D 6
ROBERTS

IND 49,195
IND 55,618

MAY 21 1999

Pharmacia & Upjohn Company
Attention: Peter J. DiRoma
Regulatory Manager
Unit 0635-298-113
7000 Portage Road
Kalamazoo, MI 49001-0199

Dear Mr. DiRoma:

Reference is made to your correspondence dated March 15, 1999, requesting that FDA issue a Written Request under Section 505A of the Food, Drug, and Cosmetic Act for Linezolid (PNU-100766).

We have reviewed your proposed pediatric study request and are unable to issue a Written Request based on your submission.

We recommend that you resubmit your proposed pediatric study request addressing all of the issues outlined in the attached review. Some specific concerns are outlined below.

1. The proposed study does not adequately address the potential use of intravenous linezolid for treatment of skin and skin structure infections in pediatric patients;

2. The pharmacokinetics and safety of linezolid in the neonatal population (including premature infants) have not been addressed;

3. Linezolid is potentially a valuable agent in the treatment of central nervous system infections including *Streptococcus pneumoniae* meningitis and CSF shunt infections. Studies of the CSF penetration of linezolid and animal models of CNS infection should be considered. Comparative studies of linezolid versus vancomycin in CNS infection (in combination with a 3rd generation cephalosporin) should also be considered;

4. Linezolid may be useful in the treatment of catheter-related bacteremia due to gram-positive organisms. Studies of linezolid versus vancomycin in this clinical entity should be considered.

Please clearly mark your submission, "PROPOSED PEDIATRIC STUDY REQUEST" in large font, bolded type at the beginning of the cover letter of the submission.

We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, contact Ms. Beth Duvall-Miller, at (301)827-2125.

Sincerely yours,

Gary K. Chikami, M.D.
Director
Division of Anti-Infective Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation IV

Attachment - (Review 10 pages)