

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
74530

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS

DIVISION OF BIOEQUIVALENCE

ANDA # 74-530

SPONSOR: Zenith Laboratories, Inc.

DRUG & DOSAGE FORM : Terazosin Hydrochloride Tablets

STRENGTHS: 1 mg, 2 mg 5 mg, & 10 mg

TYPE OF STUDY: One Fasting Study on the 5 mg Tablet

STUDY SITE: CLINICAL :

ANALYTICAL :

STUDY SUMMARY for the 5 mg Tablet:

Parameter	test (LS Geometric Mean)	ref	ratio	90% CI (log)
<u>C_{max}(pg/ml)</u>	<u>98.41</u>	<u>97.87</u>	<u>1.01</u>	<u>(0.935-1.080)</u>
<u>AUC(0-T) pgxhr/ml</u>	<u>1077.80</u>	<u>1100.32</u>	<u>0.98</u>	<u>(0.935-1.030)</u>
<u>AUC(0-Inf)pgxhr/ml</u>	<u>1123.19</u>	<u>1147.03</u>	<u>0.98</u>	<u>(0.934-1.030)</u>
<u>T_{max} hr</u>	<u>1.186</u>	<u>1.264</u>	<u>0.94</u>	
<u>Half-life hr</u>	<u>13.345</u>	<u>13.159</u>	<u>1.01</u>	

WAIVERS:

Waivers for 1 mg, 2 mg and 10 mg tablets are granted per 21 CFR section 320.22(d)(2).

DISSOLUTION :

Conditions: Paddle apparatus, 50 rpm, 900 mL of water

1 mg Tablet

Time(min)	Test Mean(range)	Ref. Mean(range)
<u>10</u>	<u>97.5</u>	<u>89.3</u>
<u>20</u>	<u>99.8</u>	<u>96.3</u>
<u>30</u>	<u>98.7</u>	<u>96.4</u>
<u>45</u>	<u>99.1</u>	<u>96.7</u>
<u>60</u>	<u>99.5</u>	<u>97.1</u>

2 mg Tablet

Time(min)	Test Mean(range)	Ref. Mean(range)
<u>10</u>	<u>96.6</u>	<u>97.2</u>
<u>20</u>	<u>98.9</u>	<u>102.9</u>
<u>30</u>	<u>98.5</u>	<u>101.4</u>
<u>45</u>	<u>98.7</u>	<u>101.2</u>

DEC 7 1995

Terazosin Hydrochloride
 Tablets, 1, 2, 5 and 10 mg
 ANDA # 74-530
 Reviewer: L. Chuang

Zenith Laboratories, Inc.
 Northvale, NJ
 Submission Date:
 July 12, 1995

**Review of an Amendment to an In-Vivo Bioequivalence Study,
 Dissolution Data and Waiver Request**

The bioequivalence study conducted by the firm on its Terazosin Hydrochloride 5 mg Tablet was found to be incomplete due to a deficiency in the dissolution testing (see attached review of 12/09/94). The firm was advised to conduct all dissolution testings for the test products in water instead of 0.1N HCl as recommended by the Office (Handbook of Drug Dissolution Standards).

The firm conducted dissolution testings according to the recommendation of the Office and the method and results are presented in Table 1 below:

Table 1 - In Vitro Dissolution Testing						
Drug (Generic Name): Terazosin Hydrochloride						
Dose Strength: 1 mg, 2 mg, 5 mg, and 10 mg						
ANDA No.: 74-530						
Firm: Zenith Laboratories						
Submission Date: 7/12/95						
I. Conditions for Dissolution Testing:						
USP XXIII Apparatus: Paddle RPM: 50						
No. Units Tested: 12						
Medium: Water Volume: 900 ml						
Tolerance: NLT % of terazosin (Q) in 30 minutes						
Reference Drug: Hvtrin [®] Tablets (Abbott)						
Assay Methodology:						
II. Results of In Vitro Dissolution Testing:						
Sampling Times (Minutes)	Test Product			Reference Product		
	Mean %	Range	%CV	Mean %	Range	%CV
	Batch # ND-190 Strength (mg): 1			Batch # 57-486-AA-21 Strength (mg): 1		
10	97.5		2.7	89.3		3.1
20	99.8		2.0	96.3		1.8
30	98.7		1.1	96.4		1.5
45	99.1		0.9	96.7		1.2
60	99.5		1.5	97.1		1.1

Sampling Times (Minutes)	Test Product Batch # ND-192 Strength (mg): 2			Reference Product Batch # 58-747-AA-21 Strength (mg): 2		
	Mean %	Range	%CV	Mean %	Range	%CV
10	96.6		2.5	97.2		5.1
20	98.9		1.4	102.9		2.3
30	98.5		1.2	101.4		1.8
45	98.7		1.0	101.2		1.6
60	98.6		1.1	101.1		1.8

