

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75014

BIOEQUIVALENCY REVIEW(S)

(3)

**OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE**

ANDA # : 75-014

SPONSOR : Alpharma

DRUG AND DOSAGE FORM : **Permethrin Creme Rinse, 1%**

STRENGTH(S) : 1%

TYPES OF STUDIES : Bioequivalence Study

CLINICAL STUDY SITE(S) :

ANALYTICAL SITE(S) :

STUDY SUMMARY : Bioequivalence study found acceptable

DISSOLUTION : N/A

DSI INSPECTION STATUS

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

PRIMARY REVIEWER : Mary M. Fanning, M.D., Ph.D.
Associate Director for Medical Affairs, Office of Generic Drugs

INITIAL : MF DATE : 9/21/99

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

INITIAL : DC DATE : 9/29/99

SEP 24 1997

ANDA #75-014
Permethrin Lotion, 1%
Reviewer: S. P. Shrivastava
WP # 75-014s.697

Alpharma
Baltimore, MD
Submission Date:
June 4, 1997

REVIEW OF AMENDMENT TO 'REFUSE TO FILE' APPLICATION

BACKGROUND

The firm had submitted an ANDA with a comparative clinical and *ex-vivo* studies for its permethrin lotion, 1%. However, the application was refused for filing (Re: OGD letter 2/13/1997), because:

1. The lotion contains high contents of protein hydrolysate and hydroxyethylcellulose.
2. The clinical study was conducted on a different formulation of permethrin than the formulation under consideration. However, *ex-vivo* studies with lice and louse eggs were conducted to bridge the differences between the two formulations,
3. The concentration of propylene glycol was higher in the test product.

The firm's representatives also had a meeting with FDA on March 26, 1997, to present the case for reconsideration of the application. The amendment is in response to the "Refuse to File" letter from the OGD.

COMMENT

1. The components of permethrin lotion, protein hydrolysate, hydroxyethylcellulose, and propylene glycol are safe for use in the formulation.
2. If appropriately designed, an *ex-vivo* study may be accepted. However, the design of the study used is inadequate to establish the bioequivalence of products. The firm should consider the following in the design:

3. The site of the *ex-vivo* study should be such that it complies with good clinical practices, and data submitted are verifiable. Pivotal study data for Alparma's another product, permethrin cream, 5% (ANDA 74-806), was found to be non-verifiable.

RECOMMENDATION

The ANDA is not acceptable for filing because of the deficiencies cited in #2.

The firm should be informed of the comments #2-3 and recommendation.

/S/

S. P. Shrivastava, Ph.D.
Division of Bioequivalence
Review Branch II

RD INITIALED S Nerurkar
FT INITIALED S Nerurkar

/S/

(For Vijay)

Date 9/24/97

Concur:

/S/

Date: 9/24/97

Rabindra Patnaik, Ph.D.
Acting Director
Division of Bioequivalence

SPS/sps/06-30-97/75014.697

cc: ANDA #75014 (Original, Duplicate), HFD-655 (SNerurkar, SShrivastava), HFD-650 (Division File), Drug File.

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-014

APPLICANT: Alparma

DRUG PRODUCT: Permethrin Creme Rinse, 1%

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

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,

A handwritten signature in black ink, appearing to read "Dale P. Conner", with a stylized flourish above the name.

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