CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76005

BIOEQUIVALENCY REVIEW(S)

4.1

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # : 76-005 SPONSOR : Taro Pharmaceuticals USA, Inc.

DRUG AND DOSAGE FORM : Econazole Nitrate Cream

STRENGTH(S) : 1%

TYPES OF STUDIES : Clinical endpoint bioequivalence study

DSI INSPECTION STATUS

Inspection needed: **NO**	Inspection status:	Inspection results:
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

ASSOCIATE DIRECTOR FOR MEDICAL AFFAIRS: DENA R. HIXON, M.D.

INITIAL : DRH DATE : 9-13-02

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : DPC DATE : 9/13/02

JAN 28

BIOEQUIVALENCY DEFICIENCIES

ANDA: 76-005 APPLICANT: Taro Pharmaceuticals, Inc..

DRUG PRODUCT: Econazole Nitrate Cream, 1%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

Your clinical endpoint study fails to demonstrate bioequivalence between your product, Econazole Nitrate Cream, 1%, and the reference listed drug (RLD), Spectazole® Cream, 1% (Ortho McNeil Pharmaceuticals) in the treatment of tinea pedis due to the following reasons:

1. The therapeutic cure should be based on mycological and clinical cure rate at week 6, and not on a mycological cure rate based on outcomes at week 4 and 6.

2. A modified intent-to-treat (MITT) population, omitting patients lost to follow-up after visit 1, was used for the comparison of the active treatment groups with the placebo arm.

3. The Evaluable population was used for the comparison of test and reference groups in the determination of bioequivalence. Patients who did not return after visit 2 or were outside the visit window of +/- 3 days for visit 3 were not included in this population.

4. The comparison between the active treatment arms and the vehicle (placebo) arm was done using the MITT population. The 90% confidence interval method is not the correct method for this analysis.

5. The 90% confidence interval for the difference in therapeutic cure rate between the test and reference drug did not meet the bioequivalence criteria.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-005 APPLICANT: Taro Pharmaceuticals, Inc.

DRUG PRODUCT: Econazole Nitrate Cream, 1%

The Division of Bioequivalence has completed its review and has no further questions at this time.

Using definitions of clinical, mycological, and therapeutic cure that incorporates results at both 4 weeks (end of treatment) and 6 weeks (2 weeks post-treatment follow up), the study submitted is adequate to demonstrate bioequivalence.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research