CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40226

BIOEQUIVALENCY REVIEW(S)

Jan

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA/AADA #40-226 SPONSOR : Vintage Pharmaceuticals
DRUG & DOSAGE FORM : Perphenazine Tablets USP
STRENGTH (s) : 2, 4, 8 and 16 mg

TYPE OF STUDY:	SD	
STUDY:	XAcceptable	□Not Applicable
DISSOLUTION :	XAcceptable	□Not Applicable
WAIVER:	XAcceptable	□Not Applicable

REVIEWER: Hoainhon Nguyen BRANCH: I
INITIAL: /S/ DATE : 1-27-98

BRANCH CHIEF : Yih-Chain Huang, Ph.D. BRANCH : I
INITIAL : /S/ DATE : 1/27/98

DIRECTOR: Dale Conner, Pharm.D.
DIVISION OF BIOEQUIVALENCE
INITIAL : /S/ DATE : 1/27/98

DIRECTOR
OFFICE OF GENERIC DRUGS
INITIAL : DATE :

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-226 APPLICANT: Vintage Pharmaceuticals

DRUG PRODUCT: Perphenazine Tablets USP, 2 mg, 4 mg, 8 mg, and 16 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,

/S/

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

Perphenazine Tablets USP
ANDA # 40-226: 2 mg, 4 mg, 8 mg & 16 mg
Reviewer: Hoainhon Nguyen
WP #40226a.d97

Vintage Pharmaceuticals
Charlotte, NC
Submission Date:
December 23, 1997

Review of a Study Amendment

The firm has submitted a study amendment in response to the Division of Bioequivalence's Deficiency Comment issued in the letter dated November 30, 1997. The Deficiency Comment, the firm's summarized Response and the DBE's Comment on the firm's Response are given below.

Deficiency Comment:

"Long-term stability data only covered a freezer (-20 °C) storage duration of 33 days (5-week study) while the actual study sample storage time lasted up to 46 days (From April 11 to May 27, 1996). The stability study is therefore insufficient."

Firm's Response:

The firm has submitted in this current amendment the requested long-term stability data. A post-study, 20-week stability study showed that the difference in perphenazine plasma concentration for controls of 0.150 ng/mL, 0.900 ng/mL and 2.50 ng/mL between Time 0 and Time 20 weeks was %, with no degradation trend observed.

DBE's Comments:

1. The firm's response to the Deficiency comment is adequate. The study results as summarized in the last review (dated November 20, 1997) are considered acceptable. The test product is shown to be equivalent to the reference product in the extent and rate of absorption as measured by log-transformed AUCs and CMAX.

2. Dissolution testing for the test and reference products, 2 mg, 4 mg, 8 mg and 16 mg, is acceptable.

3. The formulations of the lower strengths are proportionally similar to the 16 mg strength which underwent the bioequivalence study.

DBE's Recommendations:

1. The single-dose, fasting bioequivalence study conducted by Vintage Pharmaceuticals on the test product, Perphenazine Tablets, 16 mg, lot # 074045, comparing it with the reference product, Trilafon^{R} Tablets, 16 mg, lot # 4-ADM-2, has been found **acceptable** by the Division of Bioequivalence. The test product, Vintage's Perphenazine Tablets, 16 mg, is deemed bioequivalent to the reference product, Trilafon® Tablets, 16 mg, manufactured by Scherings.

2. The in-vitro dissolution testing conducted by Vintage on its Perphenazine Tablets, 2 mg, 4 mg, 8 mg and 16 mg, has been found **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 0.1N HCl at 37^{0}C using USP XXIII apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

> Not less than % of the labeled amount of perphenazine in the dosage form is dissolved in 45 minutes.

3. The firm has demonstrated that the formulations of its Perphenazine Tablets, 2, 4, and 8 mg, are proportionally similar to the 16 mg strength that underwent acceptable in vivo bioequivalence testing. The waiver of in vivo bioequivalence study requirements for the 2, 4, and 8 mg tablets is granted. The firm's Perphenazine Tablets, 2, 4 and 8 mg, are therefore deemed bioequivalent to Trilafon^{R} Tablets, 2, 4 and 8 mg, respectively, manufactured by Scherings.

