CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

203168Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

17 January 2013

NDA: **NDA 203-168/N-000**

Drug Product Name
Proprietary: Prolensa™ 0.07%
Non-proprietary: bromfenac ophthalmic solution

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
6 June 2012	7 June 2012	22 June 2012	28 June 2012
16 November 2012	19 November 2012	N/A	N/A
19 December 2012	19 December 2012	N/A	N/A

Submission History (for amendments only): Not applicable

Applicant/Sponsor
Name: ISTA Pharmaceuticals
Address: 50 Technology
Irvine, CA 92618

Representative: Paul Nowacki
Telephone: 949-789-3109

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: [redacted] (b) (4) information for a sterile topical ophthalmic drug product.

3. MANUFACTURING SITE: Bausch and Lomb Pharmaceuticals, Inc.
8500 Hidden River Parkway
Tampa, FL 33637
Registration Number 1052807

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile solution in an LDPE [redacted] (b) (4) round bottle
- Topical Ophthalmic
- 0.07%

5. METHOD(S) OF STERILIZATION: [redacted] (b) (4)

6. PHARMACOLOGICAL CATEGORY: Ophthalmic analgesic

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: The submission was provided in eCTD format. The following information requests were sent to the applicant on 1 November 2012 and 6 November 2012.

1. Provide a justification for [redacted] (b) (4)

2. Provide a copy of [redacted] (b) (4)

(b) (4)

3. Provide the raw data (plate counts) for the preservative effectiveness test results provided in tables J3-1, J3-2, and J3-3 located in the "Preservative Effectiveness Tests and Methods" document located in section 3.2.P.3.5 of the application.

4. Provide the following information regarding endotoxin testing for Prolensa™

a. The endotoxin limit for the drug product (an endotoxin limit of (b) (4) *is suggested)*
b. The test method to be used for endotoxin testing
c. Calculation of the maximum valid dilution
d. The results of inhibition/enhancement testing
e. Inclusion of the endotoxin limit and test method in the list of drug product specifications.

Responses to the information requests were provided on 16 November 2012 and 19 December 2012 and have been incorporated into the body of this review.

filename: N203168r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 203-168/N-000 is recommended for approval from the standpoint of product quality microbiology.

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 [redacted] (b) (4) at the Bausch and Lomb Tampa, FL facility.

B. Brief Description of Microbiology Deficiencies -

No product quality microbiology deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -

Not applicable.

III. Administrative

A. Reviewer's Signature _____

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

B. Endorsement Block _____

Bryan Riley, Ph.D.
Senior Microbiology Reviewer

C. CC Block

N/A

13 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

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
01/22/2013

BRYAN S RILEY
01/22/2013
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203168 **Applicant:** Ista Pharmaceuticals Inc. **Letter Date:** 6 June 2012

Drug Name: Prolensa™ **NDA Type:** Original NDA **Stamp Date:** 7 June 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		Sections P.3.3 and P.3.5
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.3.5
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.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?			Sections P.2.4 and P.3.5
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	X		AET validation was provided (P.5.3). Sterility test validation not provided.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			No such studies were requested.
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The following information request should be conveyed to the applicant: "Provide the results of bacteriostasis/fungistasis testing conducted to verify the USP sterility test for Prolensa™."

Reviewing Microbiologist 29 June 2012
Stephen E. Langille, Ph.D.
Senior Microbiology Reviewer
NDMS/OPS/CDER

Microbiology Secondary Reviewer 29 June 2012
John Metcalfe, Ph.D.
Senior Microbiology Reviewer
NDMS/OPS/CDER

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
07/02/2012

JOHN W METCALFE
07/02/2012
I concur.