DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-839/S-058/S-060
NDA 20-990/S-024/S-026

Pfizer Pharmaceuticals
Attention: Mojgan M. Moghaddassi, Pharm.D.
Regulatory Affairs
235 East 42nd Street
New York, NY 10017-3184

Dear Dr. Moghaddassi:

We acknowledge receipt of your supplemental new drug applications dated May 10, 2006 (NDAs 19-839/S-058 & 20-990/S-024) and July 27, 2006 (NDAs 19-839/S-060 & 20-990/S-026), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zoloft (sertraline hydrochloride) 25 mg, 50 mg, and 100 mg tablets (19-839) and 20 mg/ml oral concentrate (20-990).

These "Changes Being Effected" supplemental new drug applications provide for revisions to the **PRECAUTIONS**-**Pregnancy**-*Nonteratogenic Effects* section to incorporate new data pertaining to the use of selective serotonin reuptake inhibitors (SSRIs) during pregnancy as requested in our letter dated April 10, 2006, and our e-mail communication dated July 13, 2006.

Specifically, this subsection has been revised as follows (double underline font denotes additions to product labeling):

> **Pregnancy-Nonteratogenic Effects–**Neonates exposed to Zoloft and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. These findings are based on postmarketing reports. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see WARNINGS).
>
> Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1-2 per 1,000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no

corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk.

When treating a pregnant woman with ZOLOFT during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see DOSAGE AND ADMINISTRATION). Physicians should note that in a prospective longitudinal study of 201 women with a history of major depression who were euthymic in the context of antidepressant therapy at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication.

We have completed our review of these applications, and they are approved, effective on the date of this letter, for use as recommended in the enclosed labeling text.

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
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 Renmeet Gujral, Regulatory Project Manager, at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
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/

Thomas Laughren
9/14/2006 09:05:16 AM