/S/
Hoainhon Nguyen
Division of Bioequivalence
Review Branch I

RD INITIALED YHUANG
FT INITIALED YHUANG /S/ 1/27/98

Concur: /S/ Date: 1/27/98
Dale Conner, Pharm.D.
Director, Division of Bioequivalence

cc: ANDA # 40-226 (original, duplicate), HFD-652(Huang, Nguyen), Drug File, Division File

Hnguyen/01-26-98/WP #40226a.d97

Attachments: None

Perphenazine Tablets USP
ANDA # 40-226: 2 mg, 4 mg, 8 mg & 16 mg
Reviewer: Hoainhon Nguyen
WP #40226a.697

Vintage Pharmaceuticals
Charlotte, NC
Submission Date:
June 19, 1997

Review of a Study Amendment

The firm has submitted a study amendment in response to the Division of Bioequivalence's Deficiency Comments issued in the letter dated May 12, 1997. The Deficiency Comments, the firm's summarized Responses and the DBE's Comments on the firm's Responses are given below.

Deficiency Comments:

"1. Representative chromatograms submitted were not clearly identified. Code Nos. such as "NM3605", "NM3618"... were not decoded and matched with any actual study samples. The worksheet for each run should be submitted with code no. identified for each sample as well as sequences of samples as formed in each run.

The order in which representative chromatograms submitted should also be clearly explained. It appeared that some batches of chromatograms such as Batch 71 included some chromatograms that did not belong to the batch, such as the chromatograms on page 1639 (based on the run date and retention times of the chromatograms).

2. Please explain, for Batch 71 chromatograms, why retention (or scan) times of the drug and internal standard varied drastically from chromatogram to chromatogram (greater than % deviation from the expected retention times of approximately 1.2 (scan 67) and 1.5(scan 54) minutes for the drug and internal standard, respectively).

The doubling of the retention times and total run time due to adding of a guard column between the validation and the study (from 1.2 and 1.5 minutes to 2.0 and 2.4 minutes for the drug and internal standard, respectively), as explained in the analytical report (pages 1510-1511), was only observed in chromatogram

of Batches 73, 90, 92 and 100 (and not Batch 71), with expected consistency.

3. Complete peak height (or peak area) and peak height (or peak area) ratio data for all study samples, standards and quality controls assayed should be submitted with the anlytical report.

4. Long-term stability data only covered a freezer (-20 °C) storage duration of 33 days (5-week study) while the actual study sample storage time lasted up to 46 days (From April 11 to May 27, 1996). The stability study is therefore insufficient.

5. For the 4-freeze/thaw-cycle stability study, the quality control of 2.50 ng/mL showed an increase of % when compared with Time 0 control. Please explain the significant difference in the control concentrations following 4 cycles of freeze/thaw. Did actual study assays at times require 4 cycles of freeze/thaw?"

Firm's Responses:

1. The firm has provided a key for the translation of NOVOMANN numbers (i.e., NM3618) and copies of the batch worksheets for samples batches which detail sample analysis order within each batch and identify samples by subject, period, hour and NM number.

A corrected copy of Batch 71 has been submitted (Batch Worksheet and corresponding chromatograms). The firm confirmed that there was one chromatogram from Batch 104 that was inadvertently misfiled in Batch 71.

2. The firm has attributed the drastic variation in absolute retention time for analyte and internal standard in Batch 71 to possible "pump flow rate fluctuations, temperature variations, etc.". In order to adjust the shift in internal standard and analyte retention times, the analytical laboratory utilized a software that assigns expected retention time, based on the relative retention time (RRT) ratio (internal standard to analyte retention time) of a calibrator (Std 3.0 ng/ml). The RRT ranges from with an average of 0.81 and a standard deviation of 1.6%.

For Batch 71, no guard column to the analytical column was not available for use. Guard column was used for Batches 73, 90, 92 and 100.

3. The firm has submitted copies of all worksheets for sample batches with peak area and peak area ratio data for study samples, standards and quality controls.

4. *"Data was acquired up to 33 days, however, recent attempts to obtain further data were unsuccessful due to batch failure (problems with deionized water). Unfortunately, these failures depleted the available stability samples in our freezer so the study must be reinitiated."* **The new stability study started June 4, 1997, and the data from this stability study were not submitted in the current amendment.** The firm was telephoned for the data September 16, 1997 and requested that the data be faxed. However, as of September 30, 1997, the Division of Bioequivalence has not received the requested information from the firm. (See the Telephone Memo attached.)

