

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022572Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

18 November 2011

NDA: 22-572/N000

Drug Product Name

Proprietary: Mitosol Kit for Ophthalmic Use (Rx Only)

Non-proprietary: Mitomycin Kit for Ophthalmic Use (RX Only)

Review Number: 2

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
08 August 2011	08 August 2011	08 August 2011	08 August 2011

Submission History (for amendments only)

Submit Date(s)	Microbiology Review #	Review Date(s)
21 June 2010	1	23 November 2010

Submission History (for amendments only) – NA

Applicant/Sponsor

Name: Mobius Therapeutics LLC
Address: 1141 South 7th Street
St. Louis MO 63104

Representative: Ed Timm, President
Telephone: (314) 571-6205

Name of Reviewer: Denise A. Miller

Conclusion: Approve

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Resubmission of original application
2. **SUBMISSION PROVIDES FOR:** This application is for the (b) (4) lyophilization of Mitomycin. The application also provides for the assembly for the drug product into a kit (b) (4)
3. **MANUFACTURING SITES:**
Drug Product:
Intas Pharmaceuticals Limited (b) (4)
Dist. Ahmedaban
Gujarat, India
Establishment number 3003157498
Kit Assembly:
Synergetics, Inc.
3845 Corporate Centre Drive
O'Fallon MO 63368
Establishment number 021056726
(b) (4)
Midwest Sterilization
1204 Lenco Ave
Jackson MO 63755
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Dosage Form: sterile lyophilized powder for reconstitution
 - Route of Administration: topical
 - Strength/Potency: 0.2 mg/vial
5. **METHOD(S) OF STERILIZATION:** (b) (4)
6. **PHARMACOLOGICAL CATEGORY:** ophthalmic
-

B. SUPPORTING/RELATED DOCUMENTS:

1) ANDA 64-144 is referenced for the manufacture of the mitomycin lyophilized drug product. Letter of Authorization dated 26 July 2010 authorized access to ANDA 64-144 in support of NDA 22-572/N000. OGD last reviewed CMC supplements to ANDA 64-144 on 16 March 2009 and 28 May 2010 and remained acceptable.

2) DMF ^{(b) (4)} is referenced for the manufacture of the prefilled syringe containing sterile water for injection with LOA dated February 2010. DMF was reviewed on 12 Nov 2010 and is adequate in support of NDA 22-572/N000.

C. REMARKS:

1) Application is in e-CTD format.

filename: N022572N000R2.doc

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** – (b) (4)
lyophilization of the drug product. The vial of lyophilized drug product is assembled into a kit for use in ophthalmic surgery. (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, NDMS
- B. Endorsement Block** _____
Bryan S. Riley, Ph.D.
Senior Microbiologist, NDMS
- C. CC Block**
N/A

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/s/

DENISE A MILLER
11/21/2011

BRYAN S RILEY
11/21/2011
I concur.

Product Quality Microbiology Review

22 November 2010

NDA: 22-572/N000

Drug Product Name

Proprietary: Optomycin Kit for Ophthalmic Use (Rx Only)

Non-proprietary: Mitomycin Kit for Ophthalmic Use (RX Only)

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
21 June 2010	22 June 2010	23 June 2010	24 June 2010
29 July 2010 (Sequence 007)	29 July 2010	NA	NA

Submission History (for amendments only) – NA

Applicant/Sponsor

Name: Mobius Therapeutics LLC
Address: 1141 South 7th Street
St. Louis MO 63104

Representative: Ed Timm, President
Telephone: (314) 571-6205

Name of Reviewer: Denise A. Miller

Conclusion: Approvable

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original Application
2. **SUBMISSION PROVIDES FOR:** This application is for the (b) (4) lyophilization of Mitomycin. The application also provides for the assembly for the drug product into a kit (b) (4)
3. **MANUFACTURING SITES:**
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Jackson MO 63755
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Dosage Form: sterile lyophilized powder for reconstitution
 - Route of Administration: topical
 - Strength/Potency: 0.2 mg/vial
5. **METHOD(S) OF STERILIZATION:** (b) (4)
6. **PHARMACOLOGICAL CATEGORY:** ophthalmic
-

B. SUPPORTING/RELATED DOCUMENTS:

1) ANDA 64-144 is referenced for the manufacture of the mitomycin lyophilized drug product. Letter of Authorization dated 26 July 2010 authorized access to ANDA 64-144 in support of NDA 22-572/N000. OGD last reviewed CMC supplements to ANDA 64-144 on 16 March 2009 and 28 May 2010 and remained acceptable.

2) DMF (b) (4) is referenced for the manufacture of the prefilled syringe containing sterile water for injection with LOA dated February 2010. DMF was reviewed on 12 Nov 2010 and is adequate in support of NDA 22-572/N000.

C. REMARKS:

1) Application is in e-CTD format.

2) The proposed name Optomycin was not acceptable. The current proposed name is Mitosol Kit for Ophthalmic Use

3) This product is a kit which consists of (b) (4)

(b) (4)

4) Mitomycin for Injection is currently manufactured by Intas under the FDA approved ANDA 64-144. This ANDA lists several concentrations of lyophilized mitomycin. (b) (4)

(b) (4)

Since the manufacturing process is FDA approved, this review of NDA 22-572/N000 consists of a review of (b) (4) the inner procedure tray, package integrity of the inner procedure tray and the Water for Injection prefilled syringe component of the procedure tray. The manufacturing process for NDA 22-572/N000 is summarized here for context. The manufacturing information was provided in the NDA submission.

filename: N022572N000R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - This submission is approvable pending resolution of microbiological deficiencies.
- 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** – (b) (4)
lyophilization of the drug product. The vial of lyophilized drug product is assembled into a kit for use in ophthalmic surgery. (b) (4)

- B. Brief Description of Microbiology Deficiencies** – (b) (4)

- C. Assessment of Risk Due to Microbiology Deficiencies** – (b) (4)

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
11/23/2010

JAMES L MCVEY
11/23/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 22-572

Applicant: Mobius
Therapeutics LLC

Letter Date: 21 June 2010

Drug Name: Optomyacin Kit for Ophthalmic Use
NDA Type: 505 (b)(2)

Stamp Date: 21 June 2010

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?	√		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	√		
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	√		(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?		√	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	√		Preservative Efficacy is NA Container Closure was submitted
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	√		Sterility per USP <71> Endotoxin NMT (b) (4) EU/mg per USP <85>
7	Has the applicant submitted the results of analytical method verification studies?	√		B&F and E&I studies were submitted
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	NA		
9	Is this NDA fileable? If not, then describe why.	√		

Additional Comments:

The application was in an e-CTD format.

This drug product is supplied as a kit. The kit contains the vial of mitomycin lyophilized powder in a 2 mL vial. The kit includes a pre-filled syringe containing Water for Injection for which a Letter of Authorization was included to DMF (b) (4)

Denise A. Miller, Microbiologist

Date

James L. McVey, Team Leader

Date

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

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/s/

DENISE A MILLER
07/14/2010

JAMES L MCVEY
07/16/2010
I concur.