CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022434Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

8 June 2011

NDA: **22-434**

Drug Product Name
Proprietary: Argatroban Injection
Non-proprietary: not provided

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
12 January 2011	12 January 2011	13 January 2011	13 January 2011
21 April 2011	22 April 2011	N/A	N/A
6 June 2011	6 June 2011	N/A	N/A

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Eagle Pharmaceuticals Inc.
Address: 470 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Representative: Jay Catalong
Telephone: (847) 969-4897

Name of Reviewer: Stephen E. Langille

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: NDA resubmission

2. SUBMISSION PROVIDES FOR: (b) (4) of Argatroban Injection in building (b) (4) of the Cipla Limited – Goa, India facility.

3. MANUFACTURING SITE: Cipla Limited
Verna Industrial Estate
Verna, Goa 403 722
India
Registration # 3004081307

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile solution, Single dose
- Intravenous infusion
- 1 mg/mL

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Anticoagulant

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: The application was provided in eCTD format. Information requests were sent to the applicant on 7 April 2011 and 31 May 2011. Responses were provided by the applicant on 21 April 2011 and 6 June 2011 and the information contained in the responses has been integrated into the review.

filename: N022434R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 22-434 is recommended for approval from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

Not applicable.

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product will be [redacted] (b) (4) in [redacted] (b) (4) of the Cipla Goa facility.

B. Brief Description of Microbiology Deficiencies -

No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -

Not applicable

III. Administrative

A. Reviewer's Signature _____

Stephen E. Langille, Ph.D.

B. Endorsement Block

James McVey – Team Leader

C. CC Block

N/A

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/s/

STEPHEN E LANGILLE
06/09/2011

JAMES L MCVEY
06/10/2011
I concur.

Product Quality Microbiology Review

20-January-2010

NDA: 22-434

Drug Product Name
Proprietary: Argatroban Injection
Non-proprietary: not provided

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
26-September-2008	29-September-2009	Not provided	16-October-2008

Submission History (for amendments only): Not applicable

Applicant/Sponsor
Name: Eagle Pharmaceuticals Inc.
Address: 470 Chestnut Ridge Road
Woodcliff Lake, NJ 07677

Representative: Hindy Schiff
Telephone: 201-326-5309

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: (b) (4) of Argatroban Injection

3. MANUFACTURING SITE: Cipla Limited
Verna Industrial Estate
Verna, Goa 403 722
India
Registration # 3004081307

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile solution, Single dose
- Intravenous infusion
- 1 mg/mL

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Anticoagulant

B. SUPPORTING/RELATED DOCUMENTS: Not applicable

C. REMARKS: NDA 22-434 was provided as a paper submission in CTD format. The application was originally submitted on 9-September-2008. A refuse to file letter was sent to the applicant on 21-November-2008. The application was then re-filed on 30-March-2009.

filename: N022434R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 22-434 is approvable from the standpoint of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product will be (b) (4) of the Cipla manufacturing facility in Verna Goa, India.

B. Brief Description of Microbiology Deficiencies -

The applicant failed to provide updated manufacturing process control information, validation information, and stability data for the manufacture of Argatroban Injection in (b) (4) of the Cipla manufacturing facility.

C. Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiology deficiencies could result in microbial and/or endotoxin contamination of the drug product.

III. Administrative

A. Reviewer's Signature _____

Stephen E. Langille

B. Endorsement Block

James McVey – Team Leader

C. CC Block

N/A

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22434	ORIG-1	EAGLE PHARMACEUTICALS INC	ARGATROBAN INJECTION

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/s/

STEPHEN E LANGILLE
01/20/2010

JAMES L MCVEY
01/21/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 22-434 **Applicant:** Eagle Pharmaceuticals, Inc **Letter Date:** September 26, 2008

Drug Name: Argatroban Injection **NDA Type:** 505(b)(2) **Stamp Date:** September 29, 2008

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		The application is arranged in DTD format and contains sufficient information to begin the review.
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Section P.3.3
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Section P.3.5
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		The drug product is not preserved. Integrity testing was provided in section P.2.5.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	X		Section P.5.3
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?		X	Not applicable for product quality microbiology
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: Not applicable

Stephen E. Langille, Ph.D.	Date
James McVey/Team Leader	Date

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/s/

Stephen Langille
12/2/2008 03:05:06 PM
MICROBIOLOGIST

James McVey
12/2/2008 03:06:47 PM
MICROBIOLOGIST
I concur.