5. According to the firm, *"actual study samples underwent a maximum of up to 8 freeze/thaw cycles"*. The firm has generated more freeze/thaw data over 10 freeze/thaw cycles with 2 replicates at three QC concentrations, 0.150, 0.900 and 2.50 ng/ml. The concentrations were within % of the target concentrations. The % concentration difference found in the 4 cycle-freeze/thaw stability study for the 2.50 ng/ml QC was therefore likely not indicative of analyte instability.

DBE's Comments:

The firm's responses are found satisfactory except for the response No. 4 concerning the long-term stability study (See above.).

The results of the bioequivalence study are reviewed below.

Assay Methodology:

Assay Specificity:

The assay was specific for perphenazine with no significant interferences seen at the drug or internal standard retention times in the chromatograms of the pre-dose samples and blank plasma standards.

Linearity:

(Based on actual study standard curves)

The assay was linear in the range of ng/ml.

Reproducibility:

(Based on actual study quality controls)

Interday CV's were: 8.6% at 0.150 ng/ml, 9.1% at 0.900 ng/ml and 11.7% at 2.50 ng/ml.

Sensitivity:

(Based on actual study standard data)

Sensitivity limit was 0.05 ng/ml (CV% = 2.0). Any level below this limit was reported as zero.

Pre-study validation CV% for QC of 0.05 ng/ml was 10 (n=5).

Accuracy:

(Based on actual study quality controls)

Percent recovery of control samples were: 101% at 0.150 ng/ml, 103% at

0.900 ng/ml and 108% at 2.50 ng/ml.

Stability:

For long-term stability study, see Firm's Response No. 4.

Stability of processed samples in reconstitution solvent at 4^0C and at room temperature for 24 and 48 hours was confirmed(% difference). Stability of plasma samples at room temperature for 24 hours was also confirmed (% difference). Stability of 4 freeze/thaw cycles was acceptable at concentrations of 0.150 ng/mL(% difference) and 0.900 ng/mL(% difference), but questionable at 2.50 ng/mL(% difference).

Pharmacokinetic Results:

AUC(0-T) was calculated using method. AUC(0-Infinity) was calculated by : AUC(0-Infinity) = AUC(0-T) + [last measured concentration/ KEL]. CMAX and TMAX were observed values of the peak plasma concentration and time to peak plasma concentration, respectively. KEL and T1/2 were calculated from the portion of the log concentration versus time curve.

Statistical Analyses:

Analysis of variance and F-test were used to determine statistically significant (p less than 0.05) differences between treatments, sequences of treatment, subjects within sequence, and days of administration for the above pharmacokinetic parameters as well as for the plasma concentrations at each sampling time. The 90% confidence intervals for AUC's, CMAX, lnAUC's and lnCMAX were calculated, based on least squares means, using the two, one-sided t-test.

(NOTE: ANOVA was repeated with Subjects # 11 and 18 dropped from the data set due to their CMAX's (both under Treatment A) being the first non-zero plasma concentration. 90% confidence intervals for log-transformed AUCT, AUCI and CMAX without these two subjects were within [0.80;1.25] (They were [0.91;1.02], [0.93;1.04], and [0.91;1.06], respectively).)

Results:

Twenty-seven of thirty enrolled volunteers completed the clinical portion of the study. Subject # 5 was withdrawn from the study because of positive drug screen. Subjects #8 and 10 were withdrawn from the study for disruptive behavior on Day 1, Period 2. The statistical analysis was performed using 27 data sets.

There was no significant difference (alpha=0.05) between treatments for AUC (0-T), AUC (0-Infinity), CMAX, lnAUC(0-T), lnAUC(0-Infinity) and lnCMAX. The results are summarized in the tables below:

Table I

Perphenazine Comparative Pharmacokinetic Parameters

Dose = 16 mg; n = 27

Parameters	Vintage's Mean (CV%)	Trilafon® Mean (CV%)	90% C.I.	Ratio T/R
AUC (0-T) ng.hr/ml	5.373*	5.447*	[0.93;1.05]	0.99
AUC (0-Inf) ng.hr/ml	6.673* (n=21)	6.601* (n=22)	[0.94;1.08]	1.01
CMAX(ng/ml)	0.546*	0.548*	[0.92;1.08]	1.00
TMAX (hrs)	2.15(60)	2.57(53)		
KEL (1/hrs)	0.0820(28) (n=21)	0.0870(28) (n=22)		
T1/2 (hrs)	9.12(28) (n=21)	8.66(31) (n=22)		

*Geometric LS Means

Table II
Comparative Mean Plasma Levels of Perphenazine
ng/ml(CV%)
Dose = 16 mg; n = 27

Hour	Vintage's	Trilafon^{R}
0	0	0
0.50	0.317(48)	0.201(78)
1.0	0.431(37)	0.397(49)
1.5	0.509(42)	0.508(54)
2.0	0.520(55)	0.575(78)
3.0	0.551(77)	0.612(87)
4.0	0.539(86)	0.556(96)
6.0	0.465(104)	0.493(117)
8.0	0.421(104)	0.444(121)
12.0	0.229(105)	0.240(107)
16.0	0.184(110)	0.190(119)
24.0	0.0810(142)	0.0859(131)
36.0	0.0249(220)	0.0270(216)
48.0	0.0075(361)	0.0083(360)
AUC(0-T)ng.hr/ml	7.366(106)	7.706(116)
AUC(0-Inf)ng.hr/ml	9.299(95)	9.305(109)
CMAX	0.641(71)	0.671(83)

Adverse Effects:

None of the adverse reactions reported was serious. During the Test Treatment, there were mild to moderate drug-related reactions of twitching neck, blurred vision, dizziness, vomiting, restlessness, dry lips, eyes watering, tiredness, muscle spasms, stiffness, headache, elevated pulse rate, sleepiness, restlessness, teeth grinding, drowsiness, jaw stiffness, lightheadedness and sore throat (29 reactions reported by 14 subjects). During the Reference Treatment, there were mild to moderate drug-related reactions of headache, tiredness, muscle spasms, dizziness, nervousness, edginess, drooling, dry mouth, elevated blood pressure, body twitching and restlessness (19 reactions reported by 11 subjects).

III. Dissolution Testing: USP method and specifications were used.

Drug (Generic Name): Perphenazine Tablets Firm: Vintage Pharmaceuticals
Dose Strength: 16, 8, 4, and 2 mg ANDA # 40-226
Submission Date: December 6, 1996

Table - In-Vitro Dissolution Testing - USP Method

I. Conditions for Dissolution Testing:
USP XXIII Basket __ Paddle X RPM 50 No. Units Tested: 12
Medium: 0.1N HCl Volume: 900 ml
Reference Drug: (Manuf.) Trilafon[R]; Scherings
Assay Methodology: _____
USP Specification: NLT % dissolved in 45 minutes

II. Results of In-Vitro Dissolution Testing:

Sampling Times (min)	Test Product Lot # 071045 Strength (mg) 2 Mean % Dissolved	Range	(S.D.)	Reference Product Lot # 5-ADH-1 Strength (mg) 2 Mean % Dissolved	Range	(S.D)
5	84.3		(6.5)	1.0		(2.3)
15	95.8		(3.5)	62.2		(13.1)
30	96.9		(2.7)	97.9		(3.9)
45	97.4		(2.0)	103.1		(3.3)

Sampling Times (min)	Test Product Lot # 072045 Strength (mg) 4 Mean % Dissolved	Range	(S.D.)	Reference Product Lot # 4-ADK-3 Strength (mg) 4 Mean % Dissolved	Range	(S.D)
5	86.8		(6.0)	5.1		(1.3)
15	95.2		(2.2)	63.6		(11.6)
30	96.4		(1.6)	98.9		(3.1)
45	96.8		(1.3)	102.6		(2.2)

Sampling Times (min)	Test Product Lot # 073045 Strength (mg) 8			Reference Product Lot # 4-ADJ-2 Strength (mg) 8		
	Mean % Dissolved	Range	(S.D.)	Mean % Dissolved	Range	(S.D)
5	77.7		(11.4)	4.5		(1.0)
15	95.4		(2.9)	42.8		(18.0)
30	96.9		(2.8)	92.4		(6.1)
45	98.2		(2.5)	99.36		(2.4)

Sampling Times (min)	Test Product Lot # 074045 Strength (mg) 16			Reference Product Lot # 4-ADM-2 Strength (mg) 16		
	Mean % Dissolved	Range	(S.D.)	Mean % Dissolved	Range	(S.D)
5	80.8		(5.2)	0		(0)
15	95.0		(2.6)	41.6		(29.0)
30	97.1		(2.2)	88.6		(7.9)
45	97.8		(1.9)	94.7		(4.8)

IV. Comparative Formulations: See Attachments.

V. Deficiency:

The deficiency concerning the long-term stability study has not been addressed satisfactorily in this amendment. See the firm's response No. 4 above.

