CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204078Orig1s000

MICROBIOLOGY/VIROLOGY REVIEW(S)

Product Quality Microbiology Review

25 January 2013

NDA: 204078

Drug Product Name
Proprietary: Not listed
Non-proprietary: Neostigmine Methylsulfate Injection, USP

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
31 JUL 2012	31 JUL 2012	03 AUG 2012	09 AUG 2012
13 SEP 2012	13 SEP 2012	N/A	N/A
15 NOV 2012	15 NOV 2012	N/A	N/A
28 DEC 2012	28 DEC 2012	N/A	N/A
18 JAN 2013	18 JAN 2013	N/A	N/A

Applicant/Sponsor
Name: Éclat Pharmaceuticals
Address: 699 Trade Center Blvd., Suite A, Chesterfield, MO 63005
Representative: Lauren Wind, Senior Consultant, The Weinberg Group
Telephone: 202-730-4101

Name of Reviewer: Erika Pfeiler, Ph.D.

Conclusion: Recommend Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: 505(b)(2)

2. SUBMISSION PROVIDES FOR: Approval of a sterile drug that is already marketed in the United States

3. MANUFACTURING SITE:

(b) (4)

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

- Clear, colorless sterile solution, 10 ml glass vial
- Intravenous injection
- 10 ml drug product, 0.5 mg/ml and 1.0 mg/ml

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

6. PHARMACOLOGICAL CATEGORY: Reversing the effects of neuromuscular blocking agents after surgery

B. SUPPORTING/RELATED DOCUMENTS: Microbiology Review 19 of DMF (b) (4), 9 December 2011

C. REMARKS:

This application was submitted in the eCTD format.

Information requests were sent to the applicant on through the RPM on 28 August 2012, 12 October 2012, 29 November 2012, and 07 January 2013. Responses were received on 13 September 2012, 15 November 2012, 28 December 2012, and 18 January 2013. The text of the requests and responses are incorporated into the relevant sections of the review.

filename: N204078R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommend approval on the basis of product quality microbiology

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 – Product is (b) (4)

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature _____
Erika Pfeiler, Ph.D.

B. Endorsement Block_____
Stephen Langille, Ph.D.
Senior Microbiology Reviewer

C. CC Block
N/A

12 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/

ERIKA A PFEILER
01/25/2013

STEPHEN E LANGILLE
01/25/2013

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 204078 **Applicant:** Éclat Pharmaceuticals **Letter Date:** July 31, 2012

Drug Name: Neostigmine methylsulfate injection, USP **NDA Type:** 505(b)(2) **Stamp Date:** July 31, 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		
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		
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	All records are in English.
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?	X		
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?	X		
10	Is this NDA fileable? If not, then describe why.	X		Based on the applicant's response to the IR sent on August 27, 2012, the application is fileable.

Additional Comments:
Information requests to be included in the 74-day letter:

- A review of the manufacturing process and process controls is necessary. Please provide the following information:
  - A description of container-closure integrity testing methods. (b) (4) Describe the method of (b) (4). Provide justification that this method can detect (b) (4) into the drug product.
  - Provide results from preservative effectiveness testing performed in product development.
  - An overview of the building and production facilities, including
    - A facility floorplan along with an outline of product and personnel flow,
    - Production equipment locations,
    - A listing of air quality in production rooms,
  - A more thorough description of the overall manufacturing process, including,
    - A description of any (b) (4),
    - The duration of the (b) (4)
  - A description of the sterilization process for containers, closures, and production equipment,
  - A summary of environmental and personnel monitoring schedules, sites, and methods, including alert and action levels for all monitoring programs.
- More process validation information is needed for review. Please provide the following information:
  - Describe the (b) (4) studies for the (b) (4). For each (b) (4) study, state:
    - (b) (4) parameters,
    - The number (b) (4) used in the study (b) (4)
    - (b) (4)
    - Acceptance criteria for these studies and most recent results,
    - The (b) (4) schedule (b) (4)

Erika Pfeiler, Ph.D. Date

Bryan Riley, Ph.D.
Microbiology Team Leader Date

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

/s/

ERIKA A PFEILER
09/17/2012

BRYAN S RILEY
09/17/2012
I concur.