

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-024

MICROBIOLOGY REVIEW

AUG 22 2000

OFFICE OF GENERIC DRUGS, HFD-640
Microbiology Preliminary Review #1
August 16, 2000

A. 1. ANDA: 65-024

APPLICANT: Altana, Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

2. PRODUCT NAMES: Gentamicin Sulfate Ophthalmic
Ointment USP, 0.3%

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: Sterile Opht Ointment

4. METHOD(S) OF STERILIZATION: _____

5. PHARMACOLOGICAL CATEGORY: Antibiotic

B. 1. DATE OF INITIAL SUBMISSION: August 4, 1998


2. DATE OF AMENDMENT: None

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW:

C. REMARKS: The application is in NA-major status. A warning letter was issued to the drug substance supplier _____ for significant deviations from CGMP. The cited deviations will require Altana to manufacture new drug product using an acceptable source of drug substance.

D. CONCLUSIONS: The submission does not merit sterility assurance review at this time. The sponsor needs to provide new batch records using an acceptable source of drug substance. Micro will review ~~with~~ these data after they are provided. The firm is aware of the deficiencies and plans to submit new data in September 2000.


Joseph Buccine, Project Manager

cc: Original ANDA
Duplicate ANDA
Initialed by A. High

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65-024pr1.doc

NA 1/31/03

Product Quality Microbiology Review

Review for HFD-620

29 January 2003

ANDA: 65-024

Drug Product Name

Proprietary: Garamycin®

Non-proprietary: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3%

Drug Product Classification: N/A

Review Number: 1

Subject of this Review

Submission Date: August 4, 1998 and June 18, 2002 (chemistry amendment)

Receipt Date: August 5, 1998 and June 19, 2002

Consult Date: N/A

Date Assigned for Review: December 18, 2002

Submission History (for amendments only)

Date(s) of Previous Submission(s):

Date(s) of Previous Micro Review(s):

Applicant/Sponsor

Name: Altana Inc.

Address: 60 Baylis Road
Melville, NY 11747

Representative: Virginia Carman

Telephone: 631-454-7677

Name of Reviewer: Marla Stevens-Riley, Ph.D.

Conclusion: Not recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**
Altana Inc.
55 Cantiague Rock Road
Hicksville, NY 11802
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile topical ophthalmic ointment in tin tubes, 0.3%
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** antimicrobial
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** The applicant is submitting an equivalent product to CVM/CDER under ANADA 200-273, A0000. Geoffrey Wong was the microbiology reviewer of the original submission. A similar application for gentamicin sulfate ophthalmic solution 0.3% ANDA 65-121 was previously reviewed by M. Stevens-Riley, and this review contains portions of that review.

Paul DeLeo began a microbiology review of the original submission in September 1999. The review was not completed for unknown reasons. Joe Buccine prepared a "Preliminary Microbiology Review" in August 2000 (v:microrev\65-024PR1.doc) that indicated that the submission did not merit sterility assurance review due to the unacceptable source of the drug substance.

The June 18, 2002 amendment contains information regarding the production of a new exhibit batch using a new API source/manufacturer (_____). This amendment is also reviewed.

filename: v:microrev\65-024.doc

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability – Not recommended for approval on the basis of sterility assurance.**
- 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 - _____**
- B. **Brief Description of Microbiology Deficiencies - Incomplete manufacturing instructions and facility description. Incomplete in-process and process validation information is provided. Incomplete package integrity testing. Incomplete Finished Production Release Specification information.**
- C. **Assessment of Risk Due to Microbiology Deficiencies – The safety risk associated with these deficiencies is moderate.**

III. Administrative

- A. **Reviewer's Signature** Maia Stevens-Riley
- B. **Endorsement Block**
 M. Stevens-Riley, Ph.D. ^{2/14/03}
 N. Sweeney, Ph.D. *N. Sweeney*
- C. **CC Block**
 cc:
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MICROBIOLOGY REVIEW #1

Product Quality Microbiology Review

Review for HFD-620

8 July 2003

ANDA: 65-024

Drug Product Name

Proprietary: Garamycin®

Non-proprietary: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3%

Drug Product Classification: N/A

Review Number: 2

Subject of this Review

Submission Date: May 7, 2003, June 13, 2003 (telephone amendment),
and July 1, 2003 (telephone amendment).

Receipt Date: May 8, 2003, June 16, 2003, and July 2, 2003

Consult Date: N/A

Date Assigned for Review: May 21, 2003

Submission History (for amendments only)

Date(s) of Previous Submission(s): August 4, 1998 and June 18, 2002

Date(s) of Previous Micro Review(s): January 29, 2003

Applicant/Sponsor

Name: Altana Inc.

Address: 60 Baylis Road
Melville, NY 11747

Representative: Audrey Zaweski

Telephone: 631-454-7677

Name of Reviewer: Marla Stevens-Riley, Ph.D.

Conclusion: Not recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.
1. TYPE OF SUPPLEMENT: N/A
 2. SUPPLEMENT PROVIDES FOR: N/A
 3. MANUFACTURING SITE:
Altana Inc.
55 Cantiague Rock Road
Hicksville, NY 11802
 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: sterile topical ophthalmic ointment in tin tubes, 0.3%
 5. METHOD(S) OF STERILIZATION: _____
 6. PHARMACOLOGICAL CATEGORY: antimicrobial
- B. SUPPORTING/RELATED DOCUMENTS: none
- C. REMARKS: The subject amendment provides a response to the Microbiology deficiencies in the letter dated February 20, 2003. In addition, 5 teleconferences with the applicant were held on May 30, 2003, June 11, 2003, June 20, 2003, June 26, 2003, and June 27, 2003. Information submitted in the June 13, 2003 and July 1, 2003 telephone amendments will also be reviewed.

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**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability – Not recommended** for approval on the basis of sterility assurance.
- 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 – _____**
- B. **Brief Description of Microbiology Deficiencies -Lack of adequate responses to deficiency questions, incomplete new information submitted regarding _____**

- C. **Assessment of Risk Due to Microbiology Deficiencies – The safety risk associated with these deficiencies is moderate.**

III. Administrative

- A. **Reviewer's Signature** Maia Stevens-Riley
- B. **Endorsement Block**
M. Stevens-Riley, Ph.D. 10/22/03
N. Sweeney, Ph.D. Neal J. Sweeney
10-28-03
- C. **CC Block**
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MICROBIOLOGY REVIEW # 2

Product Quality Microbiology Review

Review for HFD-620

23 January 2004

ANDA: 65-024

Drug Product Name

Proprietary: Garamycin®

Non-proprietary: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3%

Drug Product Classification: N/A

Review Number: 3

Subject of this Review

Submission Date: December 15, 2003 and January 21, 2004 (telephone amendment)

Receipt Date: December 16, 2003 and January 23, 2004

Consult Date: N/A

Date Assigned for Review: December 30, 2003

Submission History (for amendments only)

Date(s) of Previous Submission(s): August 4, 1998, June 18, 2002, May 7, 2003, June 13, 2003, July 1, 2003

Date(s) of Previous Micro Review(s): January 29, 2003 and July 8, 2003

Applicant/Sponsor

Name: Altana Inc.

Address: 60 Baylis Road
Melville, NY 11747

Representative: Robert J. Anderson, Esq.

Telephone: 631-454-7677

Name of Reviewer: Marla Stevens-Riley, Ph.D.

Conclusion: Not recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**
Altana Inc.
55 Cantiague Rock Road
Hicksville, NY 11802
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile topical ophthalmic ointment in tin tubes, 0.3%
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** antimicrobial
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** The subject amendment provides a response to the Microbiology deficiencies in the letter dated October 29, 2003. A January 13, 2004 teleconference was held to clarify statements regarding a expiry made in response #8, and a January 21, 2004 telephone amendment was sent in with the clarifications.