Until all questions concerning the assay method validation are addressed adequately, the study results may not be considered valid.

V. Comments:

1. Dissolution testing for the test and reference products, 2 mg, 4 mg, 8 mg and 16 mg, is acceptable.

2. The formulations of the lower strengths are proportionally similar to the 16 mg strength which underwent the bioequivalence study.

VI. Recommendation:

The single-dose, fasting bioequivalence study conducted by Vintage Pharmaceuticals on the test product, Perphenazine Tablets, 16 mg, lot # 074045, comparing it with the reference product, Trilafon[R] Tablets, 16 mg, lot # 4-ADM-2, has been found **incomplete** by the Division of Bioequivalence due to the reasons cited in the Deficiency above.

The firm should be informed of the Recommendation and Deficiency.

/S/
Hoaimhon Nguyen
Division of Bioequivalence
Review Branch I

/S/ 10/7/97
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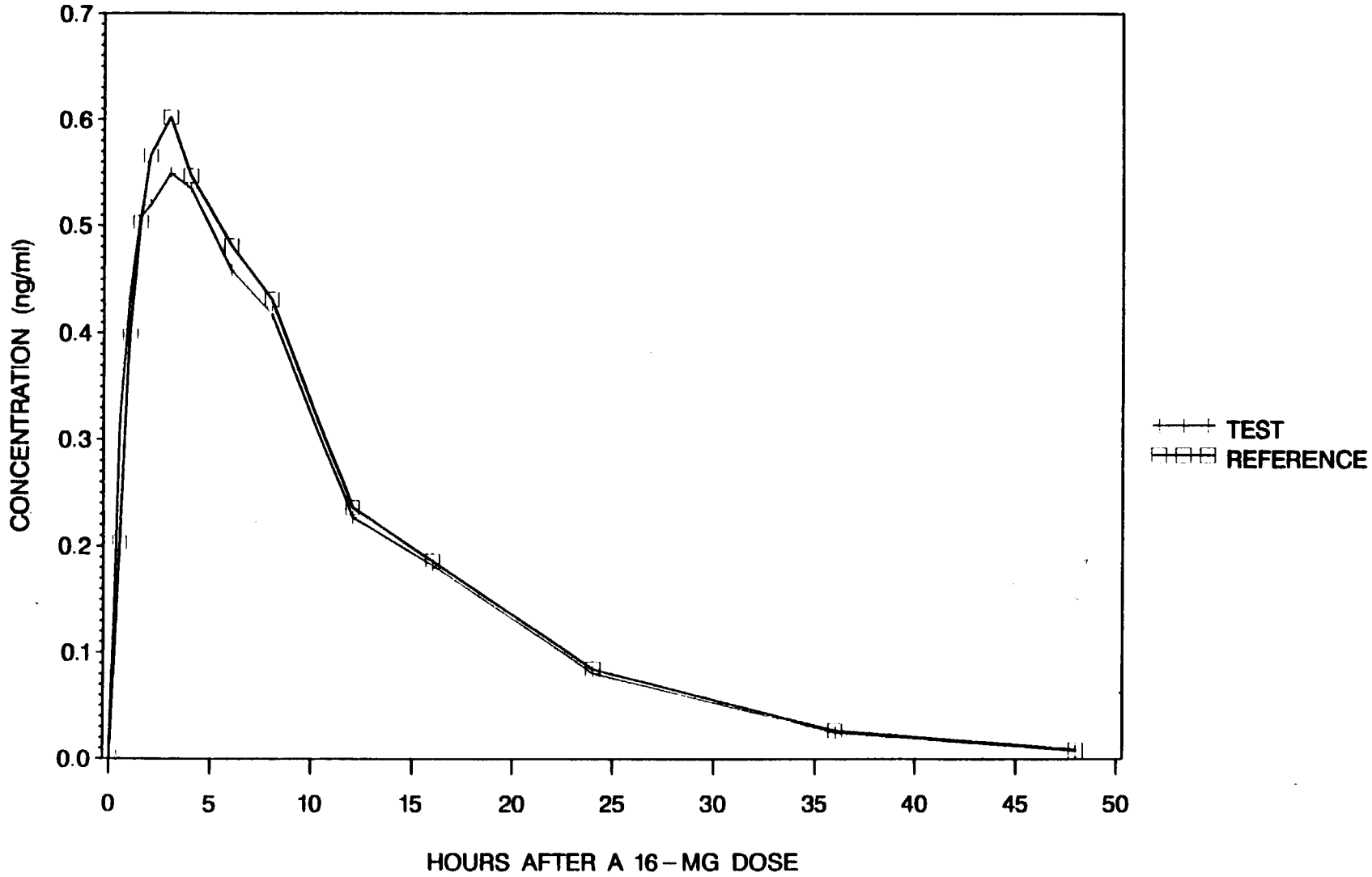
/S/
Concur: _____ Date: 11/20/97
Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence

NP # 40226 a. 697 Attachment (Page 1 of 10)

PERPHENAZINE STUDY NO. 9528044D

LEAST-SQUARES MEAN PLASMA CONCENTRATIONS (N=27)



WF # 40226 a. 697 Attachment (Page 2 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

COMPONENTS AND COMPOSITION STATEMENT
Perphenazine Tablets
2 mg

Ingredient	per tablet	Quantity per batch
Perphenazine, USP	2.00 mg	g
Microcrystalline Cellulose, NF PH101	mg	kg
Lactose Monohydrate, NF DC	mg	kg
Sodium Starch Glycolate, NF	mg	kg
Magnesium Stearate, NF	mg	g
Total Core Weight	mg	kg
Sugar Coating/Printing		
% excess is added where indicated for potential process loss associated with coating of tablets)		
Eudragit E-100	mg	g
Sucrose, NF	mg	kg
Calcium Carbonate, USP	mg	kg
Talc, USP	mg	kg
Povidone, USP K-30	mg	g
Titanium Dioxide, USP	mg	g
	mg	kg
Sucrose Syrup		
Titanium Dioxide, USP		
Povidone, USP		
Synthetic Black Iron Oxide	mg/tablet)	
Sodium Benzoate, USP		
*refer to DMF page 3561 for further quantitative information		
Isopropyl Alcohol, USP	mg	kg
Acetone, NF	mg	kg
Purified Water, USP	mg	kg
Carnauba Wax, NF	mg	g

WP # 40226 a. 697 Attachment (Page 3 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

2212 Fine Black Ink* mg g
- Pharmaceutical Glaze, Shellac, NF %
- Polyvinylpyrrolidone, Food Grade NF %
- Polyethylene Glycol 600, USP %
- Isobutyl Alcohol %
- Purified Black Iron Oxide % mcg/tablet)

*refer to DMF for further quantitative information

XI Thinner (%

Total weight mg kg

/S/ 9/30/96
Approved - Manufacturing Date

/S/ 9/30/96
Approved - Regulatory Affairs Date

WP # 40226a.697 Attachment (Page 4 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

COMPONENTS AND COMPOSITION
STATEMENT
Perphenazine Tablets
4 mg

Ingredient	per tablet	Quantity per batch
Perphenazine, USP	mg	kg
Microcrystalline Cellulose, NF PH101	mg	kg
Lactose Monohydrate, NF DC	mg	kg
Sodium Starch Glycolate, NF	mg	kg
Magnesium Stearate, NF	mg	g
Total Core Weight	mg	kg

Sugar Coating/Printing

% excess is added where indicated for potential process loss associated with coating of tablets)

Eudragit E-100	mg	g
Sucrose, NF	mg	kg
Calcium Carbonate, USP	mg	kg
Talc, USP	mg	kg
Povidone, USP K-30	mg	g
Titanium Dioxide, USP	mg	g
	mg	kg

Sucrose Syrup
Titanium Dioxide, USP
Povidone, USP
Synthetic Black Iron Oxide mg/tablet)
Sodium Benzoate, USP
*refer to DMF page 3561 for further quantitative information

Isopropyl Alcohol, USP	mg	kg
Acetone, NF	mg	kg
Purified Water, USP	mg	kg
Carnauba Wax, NF	mg	g

WP # 40226a.697 Attachment (Page 5 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

2212 Fine Black Ink*		mg	g
Pharmaceutical Glaze, Shellac, NF	%		
Polyvinylpyrrolidone, Food Grade NF	%		
Polyethylene Glycol 600, USP	%		
Isobutyl Alcohol	%		
Purified Black Iron Oxide	%	mcg/tablet)	
*refer to DMF for further quantitative information			
XI Thinner	%		
Total weight		mg	kg

/S/ 9/30/96
Approved - Manufacturing Date

/S/ 9/30/96
Approved - Regulatory Affairs Date

Wf# 40226a.697 Attachment (Page 6 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

COMPONENTS AND COMPOSITION STATEMENT
Perphenazine Tablets
8 mg

Ingredient	per tablet	Quantity per batch
Perphenazine, USP	8.00 mg	1 kg
Microcrystalline Cellulose, NF PH101	mg	kg
Lactose Monohydrate, NF DC	mg	kg
Sodium Starch Glycolate, NF	mg	kg
Magnesium Stearate, NF	mg	g
Total Core Weight	mg	kg

Sugar Coating/Printing

% excess is added where indicated for potential process loss associated with coating of tablets)

Eudragit E-100	mg	kg
Sucrose, NF	mg	kg
Calcium Carbonate, USP	mg	kg
Talc, USP	mg	kg
Povidone, USP K-30	mg	kg
Titanium Dioxide, USP	mg	g
	mg	kg

Sucrose Syrup
Titanium Dioxide, USP
Povidone, USP
Synthetic Black Iron Oxide mg/tablet)
Sodium Benzoate, USP
*refer to DMF page 3561 for further quantitative information

Isopropyl Alcohol, USP	mg	kg
Acetone, NF	mg	kg
Purified Water, USP	mg	kg
Carnauba Wax,NF	mg	g

WP# 40226 a. 697 Attachment (Page 7 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

2212 Fine Black Ink*	mg	g
Pharmaceutical Glaze, Shellac, NF	%	
Polyvinylpyrrolidone, Food Grade NF	%	
Polyethylene Glycol 600, USP	%	
Isobutyl Alcohol	%	
Purified Black Iron Oxide	% (mcg/tablet)	
*refer to DMF for further quantitative information		
XI Thinner %		
Total weight	475.23 mg	1460.610 kg

/S/ 9/30/96
Approved - Manufacturing Date

/S/ 9/30/96
Approved - Regulatory Affairs Date

WP# 40226a. 697 Attachment (Page 8 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

COMPONENTS AND COMPOSITION
STATEMENT
Perphenazine Tablets
16 mg

Ingredient	per tablet	Quantity per batch
Perphenazine, USP	16.00 mg	kg
Microcrystalline Cellulose, NF PH101	mg	kg
Lactose Monohydrate, NF DC	mg	kg
Sodium Starch Glycolate, NF	mg	kg
Magnesium Stearate, NF	mg	g
Total Core Weight	mg	kg
Sugar Coating/Printing		
% excess is added where indicated for potential process loss associated with coating of tablets)		
Eudragit E-100	mg	kg
Sucrose, NF	mg	kg
Calcium Carbonate, USP	mg	kg
Talc, USP	mg	kg
Povidone, USP K-30	mg	kg
Titanium Dioxide, USP	mg	g
	mg	kg
Sucrose Syrup		
Titanium Dioxide, USP		
Povidone, USP		
Synthetic Black Iron Oxide	mg/tablet)	
Sodium Benzoate, USP		
*refer to DMF page 3561 for further quantitative information		
Isopropyl Alcohol, USP	mg	kg
Acetone, NF	mg	kg
Purified Water, USP	mg	kg
Carnauba Wax, NF	mg	g

WP # 40226a. 697 Attachment (Page 9 of 10)

VINTAGE PHARMACEUTICALS, INC.
Perphenazine Tablets, USP
2 mg, 4 mg, 8 mg, 16 mg

2212 Fine Black Ink* mg g
Pharmaceutical Glaze, Shellac, NF %
Polyvinylpyrrolidone, Food Grade NF %
Polyethylene Glycol 600, USP %
Isobutyl Alcohol %
Purified Black Iron Oxide % (mcg/tablet)
*refer to DMF for further quantitative information
XI Thinner (%

Total weight mg kg

/S/ 9/30/96
Approved - Manufacturing Date

/S/ 9/30/96
Approved - Regulatory Affairs Date