ANDA 75-182 February 24, 2000

Mylan Technologies, Inc.
Attention: Elizabeth Ash
110 Lake Street
St. Albans, VT 05478

Dear Madam:

This is in reference to your abbreviated new drug application dated August 6, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Estradiol Transdermal System, 0.1 mg/day, (Once-a-Week Formulation).

Reference is also made to your amendments dated February 24,
March 12, May 28, and October 28, 1998; and April 14, July 26, September 3, and October 27, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Estradiol Transdermal System, 0.1 mg/day, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Climara® Transdermal System, 0.1 mg/day of Berlex Laboratories, Inc.).

The dissolution testing should be incorporated into your manufacturing controls and stability program. The "interim" dissolution test and tolerances are:

> The dissolution testing should be conducted in 500 mL of 0.3% sodium lauryl sulfate in 0.005 N NaH_2PO_4, pH 5.5, at 32^{o} C using USP 23 apparatus 5 (paddle over disk) at 100 rpm. These percentages of the labeled amount of estradiol in the dosage form should be released within the following time periods:

[ ]
[ ]
[ ]
[ ]

The "interim" dissolution test and tolerances should be finalized by submitting dissolution data for the first three production size batches in a supplemental application. The supplemental application should be submitted under Section 505(j) of the Act as a “Changes Being Effected (CBE-0)” supplement when there are no revisions to the interim specifications or when the final specifications are tighter than the interim specifications. In all other instances the supplement should be submitted under Section 505(j) of the Act as a prior approval supplement.

We note that the listed drug (RLD) referenced in your application, Climara Transdermal System of Berlex Laboratories, is subject to a period of patent protection which expires on June 29, 2010, (U.S. Patent No. 5,223,261). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, sale, offer for sale, or importation of this drug product will not infringe on this patent, or that the patent is invalid or unenforceable. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately, unless an infringement action is brought against you before the expiration of forty-five days from the receipt date of the notice provided under paragraph (2)(B)(i). You have notified FDA that Mylan Technologies, Inc. (Mylan) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Mylan within the statutory forty-five day period.

Under Section 506(A) of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98.

The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research