CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-770

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD 550

18-July-2005

NDA: 21-770/N-000-BI
21-770/N-000-AZ

Drug Product Name
Proprietary: Alphagan
Non-proprietary: Brimonidine Tartrate Ophthalmic Solution

Drug Product Classification: Standard

Review Number: 3

Subject of this Review

	21-770/N-000-BI	21-770/N-000-AZ
Submission Date	March 11, 2005	June 27, 2005
Receipt Date	March 11, 2005	June 27, 2005
Consult Date	March 11, 2005	July 8, 2005
Date Assigned for Review	March 11, 2005	July 8, 2005

Submission History (for amendments only)
Date(s) of Previous Submission(s): May 27, 2004 and September 17, 2004
Date(s) of Previous Micro Review(s): August 24, 2004 and March 2, 2005

Applicant/Sponsor
Name: Allergan Inc.
Address: 2525 DuPont Dr.
P.O. Box 19534
Irvine, CA 92623-9534

Representative:	Lewis Gryziewicz, R.Ph.
Telephone:	714-246-4470
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Amendment to original NDA

2. **SUBMISSION PROVIDES FOR:** Responses to deficiencies from review 2 (March 2, 2005)

3. **MANUFACTURING SITE:** Allergan, Inc.
8301 Mars Dr.
Waco, TX 76712

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

- Ophthalmic solution
- 0.1%
- Topical

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

5. **PHARMACOLOGICAL CATEGORY:** Adrenergic agonist agent

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** On April 13, 2005, a teleconference was held with Allergan to convey product quality microbiology concerns at the Waco facility.

filename: C:/reviews/N021770R3.DOC

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 21-770 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] processed at the Allergan Inc. manufacturing facility in Waco, Texas.

B. Brief Description of Microbiology Deficiencies -
No deficiencies were identified based upon the information provided.

C. Assessment of Risk Due to Microbiology Deficiencies -
Not applicable

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Stephen E. Langille, Ph.D.
Bryan Riley, Ph.D.

C. CC Block
In DFS

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_____ Deliberative Process

Withheld Track Number: Microbiology-1

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/s/

Stephen Langille
7/20/05 11:30:13 AM
MICROBIOLOGIST

Bryan Riley
7/20/05 12:43:59 PM
MICROBIOLOGIST

Product Quality Microbiology Review
Review for HFD 550

2-March-2005

NDA:	21-770/BC
Drug Product Name	
Proprietary:	To be determined
Non-proprietary:	Brimonidine Tartrate Ophthalmic Solution
Drug Product Classification:	Standard
Review Number:	2
Subject of this Review	
Submission Date:	September 17, 2004
Receipt Date:	September 20, 2004
Consult Date:	January 26, 2005
Date Assigned for Review:	January 26, 2005
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	May 27, 2004
Date(s) of Previous Micro Review(s):	August 24, 2004
Applicant/Sponsor	
Name:	Allergan Inc.
Address:	2525 DuPont Dr. P.O. Box 19534 Irvine, CA 92623-9534
Representative:	Lewis Gryziewicz, R.Ph.
Telephone:	714-246-4470
Name of Reviewer:	Stephen E. Langille, Ph.D.
Conclusion:	Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Amendment to original NDA

2. **SUBMISSION PROVIDES FOR:** Responses to deficiencies from review 1 (August 24, 2004)

3. **MANUFACTURING SITE:** Allergan, Inc.
8301 Mars Dr.
Waco, TX 76712

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

- Ophthalmic solution
- 0.1%
- Topical

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

5. **PHARMACOLOGICAL CATEGORY:** Adrenergic agonist agent

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** This review addresses the applicant's responses to deficiencies sent to Allergan by fax on August 24, 2004.

filename: C:/reviews/N021770R2.DOC

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 21-770 is approvable pending the resolution of microbiology deficiencies.

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 processed at the Allergan Inc., manufacturing facility in Waco, Texas.

B. Brief Description of Microbiology Deficiencies -

The Applicant failed to provide adequate information regarding equipment and [redacted] validation and the procedure for conducting media fills.

C. Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiology deficiencies listed above could result in an increased risk of product contamination during [redacted] processing.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Stephen E. Langille, Ph.D.
David Hussong, Ph.D.

C. CC Block

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/s/

Stephen Langille
3/4/05 07:52:01 AM
MICROBIOLOGIST

David Hussong
3/4/05 09:49:52 AM
MICROBIOLOGIST

Product Quality Microbiology Review
Review for HFD 550

12-July-2004

NDA:	21-770
Drug Product Name	
Proprietary:	To be determined
Non-proprietary:	Brimonidine Tartrate Ophthalmic Solution
Drug Product Classification:	
Review Number:	1
Subject of this Review	
Submission Date:	May 27, 2004
Receipt Date:	June 1, 2004
Consult Date:	June 9, 2004
Date Assigned for Review:	June 16, 2004
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	Not applicable
Date(s) of Previous Micro Review(s):	Not applicable
Applicant/Sponsor	
Name:	Allergan Inc.
Address:	2525 DuPont Dr. P.O. Box 19534 Irvine, CA 92623-9534
Representative:	Lewis Gryziewicz, R.Ph.
Telephone:	714-246-4470
Name of Reviewer:	Stephen E. Langille, Ph.D.

Conclusion: Approvable pending revision

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Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** Not applicable

2. **SUPPLEMENT PROVIDES FOR:** Not applicable

3. **MANUFACTURING SITE:** Allergan, Inc.
8301 Mars Dr.
Waco, TX 76712

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

- Ophthalmic solution
- 0.1%
- Topical

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

5. **PHARMACOLOGICAL CATEGORY:** Agonist agent

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:**

filename: C:/reviews/21-770r1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -

NDA 21-770 is approvable pending the resolution of microbiology deficiencies.

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] processed at the Allergan Inc., manufacturing facility in Waco, Texas.

B. Brief Description of Microbiology Deficiencies -

The Applicant failed to provide adequate information regarding the environmental monitoring program within the manufacturing facility, [redacted] and the procedure for conducting media fills.

C. Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiology deficiencies listed above could result in an increased risk of product contamination during [redacted] processing.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

C. CC Block

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/s/

Stephen Langille
8/24/04 09:47:25 AM
MICROBIOLOGIST

Peter Cooney
8/24/04 09:54:52 AM
MICROBIOLOGIST