NDA 21-167
NDA 20-323/S-023

Novartis Pharmaceuticals Corporation
Attention: Lynn Mellor
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Ms. Mellor:

Please refer to your new drug application NDA 21-167 dated October 19, 1999, received October 20, 1999, and supplemental NDA 20-323/S-023 dated April 19, 2000, received April 20, 2000, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vivelle (estradiol transdermal system).

We acknowledge receipt of your submissions to NDA 21-167 dated November 29 and December 3, 1999, and February 14, March 6, April 19, June 15, July 11 (2), 26, and 27, and August 2 and 14, 2000.

We also acknowledge receipt of your submissions to NDA 20-323 dated July 11 and 27, 2000.

This new drug application provides for the use of Vivelle (estradiol transdermal system) in 0.0375 mg, 0.05 mg, 0.075 mg and 0.1 mg strengths for the new indication of the prevention of postmenopausal osteoporosis. In addition, a new lower strength, 0.025 mg, system is proposed for the indication of prevention of postmenopausal osteoporosis.

We have completed the review of these applications, 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 agreed upon labeling text. Accordingly, the applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted August 14, 2000, patient package insert submitted August 14, 2000, immediate container labels submitted April 19, 2000, and backing labels submitted July 26, 2000). 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 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. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-323/

S-023." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55.

Reference is made to your correspondence dated December 3, 1999, requesting a waiver for pediatric studies under 21 CFR 314.55(c). We have reviewed the information you have submitted and agree that a waiver is justified for Vivelle for prevention of postmenopausal osteoporosis for the pediatric population. Accordingly a waiver for pediatric studies for these applications is granted under 21 CFR 314.55 at this time.

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 two copies to the Division of Reproductive and Urologic Drug Products 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, Maryland 20857

Please submit one market package of the 0.025 mg strength 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. To comply with these regulations, all 7-day and 15-day alert reports, periodic adverse drug experience (ADE) reports, field alerts, annual reports, supplements and other submissions should be addressed to the original NDA 20-323 for this drug product at the Division of Reproductive and Urologic Drug products (HFD-580), not to NDA 21-167. In the future, no submissions should be made to NDA 21-167.

If you have any questions regarding NDA 20-323/S-023, call Diane V. Moore, Regulatory Project Manager, at (301) 827-4236. Questions regarding NDA 21-167 should be directed to William C. Koch, Regulatory Project Manager, at (301) 827-6412.

Sincerely,

John K Jenkins, M.D.
Acting Director
Division of Metabolic and
Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research