CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203629Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)
Product Quality Microbiology Review

September 6, 2012

NDA: 203629/N000

Drug Product Name

Proprietary: Not Determined
Non-proprietary: Neostigmine Methylsulfate Injection, USP

Review Number: 1

Dates of Submission(s) Covered by this Review

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<th>Submit</th>
<th>Received</th>
<th>Review Request</th>
<th>Assigned to Reviewer</th>
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</thead>
</table>

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: APP Pharmaceuticals – Fresenius Kabi Group
Address: 1501 E Woodfield Road, Schaumburg, IL 60173
Representative: James Harn, Manager of RA
Telephone: 847-517-5767

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: Recommend approval.
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original NDA

2. SUBMISSION PROVIDES FOR: Neostigmine Methylsulfate


4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Injectable, 0.5 mg/mL and 1.0 mg/mL, both in a 10 mL multiple dose vial.

5. METHOD(S) OF STERILIZATION: 

6. PHARMACOLOGICAL CATEGORY: A reversal agent to the neuromuscular blocking effects of non-depolarizing muscle relaxants.

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: The New Drug Application is submitted in accordance with 505(b)(2) to seek marketing approval of Neostigmine Methylsulfate injection, USP. The application is an eCTD submission.

filename: N203629R1
Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommend approval.

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 – 

B. Brief Description of Microbiology Deficiencies - None

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

III. Administrative

A. Reviewer's Signature  

Vinayak B. Pawar, Ph.D.

B. Endorsement Block  

John W. Metcalfe, Ph.D.

C. CC Block  

N/A
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

VINAYAK B PAWAR
09/10/2012

JOHN W METCALFE
09/10/2012
I concur.
## PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

**NDA Number:** 203629  
**Applicant:** APP Pharmaceuticals  
**Letter Date:** 12/28/2011  
**Drug Name:** Neostigmine Methylsulfate USP Injection  
**NDA Type:** Original NDA  
**Stamp Date:** 12/29/2011

### Content Parameter

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<tr>
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<th>Yes</th>
<th>No</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1</td>
<td></td>
<td>X</td>
<td>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>
</tr>
<tr>
<td>2</td>
<td></td>
<td>X</td>
<td>Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?</td>
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<tr>
<td>3</td>
<td></td>
<td>X</td>
<td>Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?</td>
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<tr>
<td>4</td>
<td></td>
<td>X</td>
<td>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>
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<td>5</td>
<td></td>
<td>X</td>
<td>Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?</td>
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<td>6</td>
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<td>Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?</td>
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<td>Has the applicant submitted the results of analytical method verification studies?</td>
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<td>Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?</td>
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<tr>
<td>9</td>
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<td>X</td>
<td>Is this NDA fileable? If not, then describe why.</td>
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### Additional Comments

The drug product is [redacted] and conforms to the formulation and controls specified by USP monograph. Although there are no filing issues, per ONDQA, the manufacturing facility has been flagged for cGMP violations; OC is preparing Warning Letter as of 10/17/11 & 01/03/12 per CMS information.

*Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist*  
*John W. Metcalfe, Ph.D., Sr. Review Microbiologist*  

Reference ID: 3091148
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/s/

VINAYAK B PAWAR
02/22/2012

JOHN W METCALFE
02/22/2012
I concur.