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RESEARCH**

APPLICATION NUMBER:

204822Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

October 25, 2013

NDA: 204822

Drug Product Name

Proprietary: Travoprost Ophthalmic Solution

Non-proprietary: Travoprost 0.003% solution

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
July 15, 2013	July 15, 2013	July 16, 2013	July 19, 2013

Submission History (for 2nd Reviews or higher) - N/A

Applicant/Sponsor

Name: Alcon Laboratories, Inc
Address: 6201 S Freeway, Fortworth, Texas 76134-2099
Representative: Naj Sharif, Ph.D., Global RA Project Manager
Telephone: 817-568-6494

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 change in preservative and strength to an approved formulation.
 3. **MANUFACTURING SITE:** Alcon Research Ltd., Fort Worth Texas [ASPEX] & S.A. Alcon-Couvreur N.V., Purrs, Belgium [PURRS]
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Eye drops, 30 µg/mL per 4 or ^(b)₍₄₎ mL bottle.
 5. **METHOD(S) OF STERILIZATION:** (b) (4)
 6. **PHARMACOLOGICAL CATEGORY:** The proposed dosage and indication for Travoprost 0.003% Solution are once-daily topical ocular therapy for decrease of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** The sponsor request review of NDA 204822 which provides for a formulation containing Travoprost 30 µg/mL (also known as Travoprost 0.003% Solution), preserved with *polyquaternium-1* (POLYQUAD). Other formulations such as Travoprost 40 µg/mL eye drops, solution preserved with benzalkonium chloride (Travoprost 0.004% BAK was approved in the USA in March 2001 (NDA 21-257) and Travoprost 40 µg/mL eye drops, solution preserved with *polyquaternium-1* was approved by EMA in November 2010 which is marketed in 60 countries worldwide. This is an electronic submission.

filename: N204822R1

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** - The bulk formulation is (b) (4) plastic bottles with plugs and caps.
- B. Brief Description of Microbiology Deficiencies** – None
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A
- D. Contains Potential Precedent Decision(s)** - Yes No

Administrative

- A. Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist, OPS/CDER
- B. Endorsement Block** _____
John W. Metcalfe, Ph.D., Sr. Review Microbiologist, OPS/CDER
- C. CC Block**
N/A

14 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

VINAYAK B PAWAR
10/28/2013

JOHN W METCALFE
10/28/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204822 **Applicant:** Alcon Laboratories, **Letter Date:** July 15, 2013
Fort Worth, Texas 76134

Drug Name: Travoprost **NDA Type:** Original NDA **Stamp Date:** July 15, 2013
Ophthalmic Solution 0.003%

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		Section 3.2.P.3.3
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Section 2.3.P.3.5
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		APE-Section 3.2.P.2.5 CCI- 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?	X		Section 3.2.P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	X		(b) (4)
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
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The product will be manufactured at two sites: Alcon, Texas, USA and Alcon Purrs, Belgium. The sponsor provided sterilization validation package for both sites, the adequacy of which will be determined upon review.

Vinayak B. Pawar, Ph.D., Sr. Review Microbiologist, Primary Reviewer **Date**

John W. Metcalfe, Ph.D., Sr. Review Microbiologist, Secondary reviewer **Date**

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/s/

VINAYAK B PAWAR
08/27/2013

JOHN W METCALFE
08/27/2013
I concur.