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

<table>
<thead>
<tr>
<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
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<tbody>
<tr>
<td>12/19/2012</td>
<td>12/20/2012</td>
<td>N/A</td>
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<td>9/21/2012</td>
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<td>9/24/2012</td>
<td>9/28/2012</td>
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<td>10/19/2011*</td>
<td>10/19/2011</td>
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*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: N/A

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: N/A

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. 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:

<table>
<thead>
<tr>
<th>Content Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>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?</td>
<td></td>
<td>X</td>
<td>eCTD format</td>
</tr>
<tr>
<td>2. Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?</td>
<td></td>
<td>X</td>
<td>3.2.P.3.3; Manuf-process-and-controls.pdf</td>
</tr>
<tr>
<td>3. Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?</td>
<td></td>
<td>X</td>
<td>3.2.P.3.5; process-validation.pdf and 3.2.R.3</td>
</tr>
<tr>
<td>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?</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>5. Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?</td>
<td></td>
<td>X</td>
<td>3.2.P.2; bak-dose-range-study.pdf</td>
</tr>
<tr>
<td>6. Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?</td>
<td></td>
<td>X</td>
<td>3.2.P.3.5.1; specifications.pdf</td>
</tr>
<tr>
<td>7. Has the applicant submitted the results of analytical method verification studies?</td>
<td></td>
<td>X</td>
<td>3.2.P.5.3; various</td>
</tr>
<tr>
<td>8. Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?</td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>9. If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?</td>
<td></td>
<td></td>
<td>N/A: Multi-dose product, contains preservative</td>
</tr>
<tr>
<td>10. Is this NDA fileable? If not, then describe why.</td>
<td></td>
<td>X</td>
<td></td>
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<th>Microbiology Team Leader</th>
<th>Date</th>
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<tr>
<td>Bryan Riley, Ph.D.</td>
<td></td>
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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

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

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**Bryan S. Riley, Ph.D.**  
Senior Review Microbiologist  
Date: 18 November 2011

**Stephen E. Langille**  
Senior Review Microbiologist  
Date:  

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**Reference ID:** 3048384
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/s/

BRYAN S RILEY
11/22/2011

STEPHEN E LANGILLE
11/23/2011