DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-151/S-029
NDA 20-699/S-046

Wyeth Pharmaceuticals, Inc.
Attention: Kenneth R. Bonk
Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-1245

Dear Mr. Bonk:

We acknowledge receipt of your supplemental new drug applications dated October 31, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Effexor (venlafaxine hydrochloride) Immediate Release Tablets (NDA 20-151) and Effexor XR (venlafaxine hydrochloride) Extended Release Capsules (NDA 20-699).

The above submissions, submitted as "Prior Approval" supplemental applications, provide for revisions to the **PRECAUTIONS-Drug Interactions**-*Drugs Metabolized by Cytochrome P450 Isoenzymes*-CYP2C9 section of labeling.

Reference is also made to your electronic communication dated March 25, 2004, agreeing to revise this section of labeling, as follows, to reflect limitations of the *in vivo* information (strike through font denotes agreed upon deletions, and double underline font denotes agreed upon revisions).

> **PRECAUTIONS-Drug Interactions**-*Drugs Metabolized by Cytochrome P450 Isoenzymes*
> CYP2C9 – Venlafaxine did not inhibit CYP2C9 in vitro. ~~The clinical significance of this finding is unknown.~~ In vivo, venlafaxine 75 mg by mouth every 12 hours did not alter the pharmacokinetics of a single 500 mg dose of tolbutamide or the CYP2C9 mediated formation of 4-hydroxy-tolbutamide.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in your draft labeling and as amended above. Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the labeling (text for the package insert) submitted on October 31, 2003, and as amended above. 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 the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. 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 NDAs 20-151/S-029 & 20-699/S-046." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, 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 the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Mr. Paul David, R.Ph., Senior Regulatory Project Manager, at (301) 594-5530.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Russell Katz

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