

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
40254

BIOEQUIVALENCY REVIEW(S)

OCT - 5 1997

Trihexyphenidyl HCl
2 mg and 5 mg Tablets
ANDA # 40-254
Reviewer: Jahnvi S. Kharidia
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Vintage Pharmaceuticals, Inc.
3241 Woodpark Blvd
Charlotte, NC 28206
Submission Date:
April 28, 1997

Review of Dissolution Data and Waiver Requests

Objective:

The firm requested waivers of bioequivalence study requirements for its test products Trihexyphenidyl HCl 2 mg and 5 mg Tablets and has submitted dissolution data in support of its request.

Formulations:

Formulation of Vintage's Trihexyphenidyl HCl 2 mg and 5 mg Tablets are shown in Table 1.

Table 1. Formulation (NOT TO BE RELEASED UNDER FOI)

Ingredient (mg per tablet)	Trihexyphenidyl HCl 2 mg Tablet	Trihexyphenidyl HCl 5 mg Tablet
Trihexyphenidyl HCl	2.0	5.0
Microcrystalline Cellulose, NF PH102		
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total Weight		

Dissolution Data:

The firm has submitted comparative dissolution data on its products Trihexyphenidyl HCl 2 mg and 5 mg Tablets and the listed reference drug products Artane® (Trihexyphenidyl HCl) 2 mg and 5 mg Tablets, manufactured by Lederle using the following dissolution conditions:

Method: USP 23, apparatus I (basket) at 100 rpm
pH 4.5 acetate buffer, 900 mL
12 tablets

Specifications: NLT % in 45 minutes

Dissolution testing results are shown in Table 2.

Comments:

1. Dissolution results for the test products Trihexyphenidyl HCl 2 mg and 5 mg Tablets are acceptable.

2. Trihexyphenidyl HCl 2 mg and 5 mg Tablets are coded AA in the Orange Book.
3. Waivers of bioequivalence study requirements for the test products may be granted based on CFR 320.22 (c).

Recommendations:

1. The dissolution testing conducted by Vintage Pharmaceuticals, Inc., on its Trihexyphenidyl HCl 2 mg and 5 mg Tablets, lot #049116 and lot # 057106, respectively, is acceptable. Waivers of *in vivo* bioequivalence study requirements for the test products are granted based on CFR 320.22 (c). From the bioequivalence point of view, the Division of Bioequivalence deems the Trihexyphenidyl HCl 2 mg and 5 mg Tablets to be bioequivalent to the reference products Artane® 2 mg and 5 mg Tablets, respectively, manufactured by Lederle.
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 acetate buffer pH 4.5 at 37° C using USP 23 apparatus I (basket) at 100 rpm. The test products should meet the following specifications:

Not less than % of the labeled amount of drug in the dosage form are dissolved in 45 minutes

The firm should be informed of the above recommendations.

/S/

Jahnvi S. Kharidia, Ph.D.
 Review Branch III
 The Division of Bioequivalence

RD INITIALED RMHATRE _____ **/S/** _____ Date 9/19/97
 FT INITIALED RMHATRE _____
 Ramakant M. Mhatre, Ph.D.
 Team Leader, Branch III
 Division of Bioequivalence

Concur: _____ **/S/** _____ ^{mail} Date 10/5/97
 for Nicholas Fleischer, Ph.D.
 Director
 Division of Bioequivalence

Table 2. In Vitro Dissolution Testing

Drug (Generic Name): Trihexyphenidyl HCl Tablets
 Dose Strength: 2 mg and 5 mg
 ANDA No.: 40-254
 Firm: Vintage Pharmaceuticals Inc.
 Submission Date: April 28, 1997

I. Conditions for Dissolution Testing: USP Method

USP XXIII Basket: X Paddle: RPM: 100
 No. Units Tested: 12
 Medium: pH 4.5 acetate buffer, 900 mL
 Specifications: NLT % in 45 minutes
 Reference Drug: Artane® 2 mg and 5 mg Tablets

II. Results of In Vitro Dissolution Testing:

Sampling Times (Minutes)	Test Product Lot #049116 Strength(mg) 2 Potency: 96.3 %			Reference Product Lot #437-134 Strength(mg) 2 Potency: 99.6 %		
	Mean %	Range	%CV	Mean %	Range	%CV
10	84.2		3.44	92.9		1.40
20	90.3		2.21	98.4		1.32
30	92.2		4.01	98.6		1.22
45	94.0		3.30	98.9		1.21

Sampling Times (Minutes)	Test Product Lot #057106 Strength(mg) 5 Potency: 98.6%			Reference Product Lot #336-367 Strength(mg) 5 Potency: 104.5%		
	Mean %	Range	%CV	Mean %	Range	%CV
10	81.2		4.06	98.6		2.94
20	91.3		0.99	102.2		2.64
30	93.1		0.64	102.8		2.63
45	93.8		0.64	103.1		2.72