CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-873

MICROBIOLOGY REVIEW

DuBeau

SEP 16 1999

REVIEW TO HFD-180
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY TEAM
MICROBIOLOGY REVIEW OF AMENDMENT # 2
24 August 1999

A. 1. **NDA 20-873**
PRODUCT NAME: Angiomax (bivalirudin) Injection
APPLICANT: The Medicines Company
One Cambridge Center
Cambridge Massachusetts 02142

B. 1. **DOSAGE FORM:** Lyophilized sterile product for reconstitution in Water for Injection, USP, 250 mg/vial (lyo)
2. **METHODS OF STERILIZATION:** Aseptic Fill
3. **PHARMACOLOGICAL CATEGORY/PRINCIPAL INDICATION:** Anticoagulant for patients undergoing percutaneous transluminal coronary angioplasty.

C. 1. **DATE OF AMENDMENT # 2:** 5 August 1999
2. **ASSIGNED FOR REVIEW:** 18 August 1999
3. **DRUG PRIORITY:** 1S

D. **REMARKS:** The amendment dated August 5, 1999 contains a response to a microbiology deficiency found in the original NDA submission and in the Amendment dated April 22, 1999.

E. **CONCLUSIONS:** The NDA 20-873 is recommended for approval from the standpoint of product quality microbiology. Please see section F for Review Notes.

/S/ 24 Aug 99

Patricia F. Hughes, Ph.D.
Microbiology Reviewer

/S/ 9/16/99

cc.: Original NDA 20-873
HFD-180/Div.Files
HFD-180/JDuBeau
HFD-160/Consult Files
HFD-805/PFHughes
Drafted by PFHughes,24 August 1999
R/D Initialed by PHCooney

1 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

DuBeau

MAY 17 1999

REVIEW TO HFD-180
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY TEAM
MICROBIOLOGY REVIEW OF AMENDMENT # 1
17 May 1999

A. 1. **NDA 20-873**
PRODUCT NAME: Hirulog® (bivalirudin) Injection
APPLICANT: The Medicines Company
One Cambridge Center
Cambridge Massachusetts 02142

B. 1. **DOSAGE FORM:** Lyophilized sterile product for reconstitution in Water for Injection, USP, 250 mg/vial (lyo)
2. **METHODS OF STERILIZATION:** Aseptic Fill
3. **PHARMACOLOGICAL CATEGORY/PRINCIPAL INDICATION:** Anticoagulant for patients undergoing percutaneous transluminal coronary angioplasty.

C. 1. **DATE OF AMENDMENT # 1:** 22 April 1999
2. **ASSIGNED FOR REVIEW:** 6 May 1999
3. **DRUG PRIORITY:** 1S

D. **REMARKS:** The amendment dated April 22, 1999 contains responses to microbiology deficiencies found in the original NDA submission.

E. **CONCLUSIONS:** The NDA 20-873 is not recommended for approval from the standpoint of product quality microbiology. Please see section F for Review Notes and Section G for List of Deficiencies.

/S/ 17 May 99
Patricia F. Hughes, Ph.D.
Microbiology Reviewer

/S/ 5/17/99

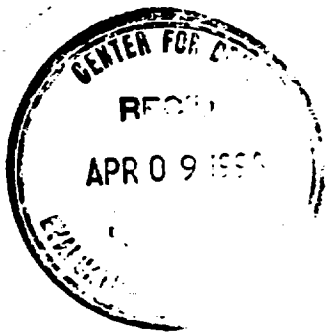
cc.: Original NDA 20-873
HFD-180/Div.Files
HFD-180/JDuBeau
HFD-160/Consult Files
HFD-160/PFHughes
Drafted by PFHughes, 17 May 1999
R/D Initialed by PHCooney

2 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

DuBeau

APR - 8 1998

REVIEW TO HFD-180
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGY REVIEW OF NDA
March 31, 1998



A. 1. **NDA 20-873**
PRODUCT NAME: Hirulog® (bivalirudin) Injection
APPLICANT: The Medicines Company
One Cambridge Center
Cambridge Massachusetts 02142

B. 1. **DOSAGE FORM:** Lyophilized sterile product for reconstitution in Water for Injection, USP, 250 mg/vial (lyo)
2. **METHODS OF STERILIZATION:** Aseptic Fill
3. **PHARMACOLOGICAL CATEGORY/PRINCIPAL INDICATION:** Anticoagulant for patients undergoing percutaneous transluminal coronary-angioplasty.

C. 1. **DATE OF SUBMISSION:** December 23, 1997
2. **ASSIGNED FOR REVIEW:** January 9, 1998
3. **DRUG PRIORITY:** 1S

D. **REMARKS:** The drug product is manufactured at _____ _____ is responsible for release of the final product and for conducting stability studies. The drug product, Hirulog®, is formulated as a lyophilized cake. The final product is aseptically filled and packaged in sterile glass vials. Each vial contains 250 mg Hirulog® and is for intravenous injection or infusion after reconstitution with 5 mL WFI (USP). For intravenous administration, the reconstituted product is further diluted with 5% Dextrose or isotonic saline.

E. **CONCLUSIONS:** The NDA 20-873 is not recommended for approval from the standpoint of product quality microbiology. Please see ~~section F~~ for Review Notes and a "List of Comments and Deficiencies" in Section G.

/S/ 3/31/98

Patricia F. Hughes, Ph.D.
Microbiology Reviewer

/S/ 4/8/98

cc.: Original NDA 20-873
HFD-180/Div.Files
HFD-180/JDuBeau
HFD-160/Consult Files
HFD-160/PFHughes
Drafted by PFHughes,03/31/98
R/D Initialed by PHCooney