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RESEARCH**

APPLICATION NUMBER:
21-994

MICROBIOLOGY REVIEW

Product Quality Microbiology Review

07 SEPT 2006

NDA: 21-994/N-000

Drug Product Name

Proprietary:

Travatan® Z (BAC-Free)

Non-proprietary:

travoprost ophthalmic solution 0.004%

Drug Product Priority Classification: S

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
18 NOV 2005	21 NOV 2005	30 NOV 2005	29 NOV 2005

Submission History (for amendments only) N/A

Applicant/Sponsor

Name:

Alcon, Inc.

Address:

P.O.Box 62

Bosch 69

CH-6331 Hunenberg

Switzerland

Representative:

Angela C. Kothe

Assoc. Dir., Reg. Affairs

Telephone:

817-551-4933

Name of Reviewer:

Robert J. Mello, Ph.D.

Conclusion:

The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
 2. **SUBMISSION PROVIDES FOR:** Request to market a new drug
 3. **MANUFACTURING SITE:** Alcon Manufacturing, Ltd., ASPEX (Alcon Sterile Products Expansion) Manufacturing Facility, 6201 South Freeway, Fort Worth, TX
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile, Preserved, Topical Ophthalmic Solution, 0.004% travoprost, packaged as 2.5ml/4ml and 5.0 ml/7.5 ml DROP-TAINER[®] plastic bottles.
 5. **METHOD(S) OF STERILIZATION:**
 - _____ - Packaging components (bottles/plugs/closures)
 - _____ - Drug Product
 6. **PHARMACOLOGICAL CATEGORY:** Ophthalmic Prostaglandins
- B. **SUPPORTING/RELATED DOCUMENTS:**
- Microbiology review dated 09 JUNE 2005 (V. Pawar) for NDA 21-862, Nevenac 0.1% Suspension.
 - Microbiology review dated 07 AUG 2000 (V. Pawar) for NDA 21-257/N-000, Travatan[®] Ophthalmic Solution
 - Microbiology review dated 09 NOV 2005 (J. Metcalfe) for NDA 21-257/SCP-016, Travatan[®] Ophthalmic Solution.
- C. **REMARKS:** The consult requests review of NDA 21-994. Six volumes of module 2 and five volumes of module 3 were submitted for review. An amendment to this NDA (21-994/N-000 BC, letter date 10 Jan 2006) was submitted in response to a request for additional information on a referenced testing standard. It is reviewed here as part of the original submission. A phone and e-mail request was sent 09 AUG 2006 to A. Kothe, Alcon Labs, for additional information on the status of the sterile filter validation of microbial retention. The report was provided for my review electronically, via e-mail, on 10 AUG 2006 and was submitted as an amendment to the NDA (NDA 21-994/N000 BC, Letter date 15 AUG 2006). A subsequent amendment was submitted (NDA 21-994/N000 BC, Letter date 01 SEPT 2006) to change the pH specification from _____ as a result of particulate generation (_____) observed at _____ at _____

An e-mail request was sent 25 AUG 2006 to A. Kothe, Alcon Labs, for additional information on the media fill program. A response was received on 07 SEPT 2006 and is incorporated into the body of this review.

Filename: N021994N000R1.doc

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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** - The application is recommended for approval from microbiology product quality standpoint.
- 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 product Travatan[®]-Z (BAC-free) is a sterile, preserved ophthalmic topical solution that does not contain the BAC/EDTA (benzalkonium chloride/edetate disodium) preservative system found in a similar drug product of the applicant (Travatan[®] Ophthalmic Solution 0.004% NDA 21-257). Travatan[®]-Z (BAC-free) obtains its preservative effectiveness by the inclusion of a _____ and _____ into plastic DROP-TAINER[®] bottles. Packaging components are _____ by _____ at a contract _____ firm.
- B. **Brief Description of Microbiology Deficiencies** – No deficiencies noted
- C. **Assessment of Risk Due to Microbiology Deficiencies** – N/A

III. Administrative

- A. **Reviewer's Signature** _____
Robert J. Mello, Ph.D.
- B. **Endorsement Block** _____
Stephen E. Langille, Ph.D.
- C. **CC Block**
In DFS

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/s/

Robert Mello
9/8/2006 03:27:53 PM
MICROBIOLOGIST

Recommend for approval

Stephen Langille
9/8/2006 03:36:46 PM
MICROBIOLOGIST

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