DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-130/S-007
NDA 21-131/S-008
NDA 21-132/S-007

Pharmacia & Upjohn Company
c/o Pfizer Inc.
Attention: James Symons
Global Regulatory Lead
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Dr. Symons:

Please refer to your supplemental new drug applications dated July 7, 2004, received July 9, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyvox™ (linezolid) Tablets (NDA 21-130), Zyvox™ (linezolid) IV Injection (NDA 21-131) and Zyvox™ (linezolid) Oral Suspension (NDA 21-132).

We acknowledge receipt of your submissions dated July 12, 2004, and January 5, 2005.

These supplemental new drug applications provide for revised labeling to address the potential for serotonin syndrome with the concomitant use of linezolid and serotonergic agents.

We completed our review of these applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling that includes the following changes:

1. In the **CLINICAL PHARMACOLOGY, Drug-Drug Interactions**, *Serotonergic agents* section, deletion of the following text.

   "The effects of other serotonin re-uptake inhibitors have not been studied"

2. In the **PRECAUTIONS** section, **General** subsection, addition of the following bolded text as a second paragraph.

   "Spontaneous reports of serotonin syndrome associated with the co-administration of ZYVOX and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been reported (see PRECAUTIONS, Drug Interactions)"

3. The **PRECAUTIONS** sections, **Drug Interactions**, *Serotonergic Agents* sub-section, should read as follows.

   "Co-administration of linezolid and serotonergic agents was not associated with serotonin syndrome in Phase 1, 2, or 3 studies. Spontaneous reports of serotonin syndrome associated with co-administration of ZYVOX and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been reported. Patients who are treated with ZYVOX and concomitant serotonergic agents should be closely observed for signs and symptoms of serotonin syndrome (e.g., cognitive dysfunction, hyperpyrexia, hyperreflexia, incoordination). If any signs or symptoms occur, physicians should consider discontinuation of either one or both agents (ZYVOX or concomitant serotonergic agents)."

4. In the **Postmarketing Experience** section, the 5th sentence should read as follows.

   "Serotonin syndrome has been reported in patients receiving concomitant serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and ZYVOX (see **PRECAUTIONS**).

The final printed labeling (FPL) must be identical to the labeling for the package insert submitted on January 5, 2005, and should contain the above described labeling changes.

Please submit an electronic version of the FPL 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 but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**FPL for approved supplement NDA 21-130/S-007, NDA 21-131/S-008, and 21-132/S-007).**" Approval of these submissions 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, HFD-410
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 Judit Milstein, Regulatory Project Manager, at (301) 827-2207.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
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/

Janice Soreth

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