Sampling Times (Minutes)	Test Product Batch # ND-193 Strength (mg): 5			Reference Product Batch # 82-449-AA-21 Strength (mg): 5		
	Mean %	Range	%CV	Mean %	Range	%CV
10	96.0		1.6	94.0		4.8
20	96.2		2.8	97.1		1.8
30	98.2		0.7	98.1		1.7
45	98.3		0.8	98.5		1.8
60	98.4		1.0	98.2		1.4

Sampling Times (Minutes)	Test Product Batch # ND-194 Strength (mg): 10			Reference Product Batch # 62-908-AA-21 Strength (mg): 10		
	Mean %	Range	%CV	Mean %	Range	%CV
10	95.8		2.0	90.3		8.3
20	99.2		0.8	98.8		2.2
30	99.8		0.7	101.0		1.4
45	100.3		0.8	101.4		1.3
60	99.9		0.8	101.2		1.5

Comment:

The above dissolution results comply with FDA's specification of "not less than % (Q) of the labeled amount of terazosin is dissolved in 30 minutes".

Waiver Request for Terazosin Hydrochloride Tablets, 1 mg, 2 mg and 10 mg:

The firm is requesting a waiver of requirement for in vivo bioequivalence study on the 1 mg, 2 mg and 10 mg products. Comparative dissolution tests were conducted by the firm on its Terazosin Hydrochloride tablets, 1 mg, 2 mg and 10 mg, compared to Hytrin^R tablets, 1 mg, 2 mg, and 10 mg, respectively, manufactured by Abbott Laboratories. The method and results were presented in Table 1. They have been found to be acceptable.

The comparative formulations of the firm's Terazosin Hydrochloride Tablet, 1 mg, 2 mg, 5 mg and 10 mg were reviewed previously (see review of 12/09/94). The ratios of the weight of each inactive ingredient to the total tablet weight are the same among the 4 strengths of products for each inactive ingredient except that of lactose monohydrate which varies from % . However, this minute difference is acceptable.

Recommendation:

1. The bioequivalence study conducted by Zenith Laboratories, Inc. on its Terazosin Hydrochloride tablet 5 mg, Lot #ND-193, comparing to Hytrin^R 5 mg tablet, lot #82-449-AA-21, manufactured by Abbott Laboratories, in fasting volunteers, has been found acceptable by the Division of Bioequivalence. The study demonstrates that Zenith's Terazosin Hydrochloride 5 mg tablet is bioequivalent to the reference product, Hytrin^R 5 mg tablet, manufactured by Abbott Laboratories, under fasting condition.
2. The dissolution testings conducted by Zenith Laboratories, Inc. on its Terazosin Hydrochloride tablets, 1 mg, 2 mg, 5 mg, and 10 mg, Lot #ND-190, #ND-192, #ND-193, and #ND-194 respectively, comparing to Hytrin^R tablet, 1 mg, 2 mg, 5 mg, and 10 mg respectively, manufactured by Abbott Laboratories, have been found acceptable by the Division of Bioequivalence. The dissolution testings should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of water at 37°C using USP 23 apparatus 2 at 50 rpm. The test products should meet the following specifications:

"not less than % of the labeled amount of terazosin in the dosage form is dissolved in 30 minutes"
3. The waiver of in vivo bioequivalence study requirements for the firm's Terazosin Hydrochloride 1 mg, 2 mg and 10 mg tablets are granted per 21 CFR320.22(d)(2). The 1mg, 2mg and

10 mg tablets of the test product are therefore deemed bioequivalent to Hytrin^R tablet, 1 mg, 2 mg, and 10 mg respectively, manufactured by Abbott Laboratories.

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Lin-whei Chuang
Division of Bioequivalence
Review Branch I

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11/16/95

Concur:

See Dec 5 yr memo
Keith Chan, Ph.D.
Director, Division of Bioequivalence

Date: *12-5/95*

cc: ANDA 74-530 (original, duplicate), HFD-600 (Hare), HFD-630, HFD-344 (CViswanathan), HFD-652 (Huang, Chuang), Drug File, Division File.

DEC 9 1994

Terazosin Hydrochloride
Tablets, 1, 2, 5 and 10
ANDA # 74-530
Reviewer: L. Chuang
WP#74530SDW.894

Zenith Laboratories, Inc.
Northvale, NJ
Submission Date:
August 1, 1994

Review of an In-Vivo Bioequivalence Study, Dissolution Data
and Waiver Request

Introduction:

Terazosin is a quinazoline derivative used for treatment of hypertension. Its vasodilatory hypotensive action is due mainly to the blockade of alpha-1 adrenoreceptors.

Relative to solution, terazosin hydrochloride administered as tablets is completely absorbed in man. It undergoes minimum first-pass metabolism. Peak plasma concentrations of about 20 ng/mL are observed at 1 hour after a 1 mg oral dose and then decline with a half-life of about 12 hours. The drug is highly bound to plasma proteins.

Food had little or no effect on the bioavailability of terazosin but delayed the time to peak concentration by about 1 hour.

Terazosin hydrochloride is commercially available as 1 mg, 2 mg, 5 mg, and 10 mg tablets.

Bioequivalence Study:

The objective of this study is to compare the bioavailability of the firm's 5 mg terazosin hydrochloride tablets with that of Hytrin^R 5 mg tablets, manufactured by Abbott Laboratories, in male volunteers under fasting conditions.

