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APPLICATION NUMBER:

21-640

MICROBIOLOGY REVIEW

Product Quality Microbiology Review Review for HFD-550

26 AUGUST 2003

NDA: 21-640

Drug Product Name

Proprietary: Vitrase

Non-proprietary: Hyaluronidase, Ovine

Drug Product Priority Classification: P

Review Number: 1

Subject of this Review

Submission Date: 4 August 2003

Receipt Date: 5 August 2003

Consult Date: 11 August 2003

Date Assigned for Review: 20 August 2003

Submission History (for amendments only)

Date(s) of Previous Submission(s): N/A

Date(s) of Previous Micro Review(s): N/A

Applicant/Sponsor

Name: ISTA Pharmaceuticals, Inc.

Address: 15279 Alton parkway, Suite 100; Irvine, CA

Representative: Marvin Garrett

Telephone: 949-788-5303

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

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:** Cardinal Health Pharmaceutical
Albuquerque, NM 87109
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Lyophilized Powder in a 5 mL glass vial for Subcutaneous Injection, — USP units/vial
 5. **METHOD(S) OF STERILIZATION:** —
 6. **PHARMACOLOGICAL CATEGORY:** Adjuvant, to increase absorption and dispersion of other drugs
- B. **SUPPORTING/RELATED DOCUMENTS:** NDA 21-414 (Vitrase)
- C. **REMARKS:** This application refers to NDA 21-414 (Vitrase) for the CMC information. This application is for a new indication for the same drug product. NDA 21-414 was recommended for approval from the standpoint of product quality microbiology on 4 March 2003. The recommended dosage has not changed.

filename: 21640.doc

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 _____**
- B. Brief Description of Microbiology Deficiencies – N/A**
- C. Assessment of Risk Due to Microbiology Deficiencies - The drug product is _____ using a properly validated manufacturing process. Therefore, the drug product presents a minimal risk from the standpoint of product quality microbiology.**

III. Administrative

- A. Reviewer's Signature _____**
- B. Endorsement Block**
 - Bryan S. Riley, Ph.D. (Microbiology Reviewer)
 - Peter H. Cooney, Ph.D. (Microbiology Supervisor)
- C. CC Block**
 - N/A

Product Quality Microbiology Assessment

See Product Quality Microbiology Review of NDA 21-414, (Vitrase, ovine hyaluronidase, recommended for approval).

ADEQUATE

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/s/

Bryan Riley
9/24/03 10:58:20 AM
MICROBIOLOGIST

Peter Cooney
9/24/03 11:00:44 AM
MICROBIOLOGIST

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Product Quality Microbiology Review

Review for HFD-550

4 MARCH 2003

NDA: 21-414

Drug Product Name

Proprietary: Vitrase

Non-proprietary: Ovine Hyaluronidase

Drug Product Potential: Priority, Therapeutic Gain

Review Number: 1

Subject of this Review

Submission Date: 7 October 2002

Receipt Date: 9 October 2002

Consult Date: 11 October 2002

Date Assigned for Review: 21 October 2002

Submission History (for amendments only)

Date(s) of Previous Submission(s): N/A

Date(s) of Previous Micro Review(s): N/A

Applicant/Sponsor

Name: ISTA Pharmaceuticals, Inc.

Address: 15279 Alton Parkway, Suite 100; Irvine, CA 92618

Representative: Marvin Garrett, VP for Reg. Affairs, Quality and Compliance

Telephone: 949-788-5303

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

Conclusion: Recommend for Approval

Product Quality Microbiology Data Sheet

- A. 1. TYPE OF SUPPLEMENT: N/A
2. SUPPLEMENT PROVIDES FOR: N/A
3. MANUFACTURING SITE: Cardinal Health Pharmaceutical
Albuquerque, NM 87109
4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND
STRENGTH/POTENCY: Lyophilized Powder in a 5 mL glass vial for
Intravitreal Injection, — USP units/vial
5. METHOD(S) OF STERILIZATION: —
6. PHARMACOLOGICAL CATEGORY: Vitreous Hemorrhage
- B. SUPPORTING/RELATED DOCUMENTS: N/A
- C. REMARKS: N/A

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Executive Summary**I. Recommendations****A. Recommendation on Approvability – _____**
_____**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 _____**
_____**B. Brief Description of Microbiology Deficiencies – N/A****C. Assessment of Risk Due to Microbiology Deficiencies – The drug product is _____ using a properly validated manufacturing process. Therefore, the drug product presents a minimal risk from the standpoint of product quality microbiology.****III. Administrative****A. Reviewer's Signature _____****B. Endorsement Block**

Bryan S. Riley, Ph.D. (Microbiology Reviewer)

Peter H. Cooney, Ph.D. (Microbiology Supervisor)

C. CC Block

. N/A

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/s/

Bryan Riley
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MICROBIOLOGIST

Peter Cooney
3/6/03 02:29:45 PM
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