CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-186

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

23-JUNE-2008

NDA: 22-186/N-000/AZ

Drug Product Name
Proprietary: AK-FLUOR
Non-proprietary: Fluorescein Injection
Drug Product Priority Classification: Standard

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
3/28/08	3/28/08	4/2/08	4/2/08

Submission History (for amendments only):

Submission Date(s)	Microbiology Review #	Review Date(s)
4/5/07	1	12/21/07

Applicant/Sponsor
Name: Akorn, Inc.
Address: 2500 Middlebrook Drive
Buffalo Grove, IL 60089-4694

Representative: Sam Boddapati, Ph.D.
Telephone: 847-353-4909

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

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

2. **SUBMISSION PROVIDES FOR:** New sterile drug product

3. **MANUFACTURING SITE:** Akorn Incorporated
1222 West Grand Ave.
Decatur, IL

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

- Sterile solution
- Injection
- 10% and 25%
- Glass vials with rubber stoppers

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

6. **PHARMACOLOGICAL CATEGORY:** Ophthalmic diagnostic

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

C. **REMARKS:** NDA 22-186 is arranged in CTD format. Blue archival jackets and scanned PDF files (provided by the project manager) were provided for review. An IQA was entered into DFS by the PAL on May 9, 2007.

filename: N022186R2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 22-186 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 - b(4)
The drug product will be [redacted], sterilized using [redacted].

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 _____
Stephen E. Langille, Ph.D.

B. Endorsement Block
David Hussong, Ph.D.

C. CC Block
N/A

5 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Microbiology- 1

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/s/

Stephen Langille
6/24/2008 11:00:08 AM
MICROBIOLOGIST
Second review of the Akorn NDA for AK-FLUOR.

David Hussong
6/24/2008 01:55:11 PM
MICROBIOLOGIST
I concur with the reviewer's recommendation for approval of this application.

Product Quality Microbiology Review

21-December-2007

NDA: 22-186

Drug Product Name
Proprietary: AK-FLUOR
Non-proprietary: Fluorescein Injection
Drug Product Priority Classification: Standard

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
4/5/07	4/6/07	4/26/07	4/26/07

Submission History (for amendments only): Not applicable

Applicant/Sponsor
Name: Akorn, Inc.
Address: 2500 Middlebrook Drive
Buffalo Grove, IL 60089-4694

Representative: Sam Boddapati, Ph.D.
Telephone: 847-353-4909

Name of Reviewer: Stephen E. Langille, Ph.D.

Conclusion: Approvable pending revision

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Original NDA

2. **SUBMISSION PROVIDES FOR:** New sterile drug product

3. **MANUFACTURING SITE:** Akorn Incorporated
1222 West Grand Ave.
Decatur, IL

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

- Sterile solution
- Injection
- 10% and 25%
- Glass vials with rubber stoppers

5. **METHOD(S) OF STERILIZATION:** [redacted] b(4)

6. **PHARMACOLOGICAL CATEGORY:** Ophthalmic diagnostic

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

C. **REMARKS:** NDA 22-186 is arranged in CTD format. Blue archival jackets and scanned PDF files (provided by the project manager) were provided for review. An IQA was entered into DFS by the PAL on May 9, 2007.

filename: N022186R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability -
NDA 22-186 is approvable pending the resolution of product quality 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 - b(4)
The drug product will be [redacted] sterilized using [redacted]

B. Brief Description of Microbiology Deficiencies -
The applicant failed to provide adequate information regarding:

- Sterilization validation cycles
- Endotoxin testing
- Sterility testing
- Stability data
- [redacted] of the container closure system

b(4)

C. Assessment of Risk Due to Microbiology Deficiencies -
Failure to address the microbiology deficiencies could result in microbial and/or endotoxin contamination of the drug product.

III. Administrative

A. Reviewer's Signature _____
Stephen E. Langille, Ph.D.

B. Endorsement Block
David Hussong, Ph.D.

C. CC Block
N/A

11 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Microbiology- 2

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/s/

Stephen Langille
1/4/2008 09:52:25 AM
MICROBIOLOGIST
Revised review for Akorn's AK-FLUOR

David Hussong
1/6/2008 11:07:04 AM
MICROBIOLOGIST
I concur with the reviewer's conclusions and comments (deficiencies) to the applicant.