DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-323/S-017, S-025, S-030

Novartis Pharmaceuticals Corporation
Attn.: Kevin Carl, Pharm.D.
Assistant Director
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Carl:

Please refer to your supplemental new drug applications dated March 19, 1998 received March 24, 1998 (S-017), October 12, 2000 received October 17, 2000 (S-025) and November 22, 2002, received November 25, 2002 (S-030), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vivelle® (estradiol transdermal system).

We acknowledge receipt of your submissions dated March 18, 2003 and January 16, 2004.

These supplemental new drug applications provide for changes in the labeling language regarding VTE in the package insert (S-017), incorporation of findings from the Heart and Estrogen/Progestin Replacement Study (HERS) Trial into the package insert at the agency's request (S-025) and revisions in the label for an increased risk of VTE, breast cancer and cardiovascular events in postmenopausal users of hormone replacement therapy as compared to non-users (S-030). The above supplements were further revised to add information from the Women's Health Initiative trial (WHI) to the package insert and patient package insert.

We have completed our review of these applications, as amended. These applications are approved, effective on date of this letter, for use of Vivelle as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the package insert and patient package insert submitted on March 18, 2003 with the revisions agreed upon submitted January 16, 2004.

Please submit the FPL electronically 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, 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 supplements NDA 20-323/S-017, S-025, S-030." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
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: agreed-upon labeling text

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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