CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022305Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

25 August 2011

NDA: 22-305/N000

Drug Product Name
Proprietary: Pur-Wash Eyewash
Non-proprietary: Purified Water, USP

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
29 Oct 2010	01 Nov 2010	10 Dec 2010	13 Dec 2010
15 Mar 2011 (SD 8)	16 Mar 2011	NA	NA
25 Mar 2011 (SD 9)	25 Mar 2011	NA	NA
9 May 2011 (SD 12)	10 May 2011	NA	NA
18 May 2011 (SD 14)	20 May 2011	NA	NA
31 May 2011 (SD 16)	01 Jun 2011	NA	NA
17 Aug 2011 (SD 18)	18 Aug 2011	NA	NA
24 Aug 2011 (SD 20)	25 Aug 2011	NA	NA

Submission History (for amendments only) – NA

Applicant/Sponsor
Name: Niagara Pharmaceuticals, Inc.
Address: 60 Innovation Drive
Flamborough, Ontario L9H 7P3

U. S. Agent: Robert Schiff
Schiff & Company
1129 Bloomfield Avenue
West Caldwell, NJ 07006
Telephone: (973) 227-1830

Name of Reviewer: Denise A. Miller

Conclusion: Approve

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original Application

2. SUBMISSION PROVIDES FOR: The manufacture of sterile eye wash solution. This is an over-the-counter (OTC) product.

3. MANUFACTURING SITE:
Niagara Pharmaceuticals, Inc.
60 Innovation Dr.
Flamborough, ON Canada L9H 7P3

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
Dosage Form: Sterile liquid
Route of Administration: topical ocular
Strength/Potency: 98.3%

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

6. PHARMACOLOGICAL CATEGORY: eye wash (OTC)

B. SUPPORTING/RELATED DOCUMENTS: NA

C. REMARKS:
1) This application is a resubmission in response to a Refuse to File (RTF) letter for the original application. This is a paper submission in non-CTD format.

2) A quality microbiology filing review had been completed for the original application in which the application was deemed fileable though it lacked (b) (4) effectiveness studies. These studies were requested in the subsequent RTF letter. (b) (4) Validation studies supporting the manufacture of the preservative free formulation were requested by the chemist in the 74 day letter. The sponsor provided these studies in two amendments (supporting documents 8 and 9).

3) An information request (IR) #1 was sent to the sponsor requesting information on the bioburden reduction methods in the manufacturing process. A response was received on 10 May 2011 (supporting document 12). The change in the bulk water specification was submitted on 20 May 2011(supporting document 14).

4) IR #2 requested the validation of the bulk solution hold time for the unpreserved formulation. A response was received on 31 May 2011 (supporting document 16).

5) A response to a Division request to add either a nozzle or eyecup to the 16 and 32 oz bottle sizes was received on 31 May 2011; the smaller sizes already had nozzles included. In the response, the sponsor agreed to add eyecups to these two sizes. The eyecups would be (b) (4) following the (b) (4) standard. Information for the sterilization validation was to be sent by 01 July 2011. It is noted that per 21 CFR 200.50 (c), eyecups or nozzles used with ophthalmic products should be sterile; a review of the validation for the eyecups would be required. The company provided the eyecup validation protocol on 28 July 2011 by e-mail. A T-con was held with the company on 02 August 2011 to discuss the deficiencies of the validation protocol for the eyecups. The company agreed to modify the protocol and submit a completed validation on 22 August 2011. An interim report was received on 18 August 2011 and the final report was received on 24 August 2011 (supporting document 20).

6) IR #3 was sent 23 August 2011 requesting a clarification with the interim report of 18 August 2011. The clarification was received by e-mail on 24 August 2011.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommend to approve from a quality microbiology standpoint.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – This eye wash solution is filled under (b) (4)

B. Brief Description of Microbiology Deficiencies – None

C. Assessment of Risk Due to Microbiology Deficiencies - NA

III. Administrative

A. Reviewer's Signature _____
Denise A. Miller, Microbiologist

B. Endorsement Block _____
James L. McVey, Team Leader

C. CC Block
N/A

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/s/

DENISE A MILLER
08/26/2011

JAMES L MCVEY
08/26/2011
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 22-305 **Applicant:** Niagara Pharmaceuticals **Letter Date:** 14 Feb 2008

Drug Name: Eye Wash **NDA Type:** 505(b)(2) **Stamp Date:** 26 Feb 2008

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		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		The drug product is (b) (4)
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	
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?		X	
7	Has the applicant submitted the results of analytical method verification studies?		X	
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The applicant should provide Preservative Effectiveness Testing results (USP <51>) (b) (4) Container Closure Integrity Validation results for all proposed container closure configurations.

Bryan S. Riley, Ph.D. Date
Senior Review Microbiologist

James L. McVey Date
OPS/NDMS Team Leader

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

/s/

Bryan Riley
4/17/2008 07:21:25 AM
MICROBIOLOGIST

James McVey
4/17/2008 11:29:06 AM
MICROBIOLOGIST
I concur.