

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-664

MICROBIOLOGY REVIEW

Product Quality Microbiology Review

Review for HFD 550

16-November-2004

NDA: 21-664-BI

Drug Product Name
Proprietary: XIBROM™
Non-proprietary: Bromfenac sodium (ophthalmic solution) 0.1%

Drug Product Classification: Standard

Review Number: 2

Subject of this Review
Submission Date: November 3, 2004
Receipt Date: November 5, 2004
Consult Date: November 5, 2004
Date Assigned for Review: November 16, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): May 24, 2004
Date(s) of Previous Micro Review(s): October 18, 2004

Applicant/Sponsor
Name: Ista Pharmaceuticals
Address: 15279 Alton Parkway
Suite 100
Irvine, CA 92618

Representative: Marvin J. Garrett
Telephone: (949) 788-5303

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

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUPPLEMENT:** Original NDA Submission
2. **SUPPLEMENT PROVIDES FOR:** Not applicable
3. **MANUFACTURING SITE:** Bausch and Lomb
Tampa, FL
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Solution
 - Topical
 - 0.1%
5. **METHOD(S) OF STERILIZATION:** _____
6. **PHARMACOLOGICAL CATEGORY:** ophthalmic anti-inflammatory
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** A teleconference was held with representatives of ISTA Pharmaceuticals on November 3, 2004 to discuss the microbiology deficiencies outlined in the first review of NDA 21-664.

filename: C:/reviews/N021664R2.DOC

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability -**
NDA 21-664 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 -**
Xibrom is _____ at the Bausch and Lomb manufacturing facility in Tampa, FL.
- 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.
Supervisor/Team Leader
- C. CC Block**
In DFS

2 Page(s) Withheld

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Draft Labeling

Deliberative Process

Withheld Track Number: Microbiology-1

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this page is the manifestation of the electronic signature.**

/s/

Stephen Langille
11/19/04 01:08:56 PM
MICROBIOLOGIST

David Hussong
11/19/04 02:14:52 PM
MICROBIOLOGIST
Micro Review 2 - Approve

Product Quality Microbiology Review

Review for HFD 550

15-October-2004

NDA: 21-664

Drug Product Name
Proprietary: XIBROM™
Non-proprietary: Bromfenac sodium ophthalmic solution) 0.1%

Drug Product Classification: Standard

Review Number: 1

Subject of this Review
Submission Date: May 24, 2004
Receipt Date: May 26, 2004
Consult Date: June 3, 2004
Date Assigned for Review: July 9, 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: Ista Pharmaceuticals
Address: 15279 Alton Parkway
Suite 100
Irvine, CA 92618

Representative: Marvin J. Garrett
Telephone: (949) 788-5303

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

Conclusion: Approval pending revision

Product Quality Microbiology Data Sheet

- A. 1. TYPE OF SUPPLEMENT: Original NDA Submission
2. SUPPLEMENT PROVIDES FOR: Not applicable
3. MANUFACTURING SITE: Bausch and Lomb
Tampa, FL
4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:
- Solution
 - Topical
 - 0.1%
5. METHOD(S) OF STERILIZATION:
6. PHARMACOLOGICAL CATEGORY: ophthalmic anti-inflammatory
- B. SUPPORTING/RELATED DOCUMENTS: None
- C. REMARKS:

filename: C:/reviews/N021664R1.DOC

Executive Summary

I. Recommendations

- A. Recommendation on Approvability -**
NDA 21-664 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 -**
Xibrom is [REDACTED] at the Bausch and Lomb manufacturing facility in Tampa, FL.
- B. Brief Description of Microbiology Deficiencies -**
The Applicant failed to provide adequate information regarding media fills conducted at the Bausch and Lomb manufacturing facility.
- C. Assessment of Risk Due to Microbiology Deficiencies -**
Media fills conducted with poor controls and standards may allow firms to overestimate their level of sterility assurance during [REDACTED] processing. This may result in microbial contamination of a drug product intended to be sterile.

III. Administrative

- A. Reviewer's Signature** _____
- B. Endorsement Block**
Stephen E. Langille, Ph.D.
Supervisor/Team Leader
- C. CC Block**
In DFS

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/s/

Stephen Langille
10/18/04 03:16:06 PM
MICROBIOLOGIST

David Hussong
10/18/04 05:03:14 PM
MICROBIOLOGIST

25-FEB-2005

FDA CDER EES

Page 1 of 2

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

| | | | |
|-------------|-----------------|----------|-------------------------|
| Application | : NDA 21664/000 | Sponsor: | ISTA PHARMS |
| Org Code | : 550 | | 15279 ALTON PKY STE 100 |
| Priority | : | | IRVINE, CA 92618 |

Stamp Date : 26-MAY-2004
SODIUM

Brand Name :XIBROM (BROMFENAC

PDUFA Date : 26-MAR-2005

HYDRATE OPHTH)

Action Goal :

Estab. Name:

District Goal: 25-JAN-2005
HYDRATE

Generic Name:BROMFENAC SODIUM

OPHTHALMIC SOL

Dosage Form: (SOLUTION)

Strength : 0.1035%

FDA Contacts: R. RODRIGUEZ
2090

Project Manager (HFD-550)301-827-

Y. LU
1-827-2182

Review Chemist (HFD-550)30

L. NG
2511

Team Leader (HFD-830)301-827-

Overall Recommendation: ACCEPTABLE on 30-NOV-2004by J. D AMBROGIO

NDA 21-664

Xibrom™ Ophthalmic Solution, 0.1035%

ISTA

Profile : CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 02-AUG-04
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

Establishment : ~~CSN~~

DMF No: _____

AADA:

Responsibilities:

Profile : CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 30-NOV-04
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION
