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RESEARCH**

APPLICATION NUMBER:

21-406

MICROBIOLOGY REVIEW

Product Quality Microbiology Review

Review for HFD-510

08 November 2004

NDA: 21-406/—

Drug Product Name

Proprietary: Fortical Nasal Spray

Non-proprietary: calcitonin-salmon

Drug Product Classification: 3S, nasal spray

Review Number: 2

Subject of this Review

Submission Date: 16 DEC 2003

Receipt Date: 18 DEC 2003

Consult Date: 08 OCT 2004

Date Assigned for Review: 10 OCT 2004

Submission History (for amendments only)

Date(s) of Previous Submission(s): 05 MAR 2003

Date(s) of Previous Micro Review(s): 18 NOV 2003

Applicant/Sponsor

Name: Unigene Laboratories, Inc.

Address: 110 Little Falls Road
Fairfield, NJ 07004

Representative: Heike Maaser, Ph.D.

Telephone: (973)401-9337

Name of Reviewer: David Hussong

Conclusion: APPROVE

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Amendment to original NDA
 2. **SUBMISSION PROVIDES FOR:** Answers to deficiency questions.
 3. **MANUFACTURING SITE:** Unigene Laboratories, 83 Fulton Street, Boonton, NJ
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** An aqueous nasal spray solution in a amber glass bottle with a cap. The solution is dispensed as 3.6 mL aliquots into glass, screw capped vials. The solution is delivered by a metered spray pump that is added when the product is first used. With each actuation of the pump 0.09 mL is delivered.
 5. **METHOD(S) OF STERILIZATION:** N/A
 6. **PHARMACOLOGICAL CATEGORY:** For treatment of post-menopausal osteoporosis (3S)
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This nasal spray formulation is non-sterile and for use during a 30-day treatment. The product is packaged with a pump mechanism that is installed by the patient upon the product's first use.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability - APPROVE
- 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 – N/A

III. Administrative

- A. Reviewer's Signature _____
- B. Endorsement Block
David Hussong/Reviewer
James McVey/Microbiology Team Leader
- C. CC Block
cc:
Original NDA 21-406/
DFS

2 Page(s) Withheld

✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Microbiology-

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

David Hussong
11/8/04 01:40:43 PM
MICROBIOLOGIST
Micro review - APPROVE

James McVey
11/9/04 07:24:43 AM
MICROBIOLOGIST

Product Quality Microbiology Review

Review for HFD-510

18 NOV 2003

NDA: 21-406

Drug Product Name

Proprietary: Fortical Nasal Spray

Non-proprietary: calcitonin-salmon

Drug Product Classification: 3S, nasal spray

Review Number: 1

Subject of this Review

Submission Date: 5 MAR 2003

Receipt Date: 05 MAR 2003

Consult Date: 21 APR 2003

Date Assigned for Review: 07 MAY 2003

Submission History (for amendments only)

Date(s) of Previous Submission(s): (none)

Date(s) of Previous Micro Review(s): (none)

Applicant/Sponsor

Name: Unigene Laboratories, Inc.

Address: 110 Little Falls Road
Fairfield, NJ 07004

Representative: (cover letter not provided)

Telephone: (cover letter not provided)

Name of Reviewer: David Hussong

Conclusion: APPROVABLE

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUPPLEMENT:** N/A (original NDA submission)
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:** Unigene Laboratories, 83 Fulton Street, Boonton, NJ (NDA, CMC section 4.2.2)
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** An aqueous nasal spray solution in a — amber glass bottle with a — cap. The solution is dispensed as 3.6 mL aliquots into glass, screw capped vials. The solution is delivered by a metered spray pump that is added when the product is first used. With each actuation of the pump 0.09 mL is delivered.
 5. **METHOD(S) OF STERILIZATION:** N/A
 6. **PHARMACOLOGICAL CATEGORY:** For treatment of post-menopausal osteoporosis (3S)
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This nasal spray formulation is non-sterile and for use during a 30-day treatment. The product is packaged with a pump mechanism that is installed by the patient upon the product's first use.

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Executive Summary**I. Recommendations**

- A. Recommendation on Approvability - APPROVABLE
- 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 – The in-process tests for the Purified Water, USP**

_____ use terminology that is inconsistent with USP, acceptance criteria for _____ that are inconsistent with FDA policy, and reference a test for _____ in a section of USP where no such test exists.

C. Assessment of Risk Due to Microbiology Deficiencies – These deficiencies pose a *moderate* risk to patient safety. Failure to detect this microorganism in the manufacturing process does not confer an absolute risk because the formulation contains a _____ . However, this species is problematic because it has a history of surviving exposure to chemical antimicrobial agents.**III. Administrative****A. Reviewer's Signature _____****B. Endorsement Block**

David Hussong/Microbiologist
Peter Cooney/Microbiology Supervisor

C. CC Block

cc:
Original NDA 21-406
HFD- 510/Division File/NDA 21-406

6 Page(s) Withheld

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 Draft Labeling

 Deliberative Process

Withheld Track Number: Microbiology