CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40303

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE
SIGN-OFF FORM

ANDA #40-303 SPONSOR : Endo Pharmaceuticals
DRUG & DOSAGE FORM : Oxycodone HCL/Acetaminophen Capsule
STRENGTH (s) : 5/500 mg

TYPE OF STUDY: SD
STUDY: ☐Acceptable XNot Applicable

DISSOLUTION : XAcceptable ☐Not Applicable

WAIVER: XAcceptable ☐Not Applicable

REVIEWER: Hoainhon Nguyen /S/ BRANCH: I
INITIAL: DATE : 7/15/98

BRANCH CHIEF : Yih-Chain Huang, Ph.D. BRANCH : I
INITIAL : /S/ DATE : 7/15/98

DIRECTOR: Dale P. Conner, Pharm.D.
DIVISION OF BIOEQUIVALENCE
INITIAL : /S/ DATE : 7/15/98

Oxycodone HCL/Acetaminophen Capsule
ANDA # 40-303: 5/500 mg USP
Reviewer: Hoainhon Nguyen
WP # 40303dw.398

Endo Pharmaceuticals
Garden City, NY
Submission Date:
March 12, 1998

Review of Dissolution Data and Waiver Request

The firm has submitted comparative dissolution data for the test and reference products in support of a request for waiver of in-vivo bioequivalence requirements for the test product in accordance with 21CFR 320.22(b).

Dissolution Results:

See the results at the end of the review.

Comments:

1. The dissolution data for the test and reference products are acceptable.

2. Oxycodone HCL /Acetaminophen capsule USP, 5/500 mg, is classified as an AA product in the agency's Approved Drug Products with Therapeutic Equivalence Evaluations Book.

Recommendations:

1. The dissolution testing conducted by Endo Pharmaceuticals on its Oxycodone HCL/Acetaminophen Capsule USP, 5/500 mg, lot # LK483, is acceptable.

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 0.1 N HCl at 37^0C using USP XXIII apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Not less than % of the labeled amounts of Acetaminophen and Oxycodone HCL in the dosage form are dissolved in 45 minutes.

2. The Division of Bioequivalence agrees that the information submitted by Endo demontrates that its proposed Oxycodone HCL/Acetaminophen Capsule, 5/500 mg, falls under 21 CFR 320.22 (b) of the Bioavailability/Bioequivalence Regulations. The waiver of an *in vivo* bioequivalence study for the test product is granted.

/S/

Hoainhon Nguyen
Division of Bioequivalence
Review Branch I

RD INITIALED YHUANG
FT INITIALED YHUANG /S/ 7/15/98

Concur: /S/ Date: 7/15/98
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

Hnguyen/07-13-98/WP # 40303dw.398

cc: ANDA # 40-303 original, HFD-652(Huang, Nguyen), Drug File, Division File

Attachment: 1 page

USP Dissolution Testing Procedure and Specifications

Drug (Generic Name): Oxycodone HCL/Acetaminophen Capsule Firm: Endo Pharmaceuticals
Dose Strength: 5/500 mg ANDA # 40-303
Submission Date: March 12, 1998

Table - In-Vitro Dissolution Testing

Conditions for Dissolution Testing:

USP XXIII Basket __ Paddle X RPM 50 No. Units Tested: 12
Medium: 0.1 N HCl Volume: 900 ml
Reference Drug: (Manuf.) Tylox; Johnson RW
Assay Methodology: _____
Specifications: NLT % dissolved in 45 minutes

Results of In-Vitro Dissolution Testing:

Test Product
Lot # LK483
Strength (mg) 5 mg Oxycodone HCL
500 mg Acetaminophen

Reference Product
Lot # PC6835P
Strength (mg) 5 mg Oxydone HCL
500 mg Acetaminophen

Acetaminophen:

Sampling Time (Min.)	Mean % Dissol.	Range	(CV%)	Mean % Dissol.	Range	(CV%)
15	97.5		(2.9)	88.0		(8.3)
30	101.1		(2.5)	96.8		(3.2)
45	102.8		(1.7)	98.8		(0.7)
60	103.4		(1.4)	99.3		(0.4)

Oxycodone HCL

Sampling Time (Min.)	Mean % Dissol.	Range	(CV%)	Mean % Dissol.	Range	(CV%)
15	105.1		(2.6)	93.8		(4.5)
30	105.4		(3.4)	96.8		(1.7)
45	105.9		(2.2)	97.2		(0.9)
60	106.5		(1.4)	97.3		(0.9)

Specifications:
NLT % @ 45 min

BIOEQUIVALENCY COMMENTS

ANDA: 40-303 APPLICANT: Endo Pharmaceuticals

DRUG PRODUCT: Oxycodone HCL/Acetaminophen Capsule USP, 5/500 mg

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,

/S/

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