CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203826Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

May 18, 2012

NDA: 203-826

Drug Product Name
Proprietary: N/A
Non-proprietary: Phenylephrine Hydrochloride Injection, USP

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
28 DEC 2011	28 DEC 2011	1 JAN 2012	27 FEB 2012
1 MAR 2012	1 MAR 2012	N/A	N/A
24 APR 2012	24 APR 2012	N/A	N/A

Applicant/Sponsor
Name: West-Ward Pharmaceutical Corp.
Address: 2 Esterbrook Lane, Cherry Hill, NJ 08003
Representative: J. Barton Kalis, Director, Regulatory Affairs
Telephone: (856) 489-2247

Name of Reviewer: Erika Pfeiler, Ph.D.

Conclusion: Recommend for Approval

Product Quality Microbiology Data Sheet

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

2. SUBMISSION PROVIDES FOR: Marketing of a sterile drug product

3. MANUFACTURING SITE: West-Ward Pharmaceutical Corp.
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
Dosage Form: Sterile injection solution, 1 ml in a (b) (4) glass vial
Route of Administration: Intravenous injection
Strength/Potency: 10 mg/ml

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

6. PHARMACOLOGICAL CATEGORY: To increase blood pressure in acute hypotensive state

B. SUPPORTING/RELATED DOCUMENTS: N/A

C. REMARKS:
This submission was in the eCTD format.

Two information requests were communicated to the applicant via the RPM. Responses were received on March 1, 2012 and April 24, 2012 and were incorporated into the relevant sections of the review.

February 9, 2012

- Provide a detailed description of the sterility and endotoxin test procedures used for the drug product. Additionally, provide summaries of the procedures and results for the tests performed with the drug product to verify that the sterility and endotoxin tests procedures are suitable for use with the drug product.

March 21, 2012

- Please clarify whether there are circumstances in which you intend to (b) (4) the final drug product by (b) (4). If you do plan to (b) (4) please provide data detailing this process, as well as a demonstration that the container closure system will maintain its integrity under these conditions.
- The specifications for this product list endotoxin limits as NMT (b) (4) of drug product, and the maximum human dose of the drug product listed for the purposes of endotoxin limit calculations is (b) (4). However, your label indications for acute hypotension with septic shock and pediatric acute hypotension list doses of (b) (4) These doses would exceed the endotoxin limit for parenteral drugs of NMT (b) (4) We recommend that you decrease the endotoxin specification for the drug product to NMT (b) (4) so as to not exceed the limit of (b) (4) in the highest hourly dose.

- Your application states that the production (b) (4) used to sterilize the final drug product (b) (4) (b) (4) o annual requalification wit (b) (4) studies, however the most recen tudies in your application are from 1997. Please provide your most recent (b) (4) studies for both (b) (4)

filename: N203826R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommend for approval on the basis of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – Product is (b) (4)

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature _____
Erika Pfeiler, Ph.D.

B. Endorsement Block_____
Bryan Riley, Ph.D.
Microbiology Team Leader

C. CC Block
N/A

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/s/

ERIKA A PFEILER
05/18/2012

BRYAN S RILEY
05/18/2012
I concur.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: March 21, 2012

TO: Quynh Nguyen
Regulatory Health Project Manager
CDER/OND/ODEI/DCRP

FROM: Erika Pfeiler, Ph.D.
Microbiologist
CDER/OPS/New Drug Microbiology Staff
(301) 796-0642

THROUGH: Bryan Riley, Ph.D.
Microbiology Team Leader
CDER/OPS/New Drug Microbiology Staff

SUBJECT: NDA: 203-826
Submission Date: 12/28/2011
Drug Product: Phenylephrine HCl, USP
Applicant: West-Ward Pharmaceutical Corp.

A product quality microbiology review of Phenylephrine HCl, USP is in progress and more information is needed. Please forward the following comments to the applicant.

Microbiology Comments:

1. The specifications for this product list endotoxin limits as NMT [redacted] (b) (4) of drug product, and the maximum human dose of the drug product listed for the purposes of endotoxin limit calculations is [redacted] (b) (4). However, your label indications for acute hypotension with septic shock and pediatric acute hypotension list doses of [redacted] (b) (4). These doses would exceed the endotoxin limit for parenteral drugs of NMT [redacted] (b) (4) We recommend that you decrease the endotoxin specification for the drug product to NMT [redacted] (b) (4) so as to not exceed the limit of [redacted] (b) (4) in the highest hourly dose.
2. Your application states that the production [redacted] (b) (4) used to sterilize the final drug product [redacted] (b) (4) undergo annual requalification with [redacted] (b) (4) studies, however the most recent [redacted] (b) (4) studies in your application are from 1997. Please provide your most recent [redacted] (b) (4) studies for both [redacted] (b) (4).

END

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/s/

ERIKA A PFEILER
03/21/2012

BRYAN S RILEY
03/21/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203826 **Applicant:** West-Ward Pharmaceutical Corp. **Letter Date:** 28 December 2011

Drug Name: Phenylephrine Hydrochloride Injection, USP **NDA Type:** 505(b)(2) **Stamp Date:** 28 December 2011

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		This is an eCTD submission
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		The drug product is (b) (4) using (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	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		The drug product is a single dose vial. CCI studies were provided.
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	Sterility and endotoxin test method verification were not provided.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	X		
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: An IR will be drafted to address the lack of microbial test method verification data.

27 January 2012

Bryan S. Riley, Ph.D. Date
Senior Review Microbiologist

John W. Metcalfe, Ph.D. Date
Senior Review Microbiologist

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/s/

BRYAN S RILEY
01/28/2012

JOHN W METCALFE
01/30/2012
I concur.