DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-684/S-044
NDA 50-750/S-011

Wyeth Pharmaceuticals, Inc.
Attention: Mary Ellen Menz, RN, MBA, JD
Manager, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, Pennsylvania 19101-8299

Dear Ms. Menz:

Please refer to your supplemental new drug applications dated June 3, 2004, received June 4, 2004, (NDA 50-684/S-044) and dated June 4, 2004, received June 7, 2004 (NDA 50-750/S-011), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zosyn® (piperacillin and tazobactam injection) (NDA 50-684), and Zosyn® (piperacillin and tazobactam injection) in Galaxy® Containers (NDA 50-750). We note that these applications are subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

These supplements provide for the revision of the information on Aminoglycosides under the Drug Interaction subsection of the Precautions section.

We completed our review of these applications, and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. The information on Aminoglycosides should be revised as follows:

> The inactivation of aminoglycosides in the presence of penicillin-class drugs has been recognized. It has been postulated that penicillin-aminoglycoside complexes form; these complexes are microbiologically inactive and of unknown toxicity. Coadministration of Zosyn with tobramycin to patients with normal renal function and mild to moderate renal impairment has been shown to modestly decrease serum concentrations of tobramycin but does not significantly affect tobramycin pharmacokinetics. When aminoglycosides are administered in combination with piperacillin to patients with end-stage renal disease requiring hemodialysis, the concentrations of the aminoglycosides (especially tobramycin) may be significantly altered and should be monitored. Since aminoglycosides are not equally susceptible to inactivation by piperacillin, consideration should be given to the choice of the aminoglycoside when administered in combination with piperacillin to these patients.

The final printed labeling (FPL) must include the revisions indicated. These revisions are terms of the approval of these applications. 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 50-684/S-044, NDA 50-750/S-011." 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 the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Susmita Samanta, M.D., Regulatory Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, M.D.
Director
Division of Anti-Infective and Ophthalmology 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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