CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204251Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

December 20, 2012

NDA: 204251

Drug Product Name
Proprietary: SIMBRINZA™ Ophthalmic Suspension
Non-proprietary: Brinzolamide 1%/Brimonidine tartrate 0.2%

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
June 19, 2012	June 19, 2012	June 28, 2012	July 05, 2012

Submission History (for amendments only) – N/A

Applicant/Sponsor
Name: Alcon Research, Ltd.
Address: 6201 South Freeway, Fort Worth, TX
Representative: Katharine Rath, Asst. Director, Reg. Affairs
Telephone: 817-302-5912

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: A topical ophthalmic containing Brinzolamide 1%/Brimonidine tartrate 0.2%

3. MANUFACTURING SITE: Alcon's ASPEX Manufacturing Facility, Fort Worth, Texas.

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Topical ophthalmic Suspension, one drop per treatment, maximum three drops daily.

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

6. PHARMACOLOGICAL CATEGORY: Reduction of elevated intraocular pressure in patients with Glaucoma and ocular hypertension.

B. SUPPORTING/RELATED DOCUMENTS: NDA 22-048, NDA 20-816 & ANDA 202305

C. REMARKS: The subject Original NDA provides for a topical ophthalmic suspension which contains Brinzolamide 1%/Brimonidine tartrate 0.2%. This application is an electronic submission.

filename: **N204251R1**

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) (4) [redacted]

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., NDMS, OPS, CDER

B. Endorsement Block _____
John W. Metcalfe, Ph.D., NDMS, OPS, CDER

C. CC Block
N/A

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/s/

VINAYAK B PAWAR
12/21/2012

JOHN W METCALFE
12/21/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204251 **Applicant:** Alcon Research **Letter Date:** June 19, 2012

Drug Name: Brinzolamide 1%/Brimonidine Tartrate 0.2% ophthalmic suspension **NDA Type:** An Original NDA for a new Ophthalmic suspension. **Stamp Date:** June 19, 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		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		In Section 3.2.P.3.5.2. Product will be manufactured at Alcon ASPEX, Texas.
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		In Section 3.2.P.3.5.3.
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		PET USP <51> tested at product development only. CCI in Section 3.2.P.3.5.7
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?			Specifications provided in Section 3.2.P.5.1.
7	Has the applicant submitted the results of analytical method verification studies?	X		USP Sterility Test– Procedure-0001126. USP Endotoxins Test-Procedure-0001160 (specifications at LT 0.5 EU/mL). Batches PSB #1 & PSB #2 tested at < 0.39 to 0.50 EU/mL)
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	X		
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			N/A
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: None

Vinayak B. Pawar, Ph.D., Primary Microbiology Reviewer **Date**

John W. Metcalfe, Ph.D., Secondary Microbiology Reviewer **Date**

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/s/

VINAYAK B PAWAR
08/09/2012

JOHN W METCALFE
08/09/2012
I concur.