

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**022184Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

3 JUNE 2009

**NDA:** 22-184

**Drug Product Name**

**Proprietary:** LUMIGAN 0.01%

**Non-proprietary:** bimatoprost ophthalmic solution

**Review Number:** 3

**Dates of Submission(s) Covered by this Review**

Letter	Stamp	Review Request	Assigned to Reviewer
28 April 2009	28 April 2009	N/A	29 April 2009

**Submission History (for amendments only)**

Submission Date(s)	Microbiology Review #	Review Date(s)
2 July 2007	1	1 February 2008
22 August 2007	1	1 February 2008
14 April 2008	2	16 April 2008

**Applicant/Sponsor**

**Name:** Allergan, Inc.

**Address:** 2525 Dupont Drive, PO Box 19534, Irvine, CA 92623-9534

**Representative:** Paul Stone

**Telephone:** 714-246-4177

**Name of Reviewer:** Bryan S. Riley, Ph.D.

**Conclusion:** Recommended for Approval

## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Amendment to an original NDA
  2. **SUBMISSION PROVIDES FOR:** An endotoxin specification for the drug product
  3. **MANUFACTURING SITE:** Allergan, Inc.  
8301 Mars Drive  
Waco, TX 76712
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile, preserved, aqueous solution in a plastic dropper tip bottle (1 mL physician sample in a 5 mL bottle, a 2.5 mL fill in a 5 mL bottle and a 5 mL and 7.5 mL fill in a 10 mL bottle) for ophthalmic administration, 0.01%.
  5. **METHOD(S) OF STERILIZATION:** (b) (4)
  6. **PHARMACOLOGICAL CATEGORY:** Elevated intraocular pressure
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This was a eCTD submission.

**filename:** N022184R3.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** – This submission is recommended for 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** – The drug product is [REDACTED]<sup>(b) (4)</sup>.
- B. Brief Description of Microbiology Deficiencies** – N/A
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Bryan S. Riley, Ph.D.  
Senior Review Microbiologist OPS/NDMS
- B. Endorsement Block** \_\_\_\_\_  
James L. McVey  
Team Leader OPS/NDMS
- C. CC Block**  
N/A

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/s/

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Bryan Riley  
6/8/2009 08:23:53 AM  
MICROBIOLOGIST

James McVey  
6/8/2009 09:46:26 AM  
MICROBIOLOGIST  
I concur.

# Product Quality Microbiology Review

16 APRIL 2008

**NDA:** 22-184 BI amendment

**Drug Product Name**

**Proprietary:** N/A

**Non-proprietary:** bimatoprost ophthalmic solution 0.01%

**Drug Product Priority Classification:** S

**Review Number:** 2

**Dates of Submission(s) Covered by this Review**

Letter	Stamp	Review Request	Assigned to Reviewer
4/14/2008	4/15/2008	N/A	N/A

**Submission History (for amendments only)**

Submission Date(s)	Microbiology Review #	Review Date(s)
7/2/2007	1	2/1/2008
8/22/2007	1	2/1/2008

**Applicant/Sponsor**

**Name:** Allergan

**Address:** 2525 Dupont Drive, PO Box 19534, Irvine, CA 92623-9534

**Representative:** Paul Stone

**Telephone:** 714-246-4177

**Name of Reviewer:** Bryan S. Riley, Ph.D.

**Conclusion:** Recommended for approval (Please see reviewer comment on page 4-5).

## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Amendment in response to a deficiency
  2. **SUBMISSION PROVIDES FOR:** An endotoxin test method for the drug product and a commitment to establish an endotoxin specification
  3. **MANUFACTURING SITE:** Allergan, Inc.  
8301 Mars Drive  
Waco, TX 76712
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile, preserved, aqueous solution in a plastic dropper tip bottle (1 mL physician sample in a 5 mL bottle, a 2.5 mL fill in a 5 mL bottle and a 5 mL and 7.5 mL fill in a 10 mL bottle) for ophthalmic administration, 0.01%.
  5. **METHOD(S) OF STERILIZATION:** (b) (4)
  6. **PHARMACOLOGICAL CATEGORY:** Elevated intraocular pressure
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This submission was made electronically in the eCTD format.

**filename:** N022184R2.doc

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**Executive Summary**

**I. Recommendations**

- A. Recommendation on Approvability** – This submission is recommended for approval on the basis of product quality microbiology (Please see reviewer comment on pages 4-5).
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – It is recommended that a Phase 4 commitment from the applicant regarding establishing an endotoxin specification be accepted as a condition of approval.

**II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – The drug 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** \_\_\_\_\_  
Bryan S. Riley, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
James L. McVey  
Microbiology Team Leader
- C. CC Block**  
N/A

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/s/

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Bryan Riley  
4/17/2008 07:14:43 AM  
MICROBIOLOGIST

James McVey  
4/17/2008 11:28:20 AM  
MICROBIOLOGIST  
I concur.

# Product Quality Microbiology Review

1 FEBRUARY 2008

**NDA:** 22-184 and amendment (BI)

**Drug Product Name**

**Proprietary:** N/A

**Non-proprietary:** bimatoprost ophthalmic solution 0.01%

**Drug Product Priority Classification:** S

**Review Number:** 1

**Dates of Submission(s) Covered by this Review**

Letter	Stamp	Review Request	Assigned to Reviewer
7/2/2007	7/3/2007	N/A	7/30/2007
8/22/2007	8/23/2007	N/A	9/4/2007

**Submission History (for amendments only):** N/A

**Applicant/Sponsor**

**Name:** Allergan

**Address:** 2525 Dupont Drive, PO Box 19534, Irvine, CA 92623-9534

**Representative:** Paul Stone

**Telephone:** 714-246-4177

**Name of Reviewer:** Bryan S. Riley, Ph.D.

**Conclusion:** Approvable pending resolution of product quality microbiology deficiencies. Please see "List of Microbiology Deficiencies" at the end of this review.

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original New Drug Application
  2. **SUBMISSION PROVIDES FOR:** A sterile ophthalmic drug product
  3. **MANUFACTURING SITE:** Allergan, Inc.  
8301 Mars Drive  
Waco, TX 76712
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile, preserved, aqueous solution in a plastic dropper tip bottle (1 mL physician sample in a 5 mL bottle, a 2.5 mL fill in a 5 mL bottle and a 5 mL and 7.5 mL fill in a 10 mL bottle) for ophthalmic administration, 0.01%.
  5. **METHOD(S) OF STERILIZATION:** (b) (4)
  6. **PHARMACOLOGICAL CATEGORY:** Elevated intraocular pressure
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This was an electronic submission in the eCTD format.

**filename:** N022184R1.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** – This submission is approvable, pending resolution of product quality microbiology deficiencies (Please see “List of Microbiology Deficiencies” at the end of this review).
- 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** – The drug product is [REDACTED] (b) (4).
- B. Brief Description of Microbiology Deficiencies** – The drug product does not have an endotoxin specification.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Excessive levels of endotoxin in the drug product could cause an inflammatory reaction in the user’s eye.

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Bryan S. Riley, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
James L. McVey  
Microbiology Team Leader
- C. CC Block**  
N/A

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/s/

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Bryan Riley  
2/4/2008 11:20:09 AM  
MICROBIOLOGIST

James McVey  
2/4/2008 01:00:17 PM  
MICROBIOLOGIST