DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-038

Upsher-Smith Laboratories, Inc.
Attention: Tanya Carone, RAC
Associate Director, New Product Regulatory Affairs
6701 Evenstad Drive
Maple Grove, MN 55369

Dear Ms. Carone:

Please refer to your May 1, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Divigel® (estradiol gel) 0.1%.

We also acknowledge receipt of your submissions dated: June 12, August 17, 30, September 11, 15, October 24, November 17 (2), December 4, 2006, January 8, 10, 2007, February 5, 9, 13, 15, 16, March 14, 30, April 6, 10, May 24, June 1, and June 4 (2), 2007.

This new drug application provides for the use of Divigel® (estradiol gel) 0.1% for the treatment of moderate to severe vasomotor symptoms associated with menopause.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert) and the May 24, 2007 submitted labeling (immediate container and carton labels) which was modified in your June 4, 2007 submission. The carton label and the single-dose foil packet (the immediate container) will specify the tradename as Divigel® and established name as (estradiol gel) 0.1%. The change to the single-dose foil packet will be made after initial launch. Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 22-038**." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division the Division of Reproductive and Urologic Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call George Lyght, R.Ph., Regulatory Health Project Manager, at (301) 796-0948.

Sincerely,

{See appended electronic signature page}

Scott Monroe M.D.
Acting Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Scott Monroe

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