CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200-890

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

05 May 2010

NDA: **200-890/N000**

Drug Product Name
Proprietary: ISOPTO® Carpine
Non-proprietary: pilocarpine hydrochloride ophthalmic solution

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
22 DEC 2009	22 DEC 2009	04 JAN 2010	05 JAN 2010

Submission History (for amendments only) – NA

Applicant/Sponsor
Name: Alcon Research, Ltd.
Address: 6201 South Freeway
Fort Worth, Texas 76134-2099
Representative: Michael C. Son Ph.D. RAC
Telephone: (817) 551-8120

Name of Reviewer: Denise A. Miller

Conclusion: Approve

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original Application

2. SUBMISSION PROVIDES FOR: The compounding and filling procedures for a sterile ophthalmic drug product.

3. MANUFACTURING SITE:
Alcon Research, Ltd.
ASPEX (Alcon Sterile Products Expansion) Manufacturing Facility
6201 South Freeway
Forth Worth, TX 76134-2099

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
Dosage Form: Sterile liquid
Route of Administration: Topical, Ocular
Strength/Potency: 1, 2 and 4%

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

6. PHARMACOLOGICAL CATEGORY: reduction of elevated intraocular presser in patients with glaucoma or ocular hypertension.

B. SUPPORTING/RELATED DOCUMENTS:
DMF (b) (4)
A review of DMF (b) (4) was not required as the information in the NDA was sufficient.
DMF (b) (4)
A review of DMF (b) (4) was not required as the information in the NDA was sufficient.

C. REMARKS:
1) The format of this application is e-CTD.
2) This is a pre-38 drug that has been marketed for many years and is on the Office of Compliance's listing of Medically Necessary Unapproved Marketed Drugs.
3) CMC Information Request was sent on 19 MAR 2010 with a request from the chemist to lower the endotoxin specification to (b) (4). Response was submitted on 15 APR 2010 with the endotoxin release specification lowered to (b) (4) (b) (4)

filename: N200890N000R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommend to approve from a quality microbiology standpoint.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – This application is for the manufacturing and (b) (4) process of a sterile preserved multi-dose ophthalmic solution.

B. Brief Description of Microbiology Deficiencies – None

C. Assessment of Risk Due to Microbiology Deficiencies - NA

III. Administrative

A. Reviewer's Signature _____
Denise A. Miller, Microbiologist

B. Endorsement Block _____
Stephen E. Langille, Ph.D.

C. CC Block
N/A

18 Pages has been withheld in full immediately following this page as B4 (CCI/TS)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200890	ORIG-1	ALCON INC	PILOCARPINE HYDROCHLORIDE OPHTHALMIC SOLUTION, 1%, 2% AND 4%

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/s/

DENISE A MILLER
05/10/2010

STEPHEN E LANGILLE
05/10/2010

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 200-890 **Applicant: Alcon, Inc.** **Letter Date:** 22-DEC-2009

Drug Name: ISOPTO Carpine **NDA Type: 505(b)(1)** **Stamp Date:** 22-DEC-2009

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?	√		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	√		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	√		
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?		√	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	√		
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	√		
7	Has the applicant submitted the results of analytical method verification studies?	√		
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	NA		
9	Is this NDA fileable? If not, then describe why.	√		

Additional Comments: this is a pre-1938 topical ophthalmic solution drug that has been on the market for over 50 years in both the United States and Europe.

Denise A. Miller, Microbiologist Date 07-JAN-2010

Bryan S. Riley, Ph.D.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200890	ORIG-1	ALCON INC	PILOCARPINE HYDROCHLORIDE OPHTHALMIC SOLUTION, 1%, 2% AND 4%

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/s/

DENISE A MILLER
01/12/2010

BRYAN S RILEY
01/12/2010
I concur.