



NDA 50-545/S-031  
NDA 50-545/S-033  
NDA 50-545/S-037

Wyeth Pharmaceuticals  
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 November 17, 1989 (S-031), May 1, 1997 (S-033), and August 25, 2000 (S-037), received November 27, 1989, May 5, 1997, and August 28, 2000, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pipracil<sup>®</sup> (piperacillin sodium) Injection. 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.

We acknowledge receipt of your submissions dated July 2 and October 15, 2002, and March 19, 2003. Your submission of March 19, 2003 constituted a complete response to our April 8, 2002 action letter.

These supplements propose the following changes:

- S-031: Additions to the **WARNINGS, PRECAUTIONS, and ADVERSE EFFECTS** sections of the package insert concerning pseudomembranous colitis and the potential interaction of piperacillin and vecuronium in the perioperative period.
- S-033: Addition of pediatric information in compliance with the December 13, 1994, Federal Register Final Notice.
- S-037: Addition of geriatric information in compliance with the August 27, 1997, Federal Register Notice.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor revision listed below:

Under **MICROBIOLOGY, Susceptibility Testing Methods, Dilution Techniques**, an asterisk and a reference are to be placed after the following statement:

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“Haemophilus species are considered susceptible if the MIC of piperacillin is  $\leq 1 \mu\text{g/mL}$ .\*

Dilution methods such as those described in the International Collaborative Study\* (*Acta Pathol Microbiol Scand* [B] 1971; suppl 217) have been used to determine susceptibility of organisms to piperacillin.”

The final printed labeling (FPL) must be identical to the submitted labeling (text for the package insert) and include the revision indicated, and must be formatted in accordance with the requirements of 21 CFR 201.66.

Please submit the FPL electronically 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, in no case 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 supplement NDA 50-545/S-031/S-033/S-037”. Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Anti-Infective Drug Products, HFD-520, and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

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, HF-2  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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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 Drug Products  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

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/s/

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Janice Soreth

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