

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**40378**

**BIOEQUIVALENCY REVIEW(S)**

(2)

**OFFICE OF GENERIC DRUGS  
DIVISION OF BIOEQUIVALENCE**

ANDA # : 40-378

SPONSOR : Upsher-Smith

DRUG AND DOSAGE FORM : Niacin Tablet

STRENGTH(S) : 500 mg

TYPES OF STUDIES : Waiver

CLINICAL STUDY SITE(S) : N/A

ANALYTICAL SITE(S) : N/A

STUDY SUMMARY : N/A

DISSOLUTION : N/A

**DSI INSPECTION STATUS**

Inspection needed: YES / <u>NO X</u>	Inspection status:	Inspection results:
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER : Andre Jackson      BRANCH : I

INITIAL : aj      DATE : 9-1-99

TEAM LEADER : Y.C. Huang      BRANCH : I

INITIAL : YCH      DATE : 9/1/99

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

INITIAL : DP      DATE : 9/1/99

**Niacin**

500 mg Tablet

ANDA # 40378

Reviewer: Andre J. Jackson

V:\Firmsnz\Upsher-Smith\Ltr&Rev.\40378W.899

**Upsher-Smith**

Minneapolis, MN.

Submission Dated:

July 19, 1999

Review of a Waiver Request

Background:

The firm submitted comparative dissolution between their product Niacin and the reference product Nicolar® manufactured by Rhone Poulenc Rorer and are requesting a waiver of the in vivo bioequivalence requirement for Niacin since it is listed as an AA drug in the orange book.

Comment:

1. The comparative formulations for the test product Niacin and the reference product Nicolar® tablet is given in Table 1.
2. The dissolution data for the test product Niacin and the reference product Nicolar® is given in Table 2.

Table 1. Comparative formulations for the test and reference products

	TEST Mg/Tablet	REFERENCE Mg/Tablet
Niacin	500	500
Dye FDC Yellow # 5		
Silicon Dioxide		
Povidone		
Microcrystalline Cellulose, NF		
Hydrogenated Vegetable Oil, NF		
Croscarmellose, NF		
Magnesium Stearate, NF		
<u>Total</u>	mg	mg

Comments:

1. Dissolution data for the test product in Table 2 is acceptable.
2. The waiver of in vivo bioequivalence requirements for the test product may be granted based upon CFR 320.22 (c).

Recommendation:

1. The dissolution study conducted by Upsher-Smith on its product Niacin 500 mg tablet lot # 64892 comparing it to the reference product Nicolar® manufactured by Rhone Poulenc Rorer has been found to be acceptable by the Division of Bioequivalence. Therefore, the waiver request for the Niacin 500 mg tablet is granted and their Niacin 500 mg tablet is deemed bioequivalent to the reference product Nicolar® 500 mg tablet, manufactured by Rhone Poulenc Rorer.
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 0.1N HCL at 37°C using USP apparatus I basket at 100 rpm. The test product should meet the following specifications:

NLT % of the labelled amount of niacin should be dissolved in 60 minutes

André J. Jackson, Ph.D.  
Division of Bioequivalence  
Review Branch I

/S/

RD INITIALED YCHuang  
FT INITIALED YCHuang

/S/

Date 8/26/99

Concur: \_\_\_\_\_  
Dale P. Conner, Pharm.D.  
Director, Division of Bioequivalence

Date 8/31/99

for

Cc: ANDA 40-378 (original, duplicate), HFD-650(Director), HFD-652(Huang, Jackson), Drug File, Division File

**Table 2. In Vitro Dissolution Testing**

Drug (Generic Name): Niacin  
 Dose Strength: 500 mg Tablet  
 ANDA No.: 40378  
 Firm: Upsher-Smith  
 Submission Date: July 19, 1999

I. Conditions for Dissolution Testing:

USP XXIII Basket: x Paddle: RPM: 100  
 No. Units Tested: 12  
 Medium: 0.1 N HCL Volume: 900 ml  
 Specifications: = NLT % in 60 min

Reference Drug: Nicolar®  
Assay Methodology: USP

ii. Results of In Vitro Dissolution Testing:

Sampling Times (Minutes)	Test Product-Niacin Tablets Lot #64892 Strength(mg) 500			Reference Product- Nicolar® Lot # P6910 Strength(mg) 500		
	Mean %	Range	%CV	Mean %	Range	%CV
10	100.3		2.5	62.9		18.3
20	100.5		2.4	90.7		7.0
30	100.4		2.4	98.9		2.6
40	100.4		2.5	100.5		2.5
60	100.7		2.3	100.8		2.4

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-378

APPLICANT: Upsher-Smith

DRUG PRODUCT: Niacin Tablets 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,

ISI



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