



**Westward**  
PHARMACEUTICAL CORP.

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February 16, 2007

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Division of Dockets Management  
Food and Drug Administration  
Dep. Of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Re: Citizen Petition/ Hydrocortisone Tablets USP, 10 mg (CORTEF<sup>®</sup>, NDA 008697)**

Dear Sirs:

The undersigned submits this petition under 21 CFR 10.25(a) and 21 CFR 10.30 to request the Commissioner of the Food and Drug Administration to determine whether a listed drug that has been voluntarily shortened from distribution and sale was shortened for safety or effectiveness reasons and if the listed drug was shortened for reasons other than for safety or effectiveness, to permit the filing of an abbreviated new drug application (ANDA).

**A. Action Requested**

The petitioner requests that the Commissioner of the Food and Drug Administration determine whether Hydrocortisone Tablets USP, 10 mg (CORTEF<sup>®</sup>, NDA 008697) manufactured by Pharmacia and Upjohn has been voluntarily shortened from distribution and sale for safety or efficacy reasons. The FDA's Division of Bioequivalence requested that we submit this petition prior to sending in our ANDA. Please see attached letter of August 4, 2006.

**B. Statement of Grounds**

The Food and Drug Administration maintains a list of drug products that are eligible for submission as ANDA's. The List, referred to as the Orange Book, contains all FDA-approved drug products. Hydrocortisone Tablets, 10 mg (CORTEF<sup>®</sup>) was approved by the FDA prior to January 1982.

Under FDA regulations, drugs are withdrawn from the list if the Agency withdraws or suspends approval of the drug product's application for reasons of safety or effectiveness. (21 CFR 314.162) The regulations also provide that the Agency must make a determination as to whether a listed drug is withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved. (21 CFR 314.161 (a)(1).

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The Petitioner has no evidence concerning the reason why Pharmacia and Upjohn shortened from distribution and sale of Hydrocortisone Tablets USP, 10 mg (CORTEF®), but nevertheless contends that the reasons were unrelated to safety or effectiveness.

The Petitioner requests that the FDA determine that Pharmacia and Upjohn's decision to shorten from distribution and sale Hydrocortisone Tablets USP, 10 mg (CORTEF®), was for reasons other than safety or effectiveness.

**C. Environmental Impact**

A claim for categorical exclusion of the requirement for submission of an environmental assessment is made pursuant to 21 CFR 25.31.

**D. Economic Impact**

Pursuant to 21 CFR 10.30(b), economic impact information is to be submitted only when requested by the commissioner. This information will promptly be submitted, if so requested.

**E. Certification**

The undersigned certifies, that to the best of her knowledge and belief, this petition includes all information and views on which the petitioner relies, and that includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,



Elizabeth A. Marro  
Senior Director, Regulatory Affairs and Quality Assurance



West-Ward Pharm. Corp.  
Attention: Liz Marro  
465 Industrial Way West  
Eatontown, NJ 07724

AUG 04 2006

Reference Number: OGD #05-1286

Dear Ms. Marro:

This letter is in response to your correspondence dated April 28, 2005. You request that the Office of Generic Drugs (OGD) provide bioequivalence recommendations regarding Hydrocortisone Tablets. You state that you have an approved application for Hydrocortisone Tablets, 20 mg. You would like to pursue additional strengths, 5 mg and 10 mg. Your application for the 20 mg strength is currently rated BP. OGD provides the following comments:

1. The 1984 Hatch-Waxman Amendments to the Federal Food Drug and Cosmetic Act (Act) require among other things that an application submitted under Section 505(j) of the Act contain "information to show that the new drug is bioequivalent to the listed drug..." A supplement is considered to be an application and it must contain all of the information required under section 505(j), including the information to demonstrate bioequivalence. Hydrocortisone is considered to be a bioequivalence problem drug product and as such requires evidence of bioequivalence in order to obtain approval for this product. Please refer to 21 CFR 320.21(c)(1).
2. Therefore, when the supplement is submitted it should contain bioequivalence study in order demonstrate bioequivalence to the listed drug:
  - a. A single dose fasting *in-vivo* bioequivalence study comparing Hydrocortisone Tablets, 20 mg, to the RLD, Cortef® (Hydrocortisone) Tablets, 20 mg.
  - b. A 4 mg dose of dexamethasone should be administered 10 hours prior to drug administration as a pre-treatment to lower endogenous hydrocortisone levels.
3. Please measure only the parent compound, hydrocortisone.
4. Hydrocortisone Tablets, 5 mg, and 10 mg, may be considered for a waiver of *in-vivo* bioequivalence testing based on (1) an acceptable bioequivalence study on the 20 mg strength, (2) acceptable dissolution testing of all strengths, and (3) proportional similarity in the formulations of all strengths.
5. Please note that the 10 mg strength of the RLD has been discontinued from the market. Please submit a Citizen's Petition to the agency to determine whether the listed drug

product was withdrawn for safety or efficacy reasons. The petition must be submitted under 21 CFR 10.25(a) and 10.30. You may submit the petition in the application.

6. Please conduct comparative dissolution testing on 12 dosage units of the test and reference products using the USP method.
7. You may submit a protocol for review prior to initiation of the studies.
8. Please provide a table that identifies every missing sample in the study. Also, for every reassayed sample, please provide a table identifying the reason(s) for reassay, as well as the original and reassayed values of the sample. Please identify which value was selected for the PK analysis. Please provide the Standard Operating Procedures (SOPs) for all types of reassays including those that describe criteria for identifying and reassaying pharmacokinetically anomalous samples. The SOP(s) should clearly state objective criteria for defining pharmacokinetic anomalies, the method of reassay, and acceptance criteria for selecting which value to report for the reassayed sample. This SOP should be in place prior to the start of the study; otherwise, the Division of Bioequivalence may not accept reassayed values of samples. Finally, please conduct all pharmacokinetic and statistical analyses using both the original as well as reassayed values.
9. The bioequivalence data to be submitted in an ANDA should be provided in a diskette or CD in SAS Transport format in two separate files as described below:
  - a. SUBJ SEQ PER TRT AUCT AUCI CMAX TMAX KE Thalf
  - b. SUBJ SEQ PER TRT C1 C2 C3 ..... Cn

Please separate each field with a blank space and indicate missing values with a period (.).

Please refer to the Guidance for Industry: "Providing Regulatory Submissions in Electronic Format-ANDAs" for information regarding the proper format at: [www.fda.gov/cder/guidance/index.htm](http://www.fda.gov/cder/guidance/index.htm) (under electronic submissions).

If you have any questions, please call Lizzie Sanchez, Pharm. D., Special Assistant to the Director, Division of Bioequivalence at (301) 827-5847. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,



Dale P. Conner, Pharm.D.

Director

Division of Bioequivalence

Office of Generic Drugs

Center for Drug Evaluation and Research