CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40191

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #40-191
SPONSOR: Vintage Pharmaceuticals, Inc.
DRUG: Meperidine Hydrochloride
DOSAGE FORM: Tablets
STRENGTH: 50 mg and 100 mg
REFERENCE PRODUCT: Winthrop's Demerol® Tablets 50 mg and 100 mg.
SUBMISSION TYPE: Waiver

STUDY SUMMARY: Not Applicable

DISSOLUTION: The comparative dissolution testing data are acceptable.

WAIVER SUMMARY: The waiver of the *in vivo* bioequivalence study for the test product, Meperidine HCl Tablets 50 mg and 100 mg is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product formulation to be bioequivalent to the reference drug Winthrop's Demerol® Tablets 50 mg and 100 mg.

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

INITIAL: /S/ DATE: 12/22/97

GROUP LEADER: Ramakant Mhatre, Ph.D. BRANCH: III

INITIAL: /S/ DATE: 12/22/97

DIRECTOR: Dale Conner, Pharm.D.
DIVISION OF BIOEQUIVALENCE

INITIAL: /S/ DATE: 12/23/97

DIRECTOR
OFFICE OF GENERIC DRUGS

INITIAL: DATE:

JAN 2 1997

Meperidine Hydrochloride
50 and 100 mg Tablets
ANDA **#40-191**
Reviewer: Z.Z. Wahba
File #40191dw.696

Vintage Pharmaceuticals, Inc.
Charlotte, NC
Submission Date:
June 05, 1996

Review of Dissolution Data and Two Waiver Requests

I. BACKGROUND

1. The firm has submitted an application for two strengths of meperidine HCl tablets and has requested waivers for *in vivo* bioequivalence testing requirements based on 21 CFR 320.22.

2 The reference listed product is Winthrop's Demerol® Tablets 50 mg and 100 mg.

3 The firm has conducted dissolution testing on the two strengths of the test products and the corresponding two strengths of Demerol® Tablets.

4 The drug product is classified "AA" in the list of the "Approved Drug Products with Therapeutic Equivalence Evaluations".

5 Meperidine hydrochloride is a narcotic analgesic. The principal actions of therapeutic value are analgesia and sedation.

II. FORMULATION

Formulation of Vintage's Meperidine Hydrochloride Tablets, 50 mg and 100 mg are presented in the following Table.

No.	Ingredient	50 mg Strength mg/tablet	100 mg Strength mg/tablet
1	Meperidine HCl, USP		
2	Pregelatinized Starch, NF		
3	Microcrystalline Cellulose, USP		
4	Sodium Starch Glycolate, NF		
5	Stearic Acid, NF		
	Total		

III. DISSOLUTION

The firm has submitted dissolution data for the test and reference products applying the following conditions:

Method:	USP 23 apparatus I (Basket) at 100 rpm
Medium:	500 ml water
Temperature:	37°C ± 0.5°C
Number of Units:	12 Tablets
Specification:	NLT % (Q) is dissolved in 45 minutes

Test product: Meperidine Hydrochloride 50 mg Tablets, lot #062105
Meperidine Hydrochloride 100 mg tablets, lot #063105

Reference product: Demerol® 50 mg and 100 mg Tablets, lot # NL419 and # NJ328, respectively

ASSAY POTENCY AND CONTENT UNIFORMITY

1. The test product assay and content uniformity

   For 50 mg Strength
   Assay mean = %
   Content uniformity = % (CV=2.0%)

   For 100 mg Strength
   Assay mean = %
   Content uniformity = % (CV=1.1%)

2. The reference product assay and content uniformity

   For 50 mg Strength
   Assay mean = %
   Content uniformity = % (CV=1.8%)

   For 100 mg Strength
   Assay mean = %
   Content uniformity = % (CV=1.7%)

Table 1. In Vitro Dissolution Testing

Drug (Generic Name): Meperidine HCl
Dose Strength: 50 mg and 100 mg
ANDA No.: 40-191
Firm: Vintage
Submission Date: June 05, 1996
File Name: 40191dw.696

I. Conditions for Dissolution Testing:

USP 23 Basket: X Paddle: RPM: 100
No. Units Tested: 12
Medium: water Volume: 500 mL
Specifications: NLT % (Q) is dissolved in 45 minutes
Reference Drug: Demerol® 50 mg and 100 mg
Assay Methodology:

II. Results of In Vitro Dissolution Testing:

Sampling Times (Minutes)	Test Product Lot #062105 Strength(mg) 50			Reference Product Lot #NL419 Strength(mg) 50		
	Mean %	Range	%CV	Mean %	Range	%CV
10	90.8		4.5	79.8		5.9
20	96.3		2.3	98.2		2.4
30	97.4		2.1	98.6		2.4
45	98.8		1.9	100.0		3.1

Sampling Times (Minutes)	Test Product Lot #063105 Strength(mg) 100			Reference Product Lot #NJ328 Strength(mg) 100		
	Mean %	Range	%CV	Mean %	Range	%CV
10	66.7		6.6	56.2		3.4
20	95.4		2.4	90.9		3.3
30	98.1		2.7	95.5		2.6
45	98.2		1.8	97.5		2.1

IV. COMMENTS

1. The drug product is classified "AA" in the list of the "Approved Drug Products with Therapeutic Equivalence Evaluations".

2. The formulations of meperidine hydrochloride 50 mg and 100 mg tablets are identically proportional.

3. The dissolution data for the test product is acceptable.

4. The waiver of in vivo bioequivalence study requirements should be granted based on 21 CFR section 320.22(c) of the Bioavailability/Bioequivalence Regulations.

V. RECOMMENDATION

1. The Division of Bioequivalence agrees that the information submitted by Vintage Pharmaceuticals, Inc. on its drug product, Meperidine HCl falls under 21 CFR section 320.22 (c) of the Bioavailability/Bioequivalence Regulations. The waiver of in vivo bioequivalence study for the drug is granted. From the Bioequivalence point of view, the Division of Bioequivalence deems the firm's test product, Meperidine HCl Tablets 50 mg and 100 mg are deemed bioequivalent to the reference listed product, Winthrop's Demerol® Tablets 50 mg and 100 mg.

2. The dissolution testing conducted by Vintage Pharmaceuticals, Inc. on its drug product, Meperidine HCl Tablets 50 mg and 100 mg is acceptable.

3. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 500 ml of H_2O, at 37°C using Apparatus I (Basket) at 100 rpm. The test product should meet the following specifications:

   Not less than % of the labeled amount of each drug in the tablet is dissolved in 45 minutes.

The firm should be informed of the recommendation.

/S/

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

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FT INITIALLED RMHATRE

/S/ 12/30/96

Concur: /S/ Date: 1/2/97
Rabindra Patnaik, Ph.D.
Acting Director
Division of Bioequivalence

cc: ANDA# 40-191, original, HFD-630 (OGD), HFD-604 (Hare), HFD-658 (Mhatre, Wahba), Drug File
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