CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206769Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

18 AUG 2014

NDA: 206-769

Drug Product Name
Non-proprietary: Argatroban Injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
28 FEB 2014	28 FEB 2014	05 MAR 2014	06 MAR 2014
03 JUN 2014	03 JUN 2014	N/A	N/A
08 JUL 2014	08 JUL 2014	N/A	N/A
22 JUL 2014	22 JUL 2014	N/A	N/A

Applicant/Sponsor
Name: Teva Pharmaceuticals USA
Address: 425 Privet Road
Horsham, PA 19044
Representative: Scott D. Tomsky
Telephone: 215-591-3142

Name of Reviewer: Jessica G. Cole, PhD

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(2) original NDA

2. SUBMISSION PROVIDES FOR: A new large volume parenteral product

3. MANUFACTURING SITE:
Teva Pharmaceutical Works Private Limited Company
Large Volume Parenteral (LVP) Plant
Gödöllö, Hungary
FEI 3002875215

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

- 250 mg/250 mL in a plastic bag
- Intravenous infusion

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

6. PHARMACOLOGICAL CATEGORY: Prophylaxis or treatment of heparin-induced thrombosis

B. SUPPORTING/RELATED DOCUMENTS: None.

C. REMARKS: This submission is in the eCTD format. The following information request was included in the 02 May 2014 74-day letter and a response was received on 22 July 2014.

1. Module 3.2.P.3.3 indicates the bioburden sample will be collected (b) (4)
2. Justify the requalificatio (b) (4)

The following information request was sent to the project manager on 27 June 2014 and a response was received on 08 July 2014.

1. (b) (4)
2.
3.

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4. (b) (4)
5. Provide a description of the growth media used for environmental monitoring. Confirm that personnel monitoring plates are incubated at a minimum of 48 hours at 32.5±2.5°C or 72 hours at 22.5±2.5°C.
6. Describe the (b) (4) container closure system.
7. Provide the sterility test and endotoxin test method verification studies.

filename: N206769R1.doc

Reference ID: 3612968

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for Approval.

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 is [redacted] (b) (4) .

B. Brief Description of Microbiology Deficiencies -

C. Contains Potential Precedent Decision(s)- ☐ **Yes** ☒ **No**

III. Product Quality Microbiology Risk Assessment

A. Initial Product Quality Microbiology Risk Assessment

CQA	Risk Factor	Prob. of Occ. (O)	Severity of Effect (S)	Detect. (D)	Risk Priority Number[6] (RPN)	Additional Review Emphasis based on Risk (in addition to normal review process)
Sterility	[redacted] (b) (4)					
Endotoxins	[redacted] (b) (4)					

B. Final Risk Assessment – The applicant has provided data sufficient to demonstrate that the risks for non-sterility and excessive endotoxin have been mitigated. These data include the validation studies and controls for the [redacted] (b) (4) process, the container closure integrity studies, and the controls for endotoxins and bioburden in the raw materials, container closure components, and finished product.

IV. Administrative

A. Reviewer's Signature _____
Jessica G. Cole, PhD

B. Endorsement Block _____
Bryan Riley, PhD

C. CC Block N/A

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/s/

JESSICA COLE
08/19/2014

BRYAN S RILEY
08/19/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206-769 **Applicant:** Teva Pharmaceuticals USA **Letter Date:** 28 February 2014

Drug Name: Argatroban Injection **NDA Type:** 505(b)(2) **Stamp Date:** 28 February 2014

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		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		This drug product is (b) (4) .
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
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		Translations were provided.
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		CCI studies were submitted.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?	X		
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			Not applicable.
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			Not applicable.
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: This is a 1 mg/mL solution in a 250 mL (b) (4) bag with an overwrap. The proposed bag has a single port and the port is closed with a stopper and a cap.

The following information request should be sent to the applicant:

1. Module 3.2.P.3.3 indicates the bioburden sample will be collected [redacted] (b) (4)
2. Justify the requalification [redacted] (b) (4)

Jessica G. Cole, PhD — 22 April 2014

Reviewing Microbiologist — Date

Bryan Riley, PhD

Microbiology Team Leader — Date

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/s/

JESSICA COLE
04/23/2014

BRYAN S RILEY
04/23/2014
I concur.