CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40231

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #40-231
SPONSOR: Pharmaceutical Associates, Inc.
DRUG: Chlorpromazine HCl
DOSAGE FORM: Oral Concentrate
STRENGTH: 30 mg/mL
REFERENCE PRODUCT: SmithKline Beecham's Thorazine® Oral Concentrate 30 mg/mL.
SUBMISSION TYPE: Waiver

STUDY SUMMARY: Not Applicable

DISSOLUTION: Not Applicable

WAIVER SUMMARY: The waiver of the *in vivo* bioequivalence study for the test product, Chlorpromazine HCl Oral Concentrate, 30 mg/mL is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product formulation to be bioequivalent to the reference drug SmithKline Beecham's Thorazine® Oral Concentrate 30 mg/mL.

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

INITIAL: /S/ DATE: 4/10/97

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

INITIAL: /S/ DATE: ~~4/17/97~~ 5/7/97

DIRECTOR: Nicholas Fleischer, Ph.D.
DIVISION OF BIOEQUIVALENCE

INITIAL: /S/ DATE: 5/19/97

DIRECTOR
OFFICE OF GENERIC DRUGS

INITIAL: _____ DATE: _____

MAY 13 1997

Chlorpromazine HCl
Oral Concentrate, 30 mg/mL
ANDA #**40-231**
Reviewer: Z.Z. Wahba
File# 40231w.d96

Pharmaceutical Associates, Inc.
Greenville, SC
Submission Date:
December 20, 1996

REVIEW OF A WAIVER REQUEST

I. BACKGROUND

The firm has requested a waiver of in vivo bioavailability study requirements for its drug product, Chlorpromazine Hydrochloride Oral Concentrate, 30 mg/mL. The reference drug product is SmithKline Beecham's Thorazine® Oral Concentrate 30 mg/mL.

II. FORMULATION COMPOSITION (should not be released under FOI)

Ingredient	mg/mL
Chlorpromazine HCl, USP	30 mg
Saccharin Sodium, USP %	mg
Sodium Benzoate, NF %	mg
Edetate Calcium Disodium %	mg
Citric Acid, USP %	mg
Ascorbic Acid, USP %	mg
Sodium Bisulfite, FCC %	mg
Glycerin, USP %	mL
Propylene Glycol, USP %	mL
PFC 9772 Ideal Vanilla	mL
Sodium Hydroxide, NF	to adjust pH
Purified Water, USP q.s. to	mL

Note: the reference product contains the following inactive ingredients: calcium disodium edetate, citric acid, flavors, hydroxypropyl methylcellulose, propylene glycol, saccharin sodium, sodium benzoate, water and trace amounts of other inactive ingredients.

III. COMMENTS

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

2. The test drug product does not contain any inactive ingredient(s) that is known to significantly affect absorption of the active drug ingredient or therapeutic moiety.

3. The concentrations that are provided in the statement of chemical composition for all the inactive ingredients except edetate calcium disodium and citric acid fall in the acceptable range of the Agency's Inactive Ingredient Guide. For edetate calcium disodium concentration, once it is diluted as specified in the drug labeling (each dose to be diluted in 60 mL water or fruit juice) the percentage of the concentration falls in the acceptable range of edetate calcium disodium oral solution that is reported in the Agency's Inactive Ingredient Guide. Citric acid is a natural product and present in a lot of food produces and products. Vanilla is used as a flavoring ingredient. Concentrations of citric acid and vanilla that are provided in statement of chemical composition should not cause any safety problems.

4. The waiver of in vivo bioequivalence study requirements should be granted based on 21 CFR section 320.22(b)(3) of the Bioavailability/Bioequivalence Regulations.

IV. RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Pharmaceutical Associates, Inc. for its drug product, Chlorpromazine Hydrochloride Oral Concentrate, 30 mg/mL, falls under 21 CFR section 320.22(b)(3) 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 Chlorpromazine Hydrochloride Oral Concentrate, 30 mg/mL, manufactured by Pharmaceutical Associates, Inc. to be bioequivalent to the reference product, SmithKline Beecham's Thorazine® Oral Concentrate 30 mg/mL.

The firm should be informed of the recommendation.

/S/

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

RD INITIALED RMHATRE
FT INITIALED RMHATRE /S/ 5/7/97

Concur: /S/ Date: 5/13/97
for Nicholas Fleischer, Ph.D.
Director
Division of Bioequivalence

cc: ANDA# 40-231, original, HFD-630 (OGD), HFD-604, HFD-658 (Mhatre, Wahba), Drug File
ZZWahba/040497/041097/050697/file #40231w.d96