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RESEARCH**

APPLICATION NUMBER:
22-038S000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

Review for Division of Reproductive and Urologic Products

28 September 2006

NDA: 22-038

Drug Product Name

Proprietary: Divigel®

Non-proprietary: estradiol gel 0.1% (USL-221)

Drug Product Priority Classification: S1

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
May 1, 2006	NA	August 22, 2006	August 31, 2006

Submission History (for amendments only) - NA

Applicant/Sponsor

Name: Upsher-Smith Pharmaceuticals

Address: Maple Grove, MN 55369

Representative: Carol, Subialka

Telephone: 763-315-2206

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Pre-NDA Review issue
 2. **SUBMISSION PROVIDES FOR:** Deletion of microbial limits
 3. **MANUFACTURING SITE:** Maple Grove, MN
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Estradiol Gel 0.1%
 5. **METHOD(S) OF STERILIZATION:** (b) (4)
 6. **PHARMACOLOGICAL CATEGORY:** Estrogen therapy
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** A consult was submitted to find out if the sponsor's request to delete Microbial Limits Testing in the Divigel NDA 22-038 submission. The Sponsor was informed at the Pre-NDA meeting (IND 51, 246 – June 22, 2005) that this request would be a microbiology review issue. A single volume of the document to support their request was sent on May 1, 2006. This review specifically addresses that issue.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – The proposal to delete Microbial Limit Testing for the Divigel® product is acceptable based on the antimicrobial efficacy testing of Divigel® USL-221 formulation containing (b) (4) alcohol.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – There are no changes in the previously approved manufacturing processes. A change is requested in the Microbial Limits Testing.
- B. Brief Description of Microbiology Deficiencies - None**
- C. Assessment of Risk Due to Microbiology Deficiencies - NA**

III. Administrative

- A. Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D.
- B. Endorsement Block** _____
James McVey
- C. CC Block**
N/A

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

/s/

Vinayak Pawar
10/3/2006 03:30:52 PM
MICROBIOLOGIST

Deletion of Microbial Limits Test recommended for approval from
microbiology standpoint.

James McVey
10/4/2006 01:28:25 PM
MICROBIOLOGIST