

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

206276Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Product Quality Microbiology Review

31 December 2014

NDA: 206276

Drug Product Name

Proprietary: PAZEO

Non-proprietary: Olopatadine Hydrochloride Ophthalmic Solution,
0.77%

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
30 July 2014	30 July 2014	12 August 2014	21 August 2014
5 December 2014	5 December 2014	N/A	N/A
17 December 2014	17 December 2014	N/A	N/A

Submission History (for 2nd Reviews or higher): Not applicable

Applicant/Sponsor

Name: Alcon
Address: 601 South Freeway
Fort Worth, TX 76134-2099
Representative: Naj Sharif, Ph.D.
Telephone: 817-568-6494

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original Submission – Priority Review
 2. **SUBMISSION PROVIDES FOR:** (b) (4) processing information for two manufacturing sites and multiple contract manufacturing sterilization sites for container closure components.
 3. **MANUFACTURING SITES:** Alcon Research, Ltd.
6201 South Freeway
Fort Worth, Texas 76134
Drug Establishment Registration No.
1610287

and

sa Alcon-Couvreur nv
Rijksweg 14
B-2870 Puurs
Belgium
Drug Establishment Registration No.
3002037047
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Sterile Ophthalmic Solution
 - Topical
 - 0.77%
 5. **METHOD(S) OF STERILIZATION:** (b) (4) processing
 6. **PHARMACOLOGICAL CATEGORY:** Treatment of itching associated with allergic conjunctivitis
- B. **SUPPORTING/RELATED DOCUMENTS:** Not applicable
- C. **REMARKS:** The application was provided in eCTD format.

filename: N206276r1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - Recommended for Approval
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - Not applicable

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

The drug product will be (b)(4) filled into 4 ml LDPE dropper bottles. The HPMC solution will be (b)(4) olopatadine solution. (b)(4)

B. Brief Description of Microbiology Deficiencies -

No deficiencies were identified based upon the information provided.

C. Contains Potential Precedent Decision(s)- Yes No

III. Product Quality Microbiology Risk Assessment

A. Initial Product Quality Microbiology Risk Assessment

CQA	Risk Factor	Prob. of Occ. (O)	Modifier for O ^(3,4,5)	Severity of Effect (S)	Detect. (D)	Risk Priority Number ⁶ (RPN)	Additional Review Emphasis based on Risk (in addition to normal review process)
Ster.	(b)(4)	10	-1	5	5	225	Simulations and interventions conducted during media fills, Environmental monitoring

(b)(4)

(b) (4)



RPN <50 = **Low Risk**; RPN 50-120 = **Moderate Risk**; RPN >120 = **High Risk**

B. Final Risk Assessment - The applicant has presented adequate information to mitigate risks outlined in the initial product quality microbiology risk assessment.

IV. Administrative

- A. Reviewer's Signature** _____
Stephen E. Langille, Ph.D.
Senior Microbiology Reviewer
- B. Endorsement Block**
Bryan Riley, Ph.D. – Acting NDMS Team Leader
- C. CC Block**
N/A

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/s/

STEPHEN E LANGILLE
01/05/2015

BRYAN S RILEY
01/05/2015
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206276

Applicant: Alcon Research Ltd.

Letter Date: 30 July 2014

Drug Name: Olopatadine
Hydrochloride Ophthalmic Solution
0.77%

NDA Type: Original NDA

Stamp Date: 30 July 2014

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 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 P.2.5 and section P.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		Section P.2.5
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section P.5
7	Has the applicant submitted the results of analytical method verification studies?	X		Section P.5
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	N/A		No such studies were requested from the NDMS
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?	N/A		The drug product is preserved.
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: None.

Stephen E. Langille, Ph.D.
Senior Microbiology Reviewer

12 August 2014

John Metcalfe, Ph.D.
Senior Microbiology Reviewer

12 August 2014

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

/s/

STEPHEN E LANGILLE
08/12/2014

JOHN W METCALFE
08/12/2014
I concur.