NDA 20-847

Fournier Research, Inc.
Attention: Mr. R. Lance Boyett
Director, Clinical Development
9 Law Drive
Fairfield, NJ 077004

Dear Mr. Boyett:

Please refer to your new drug application (NDA) dated August 7, 1997, received August 12, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Esclim® (estradiol transdermal system) 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/24 hrs.

We acknowledge receipt of your submissions dated August 12, October 6, 23, 24(3) and 27, November 10, 14 and 26, December 1 and 5, 1997; February 3 and 12, March 5, April 10 and 28, May 12, June 10, July 1, 15, 28(2), 30(2) and July 31(2), and August 3, 1998. The user fee goal date for this application is August 12, 1998.

This new drug application provides for the use of Esclim (estradiol transdermal system) 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/24 hours for the treatment of:

1. moderate to severe vasomotor symptoms associated with the menopause;

2. vulval and vaginal atrophy; and

3. hypoestrogenism due to hypogonadism, castration, or primary ovarian failure.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert dated August 3, 1998 and patient package insert dated July 30, 1998 and immediate container and carton labels dated July 31, 1998). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-847." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitment specified in your submission dated July 15, 1998. This commitment, along with any completion dates agreed upon, is listed below.

> To provide results from the testing of , that is being done for information purposes, in conjunction with the . The results will be included in the NDA annual report for the product.

Please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

> Division of Drug Marketing, Advertising, and Communications, HFD-40
> Food and Drug Administration
> 5600 Fishers Lane
> Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Diane Moore, Project Manager, at (301) 827-4260.

Sincerely,

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research