



NDA 21-130/S-016/S-017
NDA 21-131/S-013/S-014
NDA 21-132/S-014/S-015

Pfizer Global Pharmaceuticals
Attention: Nadia Kirzecky, Ph.D.
Associate Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Dr. Kirzecky:

Please refer to your supplemental new drug applications dated December 21, 2006, received December 22, 2006, and dated March 15, 2007, received March 16, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number	Supplement Number	Name of Drug Product
21-130	016 (12-21-06)/017 (3-15-07)	Zyvox [®] (linezolid) Tablets
21-131	013 (12-21-06)/014 (3-15-07)	Zyvox [®] (linezolid) IV Injection
21-132	014 (12-21-06)/015 (3-15-07)	Zyvox [®] (linezolid) for Oral Suspension

These supplemental new drug applications provide for amendment to the package insert with the information from the Phase 3 clinical trial A5951060 (M/1260/0080) "Linezolid vs. Vancomycin/Oxacillin/Dicloxacillin in the Treatment of Catheter-Related Gram-Positive Bloodstream Infections."

We also acknowledge receipt of your submissions dated February 2 and 16, March 19, April 20 and 24, May 14, December 5, 2007, and June 5, 2008.

We completed our review of these applications as amended, and these applications are approved, effective on the date of this letter, for use as recommended in the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format submitted on June 5, 2008.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling submitted on June 5, 2008. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved supplements NDA 21-130/S-016/S-017, NDA 21-131/S-013/S-014, NDA 21-

132/S-014/S-015". Approval of these submissions by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable. Your supplemental new drug applications (NDAs) identified above are not applications for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Therefore, there are no pediatric assessments required in conjunction with these supplemental NDAs.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)). This provision took effect on March 25, 2008.

Since Zyvox[®] (linezolid) was approved on April 18, 2000, for the treatment of adult patients with vancomycin-resistant *Enterococcus faecium* infections, nosocomial pneumonia, complicated and uncomplicated skin and skin structure infections, and community-acquired pneumonia, we have become aware of cases of fatal arrhythmias noted among patients who received Zyvox[®] (linezolid) in Study A5951060 that may be related to Zyvox[®] (linezolid) administration. This information was not available when Zyvox[®] (linezolid) was granted marketing authorization for the treatment of adult patients with vancomycin-resistant *Enterococcus faecium* infections, nosocomial pneumonia, complicated and uncomplicated skin and skin structure infections, and community-acquired pneumonia. The cases of fatal arrhythmias in Study A5951060 are considered to be "new safety information" as defined in FDAAA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk, that is, the risk of fatal arrhythmia.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to assess this signal of a serious risk.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess this signal of a serious risk.

NDA 21-130/S-016/S-017

NDA 21-131/S-013/S-014

NDA 21-132/S-014/S-015

Page 3

Therefore, based on appropriate scientific data, FDA has determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct a clinical trial:

1. A clinical trial to assess the risk of QT prolongation.

The timetable you submitted on June 3, 2008 states that you will conduct this trial according to the following timetable:

Final Protocol Submission:	by December 31, 2008
Initiate (i.e. first subject dosed) and complete (i.e. last subject last visit) trial:	by March 31, 2009
Summary of Trial Results:	by July 31, 2009
Final Report Submission:	by September 30, 2009

Submit protocols to your INDs [49,195 and 55,618] with a cross-reference letter to NDAs [21-130, 21-131, 21-132]. Submit all final reports to NDA 21-130, NDA 21-131, and NDA 21-132.

Use the following designators to prominently label all submissions, including supplements, relating to this postmarketing clinical trial as appropriate:

- **Required Postmarketing Protocol under 505(o)**
- **Required Postmarketing Final Report under 505(o)**
- **Required Postmarketing Correspondence under 505(o)**

You are required to report periodically to FDA on the status of this clinical trial pursuant to sections 505(o)(3)(E)(ii) and 506B of the FDCA, as well as 21 CFR 314.81. Under section 505(o)(3)(E)(ii), you are also required to periodically report to FDA on the status of any study or trial otherwise undertaken to investigate a safety issue associated with Zyvox[®] (linezolid).

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
Suite 12B05
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).

NDA 21-130/S-016/S-017

NDA 21-131/S-013/S-014

NDA 21-132/S-014/S-015

Page 4

If you have any questions, call Susmita Samanta, MD, Regulatory Project Manager, at 301-796-1400.

Sincerely,

{See appended electronic signature page}

Katherine Laessig, M.D.

Deputy Director

Division of Anti-Infective and Ophthalmology
Products

Office of Antimicrobial Products

Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Kathrine Laessig
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