

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
40199

BIOEQUIVALENCY REVIEW(S)

Acetaminophen and
Oxycodone HCl
Capsule, 500 mg/5 mg
ANDA # 40-199
Reviewer: L. Chuang

OCT 28 1996

Amide Pharmaceutical, Inc.
Little Falls, NJ
Submission Date:
July 9, 1996

Review of a Waiver Request

Oxycodone is a semisynthetic narcotic analgesic with multiple actions qualitatively similar to those of morphine. Its principal actions of therapeutic value in the drug product are analgesia and sedation. Acetaminophen is a non-opiate, non-salicylate analgesic and antipyretic.

The reference listed drug product is Tylox capsule (acetaminophen/oxycodone HCl, 500 mg/5 mg) manufactured by RW Johnson Pharmaceutical approved under NDA #88790 on 12/12/84.

The firm requests a waiver from the human *in vivo* bioequivalence testing requirements because acetaminophen/oxycodone HCl capsule, 500 mg/5 mg, is rated AA in Approved Drug Products with Therapeutic Equivalence Evaluation, and the comparative dissolution testing data of the test and reference drug products conducted by the firm are presented below:

In Vitro Dissolution Testing							
Drug (Generic Name): Acetaminophen/Oxycodone HCl Dose Strength: 500 mg/5 mg ANDA No.: 40-199 Firm: Amide Pharmaceutical, Inc.							
I. Conditions for Dissolution Testing:							
USP XXIII Apparatus: Paddle RPM: 50 No. Units Tested: 12 Medium: 0.1 N Hydrochloric Acid Volume: 900 ml Tolerance: NLT % (Q) of both ingredients in 45 minutes Reference Drug: Tylox Capsule (RW Johnson/McNeil) Assay Methodology:							
II. Results of In Vitro Dissolution Testing:							
Sampling Times (Minutes)	Test Product Lot # 6069A Strength (mg): 500/5 Amount of Acetaminophen Dissolved			Reference Product Lot # PE6914R Strength (mg): 500/5 Amount of Acetaminophen Dissolved			
	Mean %	Range	%CV		Mean %	Range	%CV

20	95.5		1.3	97.7		0.3
30	97.6		1.3	100.0		0.3
45	99.8		1.4	102.1		0.3
	Amount of Oxycodone Dissolved			Amount of Oxycodone Dissolved		
20	97.6		1.7	91.0		1.8
30	98.6		1.6	94.5		1.8
45	98.3		1.6	100.5		2.0
Content Uniformity N=10 (CV) = 99.5% (0.8%) for Acetaminophen in Test Drug Content Uniformity N=10 (CV) = 98.7% (1.1%) for Oxycodone in Test Drug						

The formulation of the test drug product is presented below:

<u>Ingredient</u>	<u>Amount per Tablet of Test Product</u>
✓ Oxycodone Hydrochloride	mg
✓ Acetaminophen	mg
✓ Pregelatinized Starch	mg
✓ Talc	mg
✓ Magnesium Stearate	mg

Capsule: Empty gelatin capsules, size 0, white opaque/strawberry opaque
% excess added to compensate for moisture content

Comment:

The test drug is in conventional dosage form and does not present bioequivalence problems. It also has met the proper *in vitro* dissolution standard that is acceptable to the specification published in USP 23. Therefore, a waiver from the human *in vivo* bioequivalence testing requirements is granted.

Recommendation:

1. The Division of Bioequivalence agrees that the information submitted by Amide Pharmaceutical, Inc. demonstrates that Acetaminophen/Oxycodone HCl Capsule, 500 mg/5 mg, falls under 21 CFR Section 320.22 (c) of the Bioavailability/Bioequivalence Regulations. The waiver of in vivo bioequivalence study for the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test capsule to be bioequivalent to Tylox capsule, 500 mg/5 mg, manufactured by RW Johnson Pharmaceutical.

2. The dissolution testing conducted by Amide Pharmaceutical, Inc. on its Acetaminophen/Oxycodone HCl Capsule, 500 mg/5 mg, Lot #6069A, 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 hydrochloric acid at 37° C using USP 23 apparatus II (paddle) at 50 rpm. The test product should meet the following specifications:

Not less than % of the labeled amounts of both acetaminophen and oxycodone are dissolved in 45 minutes.

/S/

10/28/96

Lin-whei Chuang
Division of Bioequivalence
Review Branch I

Jan

RD INITIALED YHUANG
FT INITIALED YHUANG

/S/

10/28/96

Concur

/S/

Date:

10/28/96

Rabindra Patnaik, Ph.D.

Acting Director, Division of Bioequivalence

cc: ANDA 40199 (original, duplicate), Chuang, HFD-652, (Huang, Chuang), Drug File, Division File.

First Draft, LWC, 09/26/96, c:\wpfiles\40199w.796

Final Pink LWC, 10/01/96, x:\new\firm\am\amide\lrs&rev\40199dw.796