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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability – Not recommended** for approval on the basis of sterility assurance.
- 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 – _____**
- B. **Brief Description of Microbiology Deficiencies -Lack of adequate responses to deficiency questions, incomplete new information submitted regarding _____**

- C. **Assessment of Risk Due to Microbiology Deficiencies – The safety risk associated with these deficiencies is moderate.**

III. Administrative

- A. **Reviewer's Signature** Macla Stevens-Riley
- B. **Endorsement Block**
 M. Stevens-Riley, Ph.D. 2/27/04
 N. Sweeney, Ph.D. N. J. Sweeney
- C. **CC Block**
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MICROBIOLOGY REVIEW #3

Product Quality Microbiology Review

Review for HFD-630

16 April 2004

ANDA: 65-024

Drug Product Name

Proprietary: Garamycin®

Non-proprietary: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3%

Drug Product Classification: N/A

Review Number: 4

Subject of this Review

Submission Date: April 2, 2004

Receipt Date: April 5, 2004

Consult Date: N/A

Date Assigned for Review: April 7, 2004

Submission History (for amendments only)

Date(s) of Previous Submission(s): August 4, 1998, June 18, 2002, May 7, 2003, June 13, 2003, July 1, 2003, December 15, 2003, January 21, 2004

Date(s) of Previous Micro Review(s): January 29, 2003, July 8, 2003, January 23, 2004

Applicant/Sponsor

Name: Altana Inc.

Address: 60 Baylis Road
Melville, NY 11747

Representative: Robert J. Anderson, Esq.

Telephone: 631-454-7677

Name of Reviewer: Marla Stevens-Riley, Ph.D.

Conclusion: Not recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**
Altana Inc.
55 Cantiague Rock Road
Hicksville, NY 11802
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile topical ophthalmic ointment in tin tubes, 0.3%
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** antimicrobial
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** The subject amendment provides a response to the Microbiology deficiencies in the letter dated March 1, 2004. A March 24, 2004 teleconference was held to clarify information that would be needed for this amendment.

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**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability – Not recommended for approval on the basis of sterility assurance.**
- 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** _____
- B. **Brief Description of Microbiology Deficiencies -**
- C. **Assessment of Risk Due to Microbiology Deficiencies – The safety risk associated with these deficiencies is moderate.**

III. Administrative

- A. **Reviewer's Signature** Macla Stevens-Riley 5/25/04
- B. **Endorsement Block**
 M. Stevens-Riley, Ph.D.
 N. Sweeney, Ph.D. *N. J. Sweeney*
5-25-04
- C. **CC Block**
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MICROBIOLOGY REVIEW #4

Product Quality Microbiology Review

Review for HFD-630

29 June 2004

ANDA: 65-024

Drug Product Name

Proprietary: Garamycin®

Non-proprietary: Gentamicin Sulfate Ophthalmic Ointment USP, 0.3%

Drug Product Classification: N/A

Review Number: 5

Subject of this Review

Submission Date: June 28, 2004

Receipt Date: June 29, 2004

Consult Date: N/A

Date Assigned for Review: June 28, 2004

Submission History (for amendments only)

Date(s) of Previous Submission(s): August 4, 1998, June 18, 2002, May 7, 2003, June 13, 2003, July 1, 2003, December 15, 2003, January 21, 2004, April 2, 2004

Date(s) of Previous Micro Review(s): January 29, 2003, July 8, 2003, January 23, 2004, April 16, 2004

Applicant/Sponsor

Name: Altana Inc.

Address: 60 Baylis Road
Melville, NY 11747

Representative: Robert J. Anderson, Esq.

Telephone: 631-454-7677

Name of Reviewer: Marla Stevens-Riley, Ph.D.

Conclusion: Recommended for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**
Altana Inc.
55 Cantiague Rock Road
Hicksville, NY 11802
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile topical ophthalmic ointment in tin tubes, 0.3%
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** antimicrobial
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** The subject amendment provides a response to the Microbiology deficiencies in the letter dated May 28, 2004. A June 25, 2004 teleconference was held to clarify information that would be needed for this amendment.

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**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary

I. Recommendations

- A. Recommendation on Approvability – Recommended for approval on the basis of sterility assurance.**
- 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 _____**
- B. Brief Description of Microbiology Deficiencies -none**
- C. Assessment of Risk Due to Microbiology Deficiencies – The safety risk associated with this product is low.**

III. Administrative

A. Reviewer's Signature Mala Stevens-Riley

B. Endorsement Block
 M. Stevens-Riley, Ph.D.
 N. Sweeney, Ph.D.

6/29/04
N. J. Sweeney
6-29-04

C. CC Block
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MICROBIOLOGY REVIEW #5