

20-164/S-008 and 20-164/S-010: Qualification of a 40 mg pre-filled syringe (Lovenox), the recommended dosage for the new indication of the prevention of deep vein thrombosis after hip replacement surgery.

20-164/S-011: Update specifications and analytical methods for Lovenox to harmonize methods worldwide.

20-164/S-012: Qualification for an additional filling line (line 3) in the manufacture of the approved 30 mg/0.3 ml Lovenox.

**APPLICANT:** Rhone-Poulenc Rorer Pharmaceuticals Inc.  
500 Arcola Road  
P.O. Box 1200  
Collegeville, PA 19426-0107

**2. PRODUCT NAMES:** Lovenox (enoxaparin) injection pre-filled syringe

**3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:**

Lovenox is available in prefilled syringes (10 mg enoxaparin sodium per 0.1 ml WFI, anti-Factor Xa activity is 1000 IU per every 10 mg of drug). The solution is preservative free and intended for use only as a single-dose injection.

Lovenox Injection is administered by subcutaneous injection. It must not be administered by intramuscular injection.

**4. METHOD(S) OF STERILIZATION:**

**5. PHARMACOLOGICAL CATEGORY:** Lovenox is indicated for prevention of deep vein thrombosis following hip replacement surgery.

**B. 1. DATE OF INITIAL SUBMISSION:**

NDA 20-164/S-008: December 27, 1996

NDA 20-164/S-010: March 29, 1996

NDA 20-164/S-011: April 15, 1996

NDA 20-164/S-012: May 24, 1996

2. AMENDMENT: None
3. RELATED DOCUMENTS: NDA 20-164
4. ASSIGNED FOR REVIEW: July 15, 1996
5. DATE OF CONSULT REQUEST:  
NDA 20-164/S-008, S-010, S-011: July 10, 1996  
NDA 20-164/S-012: July 5, 1996

C. REMARKS:

Supplement S-008, S-010 and S-011 were submitted in response to the FDA Chemist's request for additional information. With regard to microbiology issues, these supplements provide the alternate methods used in endotoxin determinations. The same validation data was provided for all three supplements, and they are the subject of this review.

Supplement S-012 provides for an additional filling line (line 3) for use in the manufacture of the approved 30 mg/0.3 ml Lovenox.

D. CONCLUSIONS:

The submissions are recommended for approval for issues concerning microbiology.

APPEARS THIS WAY  
ON ORIGINAL

/S/  
Brenda Uratani, Ph.D.

9/16/96

/S/ 9/16/96

cc:

NDA 20-164/S-008, S-010, S-011, S-012  
HFD-180/ Div. File  
HFD-805 /Uratani  
HFD-180/CSO/ K. Oliver  
drafted by: Brenda Uratani, 9/16/96  
R/D initialed by P.Cooney, 9/16/96

APPEARS THIS WAY  
ON ORIGINAL