

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203510Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

December 28, 2012

NDA 203510:

Drug Product Name

Proprietary:

Non-proprietary: Phenylephrine hydrochloride

Review Number: 1

Dates of Submission(s) Covered by this Review

| Submit | Received | Review Request | Assigned to Reviewer |
|---------------|-----------------|-----------------------|-----------------------------|
| 12/19/2012 | 12/20/2012 | N/A | N/A |
| 9/21/2012 | 9/21/2012 | 9/24/2012 | 9/28/2012 |
| 10/19/2011* | 10/19/2011 | N/A | N/A |

*RTF

Submission History (for amendments only): N/A

Applicant/Sponsor

Name: Paragon BioTeck, Inc.

Address: 11501 SW Pacific Highway, Suite 201, Tigard, OR 97223

Representative: Parick H. Witham

Telephone: 888-424-1192

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
 2. **SUBMISSION PROVIDES FOR:** Manufacture of a sterile drug product
 3. **MANUFACTURING SITE:** [REDACTED] (b) (4)
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Preserved Multi-dose Ophthalmic solution in a dropper bottle, 2.5 % and 10%
 5. **METHOD(S) OF STERILIZATION:** [REDACTED] (b) (4)
 6. **PHARMACOLOGICAL CATEGORY:** pupil dilation
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** An information request was sent to the sponsor on November 15, 2012 and a Response was received on 12/20/2012. A review of the original submission and the 12/20/2012 response is included herein. The submission is in eCTD format

filename: N203510r1.doc

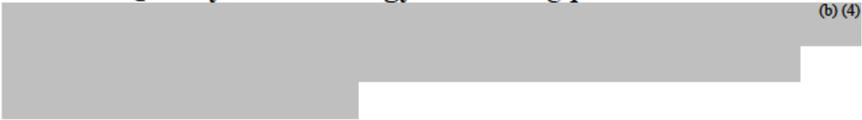
Executive Summary

I. Recommendations

- A. **Recommendation on Approvability –**
NDA 203510 is recommended for approval from the standpoint 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 –** The drug product is
 (b) (4)

- B. **Brief Description of Microbiology Deficiencies**
No product quality microbiology deficiencies were identified based upon the information provided.

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

III. Administrative

- A. **Reviewer's Signature** _____
Steven P. Donald, M.S.

- B. **Endorsement Block** _____
Bryan Riley, Ph.D.
Team Leader

- C. **CC Block**
N/A

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/s/

STEVEN P DONALD
01/02/2013

BRYAN S RILEY
01/03/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203510 **Applicant:** Paragon Biotech Inc. **Letter Date:** Sept. 21, 2012

Drug Name: Phenylephrine hydrochloride ophthalmic **NDA Type:** 505(b)(2) **Stamp Date:** Sept. 21, 2012

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 | | eCTD format |
| 2 | Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product? | X | | 3.2.P.3.3; Manuf-process-and-controls.pdf |
| 3 | Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product? | X | | 3.2.P.3.5; process-validation.pdf and 3.2.R.3 |
| 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 | | 3.2.P.2; bak-dose-range-study.pdf |
| 6 | Has the applicant submitted microbiological specifications for the drug product and a description of the test methods? | X | | 3.2.P.3.5.1; specifications.pdf |
| 7 | Has the applicant submitted the results of analytical method verification studies? | X | | 3.2.P.5.3; various |
| 8 | Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions? | | | N/A |
| 9 | If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data? | | | N/A: Multi-dose product, ^{(b)(4)} contains preservative |
| 10 | Is this NDA fileable? If not, then describe why. | X | | |

Additional Comments: Multi-dose ophthalmic; Original submission dated October 19, 2011. Refusal to file letter dated December 16, 2011. Resubmission date is September 20, 2012. Resubmission includes additional batches for stability studies. Priority review status.

Reviewing Microbiologist
Steven P. Donald, M.S.

Date

Microbiology Team Leader
Bryan Riley, Ph.D.

Date

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/s/

STEVEN P DONALD
10/04/2012

BRYAN S RILEY
10/05/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203510 **Applicant:** Paragon Biotech Inc. **Letter Date:** 19 October 2011

Drug Name: Phenylephrine hydrochloride ophthalmic **NDA Type:** 505(b)(2) **Stamp Date:** 21 October 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 | | 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 | | (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 | | |
| 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? | X | | |
| 9 | Is this NDA fileable? If not, then describe why. | X | | |

Additional Comments: The drug product is a multi-dose ophthalmic.

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

18 November 2011

Date

Stephen E. Langille
Senior Review Microbiologist

Date

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/s/

BRYAN S RILEY
11/22/2011

STEPHEN E LANGILLE
11/23/2011