CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-200/S-001

BIOEQUIVALENCE REVIEW(S)

21

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # 76-200 SPONSOR : Corepharma LLC

DRUG AND DOSAGE FORM: Acetaminophen ER Tablets

STRENGTH(S) : 650 mg

TYPES OF STUDIES : N/A.
CLINICAL STUDY SITE(S) : N/A
ANALYTICAL SITE(S) :N/A

STUDY SUMMARY: N/A

DISSOLUTION : The dissolution testing is acceptable.

DSI INSPECTION STATUS

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

PRIMARY REVIEWER : Zakaria Z. Wahba, Ph.D. BRANCH : III

INITIAL : ZZW DATE : 10/3/02

TEAM LEADER : Gur-Jai Pal Singh, Ph.D. BRANCH : III

INITIAL : GJPS DATE : 10/3/02

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

INITIAL : DPC DATE : 10/3/02

Acetaminophen Extended Release Tablets
650 mg
ANDA **76-200**
Reviewer: Z. Wahba
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Corepharm LLC
Middlesex, NJ
Submission Date:
April 18, 2002

Review of A Study Amendment

Background

- The firm previously submitted two in vivo bioequivalence studies under fasting and non-fasting conditions comparing its Acetaminophen Extended Release Tablet, 650 mg, to McNeil Consumer Healthcare's Tylenol® Arthritis Pain Extended Relief Caplet, 650 mg. The submission was reviewed and was found acceptable by the Division of Bioequivalence (the review date 09/26/01).

- In this submission, the firm has submitted a "Changes Being Effected" to its Acetaminophen Extended Release Tablet, 650 mg (ANDA #76-200). The dissolution data for the first three validation batches are provided as per the requirement for approval of drug product.

DISSOLUTION DATA
(information in the Amendment 04/18/02 attachment, volume A 2.1).

Results of *In Vitro* Dissolution Testing.

No. Units Tested: 12 tablets
USP 25 apparatus: 2 (Paddle)
Medium: Simulated Gastric Fluid without enzyme, pH 1.2
Volume: 900 mL
RPM: 50
Temperature: 37°C
Specification:

Time (min)	Mean (% of claim)
15	[redacted]
60	[redacted]
180	NLT [redacted]

Sampling Times (Min)	Acetaminophen ER Tablets Lot #CPA223 Strength(mg) 650 mg			Acetaminophen ER Tablets Lot #CPB213 Strength(mg) 650 mg		
	Mean	Range	%CV	Mean	Range	%CV
15	53.9	[redacted]	3.6	54.2	[redacted]	2.6
30	59.8		3.1	60.3		1.8
45	63.3		3.2	64.1		2.4
60	67.6		3.5	69.0		2.6
120	79.4		3.2	83.5		3.7
180	88.4		2.3	94.0		1.2
Sampling Times (Min)	Acetaminophen ER Tablets Lot #CPB214 Strength(mg) 650 mg					

	Mean	Range	%CV	Mean	Range	%CV
15	54.6		3.3			
30	59.2		2.0			
45	63.9		2.3			
60	69.8		3.3			
120	83.7		5.2			
180	93.8		2.4			

Comment on the dissolution data:
The dissolution testing and data for the three lots are acceptable.

Recommendations

The dissolution testing and data submitted by the firm are 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 Simulated Gastric Fluid without enzyme pH 1.2 using USP 25 apparatus II (paddle) at 50 rpm. The test product should meet the following specifications:

Time (min)	Mean (% of claim)
15	___
60	___
180	NLT ___

Zakaria Z. Wahba

Zakaria Z. Wahba, Ph.D.
Review Branch III
Division of Bioequivalence

RD INITIALED GJPSINGH
FT INITIALED GJPSINGH Date: 10-3-02

Concur: Dale P. Conner Date: 10/3/02
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:76-200 APPLICANT: Corepharma LLC

DRUG PRODUCT: Acetaminophen Extended Release Tablets, 650 mg.

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

We acknowledge that the following dissolution testing has been incorporated into your stability and quality control programs:

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 Simulated Gastric Fluid without enzyme pH 1.2 using USP 25 apparatus II (paddle) at 50 rpm. The test product should meet the following specifications:

Time (min)	Mean (% of claim)
16	[redacted]
60	[redacted]
180	NLT [redacted]

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 P. Conner

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

CC:ANDA 76-200
DIVISION FILE
HFD-651/ Bio Drug File
HFD-658/ Reviewer
HFD-658/ Team Leader

Endorsements:
HFD-658/ Z. Wahba ZW 10/3/02
HFD-658/ GJP Singh GJPS 10/3/02
HFD-650/ D. Conner AMH 10/3/02

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BIOEQUIVALENCY - ACCEPTABLE

Submission date: 04/18/02

1. Study Amendment (STA).

Strength: 650 mg
Outcome: AC

NOTE:

AC - Acceptable
NC - No Action
UN - Unacceptable
IC - Incomplete

Outcome Decision: ACCEPTABLE

WINBIO COMMENTS: **ACCEPTABLE**

APPEARS THIS WAY
ON ORIGINAL