CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40276

BIOEQUIVALENCY REVIEW(S)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-276 APPLICANT: Purepac Pharmaceutical Co.

DRUG PRODUCT: Phentermine HCl 37.5 mg tablets

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

The dissolution testing will need to be incorporated into your stability and quality control programs as specified in USP 23.

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,

Dale Conner

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

Phentermine Hydrochloride
37.5 mg Tablets
ANDA #40-276
Reviewer: Moheb H. Makary
WP #40276D.997

Purepac Pharmaceutical Co.
Elizabeth, NJ
Submission Date:
September 11, 1997

Review of a Dissolution Data and Waiver Request

I. Objective:

The firm has requested a waiver of the in vivo bioequivalence study requirements for its Phentermine HCl 37.5 mg Tablets. The firm conducted dissolution testing on its test product comparing it to Lemmon's Adipex-P^R 37.5 Tablets.

Phentermine Hydrochloride Tablets are coded AA for various strengths in the Orange Book.

II. Dissolution Testing:

The following USP 23 conditions were used:

Apparatus:	2 (paddle) at 50 rpm
Medium:	900 mL of water
Test product:	Purepac's Phentermine HCl, 37.5 mg Tablets, lot #P1-985
Reference product:	Lemmon's Adipex-P^R (Phentermine HCl 37.5 mg) Tablets, lot #7147, Exp. 10/99
Specifications:	NLT (Q) of the labeled amount of Phentermine is dissolved in 45 minutes.

The dissolution testing results are shown in Table I.

III. Formulation:

The formulation of the test product is shown in Table II.

IV. Comment:

The dissolution testing results for the test product met the USP specifications.

V. Recommendations:

1. The dissolution testing conducted by Purepac Pharmaceutical Co., on its Phentermine Hydrochloride, 37.5 mg Tablets, lot #P1-985, is acceptable. The waiver of the in vivo bioequivalence study requirements is granted for the test product Phentermine Hydrochloride, 37.5 mg Tablets based on 21 CFR 320.22 (c). The Division of Bioequivalence deems Phentermine Hydrochloride, 37.5 mg Tablets, manufactured by Purepac Pharmaceutical Co., to be bioequivalent to Adipex-P^{R} 37.5 mg Tablets, manufactured by Lemmon Inc.

2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 mL of water, at 37 °C using USP 23 apparatus 2 (paddle) at 50 rpm.
The test product should meet the following specifications:

> Not less than % of the labeled amount of Phentermine in the dosage form is dissolved in 45 minutes.

The firm should be informed of the above recommendations.

/S/

Moheb H. Makary, Ph.D.
Division of Bioequivalence
Review Branch III

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Concur: /S/ Date: 1/9/98

Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

Table I In Vitro Dissolution Testing

Drug (Generic Name): Phentermine Hydrochloride
Dose Strength: 37.5 mg Tablets
ANDA No.:40-276
Firm: Purepac Pharmaceutical Co.
Submission Date: September 11, 1997
File Name: 40276D.997

I. Conditions for Dissolution Testing:

USP 23 Basket: Paddle: X RPM: 50
No. Units Tested: 12
Medium: 900 mL of water
Specifications: NLT % in 45 minutes
Reference Drug: Adipex 37.5 mg Tablets
Assay Methodology:

II. Results of In Vitro Dissolution Testing:

Sampling Times (Minutes)	Test Product Lot #P1-985 Tablet Strength(mg) 37.5			Reference Product Lot # 7147 Tablet Strength(mg) 37.5		
	Mean %	Range	%CV	Mean %	Range	%CV
10	83.4		5.5	88.3		2.7
20	93.7		1.7	95.8		2.5
30	93.9		1.3	96.3		2.3
45	94.3		1.3	96.4		2.3
60	94.3		0.6	96.5		2.3