DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-222

TAP Pharmaceutical Products Inc.
Attention: Donna Helms
Associate Director, Regulatory Affairs
675 North Field Drive
Lake Forest, IL 60045

Dear Ms. Helms:

Please refer to your new drug application (NDA) dated December 28, 1999, received December 29, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Spectracef™ (cefditoren pivoxil) Tablets, 200 mg.

We acknowledge receipt of your submissions dated November 8, 20, 21, 27, and 28, 2000; December 8, 14, and 26, 2000; January 8, 14, 15, and 29, 2001; February 5, 8, and 28, 2001; March 1, 2001; April 27, 2001; June 13 and 26, 2001; July 12, 23, and 30, 2001; August 10, 15, 17, 21, and 23, 2001.Your submission of March 1, 2001, constituted a complete response to our October 27, 2000, action letter.

This new drug application provides for the use of Spectracef™ (cefditoren pivoxil) Tablets for the treatment of acute bacterial exacerbation of chronic bronchitis, pharyngitis/tonsillitis, and uncomplicated skin and skin structure infections.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the Guidance for Industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. 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 NDA 21-222." Approval of this submission by FDA is not required before the labeling is used.

We remind you of the postmarketing study commitments agreed to in your submission dated August 21, 2001. These commitments are listed below.

1. Conduct a clinical study in patients receiving cefditoren treatment including those at increased risk for clinically significant effects of carnitine depletion to assess changes in serum concentrations of carnitine. In addition to biochemical assessment of alterations in carnitine metabolism, clinical monitoring for manifestations of carnitine deficiency should also be performed.

Protocol submission:	Within 15 months of the date of this letter
Study start:	Within 18 months of the date of this letter
Final report submission:	Within 30 months of the date of this letter

2. Conduct an *in vitro* study to assess the potential for cefditoren pivoxil to influence the metabolism of co-administered drugs using human microsomes and probe substrates for cytochrome P450 isozymes. Concentrations of cefditoren to be studied should exceed concentrations observed in subjects receiving cefditoren pivoxil 400 mg twice daily. Refer to the April 1997 FDA Guidance for Industry titled *Drug Metabolism/Drug Interaction Studies in the Drug Development Process: Studies In Vitro* for additional information.

Protocol submission:	Within 2 months of the date of this letter
Study start:	Within 3 months of the date of this letter
Final report submission:	Within 6 months of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical protocols and all final study reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until September 2004. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the

waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. We acknowledge receipt of your May 30, 2000, submission of a "Proposed Pediatric Study Request" (PPSR). We refer to the Agency's letter dated May 11, 2001, that outlines why we were unable to issue a Written Request letter based on your submission. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Anti-Infective Drug Products and two copies of both the promotional materials and the package insert directly to:

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

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Beth Duvall-Miller, Regulatory Health Project Manager, at (301) 827-2125.

Sincerely yours,

{See appended electronic signature page}

M. Dianne Murphy, M.D.
Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure