DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-258

Berlex Laboratories, Inc.
Attn: Geoffrey Millington
Manager, Drug Regulatory Affairs
340 Changebridge Road
P.O. Box 1000
Montville, NJ 07450-1000

Dear Mr. Millington:

Please refer to your new drug application (NDA) dated June 29, 2000, received June 29, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Climara Pro™ (estradiol/levonorgestrel) 0.045 mg/0.015 mg/day transdermal system.

We acknowledge receipt of your submissions dated August 20 and 30, 2001, October 22, 2001, March 4 and 26, November 13 and December 13, 2002, January 27, February 20, March 18 and 24, July 18, September 19, October 6 and 24, November 6, 12, 19 and 20, 2003. The September 19, 2003 submission constituted a resubmission to this application.

This new drug application provides for the use of Climara Pro™ (estradiol/levonorgestrel) 0.045 mg/0.015 mg/day transdermal system for the treatment of moderate to severe vasomotor symptoms associated with menopause.

We 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 immediate container and carton labels submitted October 24, 2003. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and unapproved new drug.

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 21-258**." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission dated November 19, 2003. This commitment is listed below.

1. To conduct a study to determine the lowest effective dose of Climara Pro

Protocol Submission:	Within 6 months of the date of this letter
Study Start:	Within 6 months of reaching protocol agreement with DRUDP
Final Report Submission:	Within 6 months of the study completion

Submit the clinical protocol to your IND for this product. Submit the final study report to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of the commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and number of patients entered into the study. All submissions, including supplements, relating to this postmarketing study commitment must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

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 and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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 Kassandra Sherrod, R.Ph., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Director
Division of Reproductive and Urologic Drug 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/

Daniel A. Shames
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