

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020807

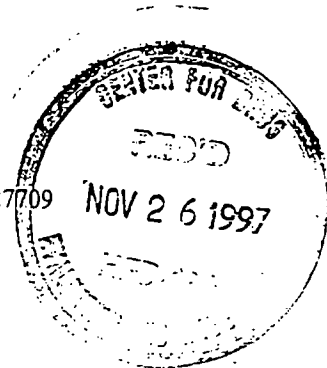
MICROBIOLOGY REVIEW(S)

Attachment I

REVIEW TO HFD-180
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF AMENDMENT # 1
November 24, 1997

NOV 25

NOV 25 1997



- A. 1. NDA 20-807 **APPLICANT:** Hoechst Marion Roussel
Frankfurt am Main, Germany
U.S. Agent: Clintrials Research, Inc.
P.O. Box 13991
Research Triangle Park, NC 27709
2. **PRODUCT NAMES:** Lepirudin
Refludan[®]
r-hirudin (HBW 023)
3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:**
Sterile Powder for Intravenous Injection or Infusion in 50 mg vials
4. **PHARMACOLOGICAL CATEGORY:** Anti-coagulation in adult patients with heparin-associated thrombocytopenia (HAT) type II and thromboembolic disease.
5. **RELATED DOCUMENTS:**

- B. 1. **DATE OF Amendment # 1:** October 2, 1997 (Subject of this review)
2. **ASSIGNED FOR REVIEW:** November 10, 1997

APPEARS THIS WAY
ON ORIGINAL

D. **CONCLUSIONS:** The NDA is recommended for approval from the standpoint of product quality microbiology.

APPEARS THIS WAY
ON ORIGINAL

ISI

11/24/97

Patricia F. Hughes, Ph.D.
Review Microbiologist

- cc.: Original NDA 20-807
HFD-160/Consult File
HFD-160/PFHughes
HFD-180/Division File
HFD-180/DuBeau

ISI 11/25/97

APPEARS THIS WAY
ON ORIGINAL

Drafted by P.F.Hughes/11/24/97
R/D initialed by P. Cooney

REVIEW TO HFD-180
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF NDA
February 26, 1997

- A. 1. **NDA 20-807** **APPLICANT:** Behringwerke AG
Marburg, FDG
U.S. Agent: Clintrials Research, Inc.
P.O. Box 13991
Research Triangle Park, NC 27709
2. **PRODUCT NAMES:** Lepirudin
Refludan®
r-hirudin (HBW 023)
3. **DOSAGE FORM AND ROUTE OF ADMINISTRATION:**
Sterile Powder for Intravenous Injection or Infusion in 50 mg vials
4. **PHARMACOLOGICAL CATEGORY:** Anti-coagulation in adult patients with heparin-associated thrombocytopenia (HAT) type II and thromboembolic disease.
5. **RELATED DOCUMENTS:**



- B. 1. **DATE OF INITIAL SUBMISSION:** December 31, 1997
2. **ASSIGNED FOR REVIEW:** February 13, 1997

APPEARS THIS WAY
ON ORIGINAL

C. **REMARKS:** The NDA is classified as a Priority I submission. Lepirudin is a recombinant protein secreted from yeast cells (*Saccharomyces cerevisiae*) transfected with an expression vector containing the hirudin gene. The recombinant protein consists of 65 amino acids and has a molecular weight of 7000 daltons. The protein is identical to one of the isoforms of the native protein except for the substitution of leucine for isoleucine at the N-terminal of the molecule and the absence of a sulfate group on the tyrosine residue at position 63.

D. **CONCLUSIONS:** The NDA is approvable from the standpoint of microbiology pending resolution of certain microbiological issues.

APPEARS THIS WAY
ON ORIGINAL

/s/ _____ -2/26/97

Patricia F. Hughes, Ph.D.
Review Microbiologist

- cc.: Original NDA 20-807
HFD-160/Consult File
HFD-160/PFHughes
HFD-180/Division File
HFD-180/M.Folkendt
HFD-180/M.Ysern
Drafted by P.F.Hughes/02/26/97
R/D initialed by P. Cooney/02/26/97

/s/ 2/26/97

APPEARS THIS WAY
ON ORIGINAL