The protocol of the study was prepared by _____ at _____ The clinical portion of the study was conducted during the period of March 26 through April 12, 1994 with _____ as the principal investigator and _____ as the clinical director. The analytical process was conducted at _____ during the period of April 15 through May 5, 1994 with _____ as the analytical investigator.

The design is a single-dose, 2-period, 2-treatment crossover of the test product, Zenith's Terzosin 5 mg Tablet and Hytrin^R 5 mg tablets, manufactured by Abbott Laboratories, in male volunteers under fasting conditions. The St. Charles Community Institutional Review Board approved the protocol and the informed consent form on February 7, 1994.

Thirty-six (36) healthy males, 19-41 years old, weighing within \pm 10% of the ideal weight for height and body frame were recruited. The screening procedures included physical examination, ECG, hematology, blood chemistries, urinalysis, infectious diseases (hepatitis B and HIV) screening and drugs-of-abuse screening.

The exclusion criteria were: history of chronic alcohol consumption, drug addiction, serious illness of any major organs or allergic response to terazosin and related drugs; tobacco usage; blood donation within 1 month prior to the start of the study; intake of any investigational drug; exposure to any known hepatic enzyme inducing or inhibiting agents within 30 days prior to study initiation; and blood pressure less than 60 mmHg after sitting for 3 minutes.

All 36 volunteers were instructed not to take any drugs for two weeks prior to the start of the study, abstain from consuming caffeine and/or xanthine products for 3 days prior to dosing and during the period when blood samples were being collected, abstain from consuming alcohol for 2 days prior to dosing and during the period when blood samples were being collected, and sign the informed consent form. All subjects were fasting for 10 hours prior and 4 hours after subjecting to one of the following randomly assigned drug treatments :

Treatment A - Test Drug: Terazosin tablet, 1 x 5 mg, Zenith lot #ND-193, potency 98.4% and lot size of tablets.

Treatment B - Reference Drug: Hytrin^R tablet, 1 x 5 mg, Abbott lot #82-449-AA-21, expires at 1/1/97, potency 97.7%.

Each treatment was taken with 240 mL of water. All subjects remained seated for 5 hours post-dose, released from the clinical facilities at 24 hour post-dose and returned at 36, 48 and 60 hours post-dose. Blood samples (10 mL each) were drawn into Vacutainers with EDTA at 0, 0.17, 0.33, 0.5, 0.75, 1, 1.5, 2, 3, 5, 8, 10, 12, 16, 24, 36, 48 and 60 hours. Plasma samples were stored at -20°C and shipped to on April 13, 1994.

Resting blood pressure and pulse rate were recorded at 0, 1, 2, 3, 4, 5, 6, 8, 12 and 24 hours post-dose. The washout period between the administration of each formulations was 15 days. Hematology, blood chemistries and urinalysis were conducted at the end of the study.

Analytical Method:

Method Validation:

Results:

Subject #30 suffered from flu symptoms during the wash-out period and was dropped from the study. Thirty-five subjects completed the study. Thirty-nine (39) adverse events were reported by 19 subjects, 16 during treatment A and 23 during treatment B. The majority of the adverse experiences (26 out of 39) was low blood pressure and the remaining complaints were headache, lightheadedness, fatigue, nausea, near syncope and parasternal pain. Almost all were considered to be highly probably related to the drug administered.

Mean blood pressures and pulse rate data obtained from safety monitoring procedures indicated decrease of both systolic and diastolic pressures at 1 hour post-dose. The systolic pressure returned to baseline by 12 hours post-dose and diastolic pressure did not return to baseline until 24 hours post-dose. This phenomenon was similar for both test and reference drugs. Pulse rates seemed to be elevated all through the monitoring period (1-24 hours post-dose) for both products.

Hematology, blood chemistries and urinalysis conducted at the end of the study did not reveal any clinically significant abnormality.

The 1260 study samples were assayed in 19 runs. Each run consisted of a 9-point standard curve and duplicates of QC samples. A run was considered valid if the correlation coefficient was ≥ 0.99 and at least 2/3 of the QC samples were within $\pm 20\%$ of the expected values. At least one QC sample from each concentration must be within $\pm 20\%$ for the run to be accepted. The SOP limits for the standards were $\pm 20\%$ of theoretical values. Out of the 171 standards, 3 were outside the SOP limits, 1 ng/mL of run #17, 2 ng/mL of run #16 and 10 ng/mL of run #10. Out of 114 QC samples, only 1 was outside the $\pm 20\%$ limits. All runs were valid with satisfactory linearity, accuracy and precision. Only 1 out of the 1260 study samples was repeated due to anomalous value. This sample was repeated twice and the median value was used in the final report.

The mean plasma concentrations of terazosin at each sampling point after both treatments in 35 subjects and the mean pharmacokinetic parameters are presented below in Table 1.

The SAS GLM procedure was used for the analysis of variance. The model included sequence, subject within sequence, period and treatment. There were no significant differences between the two periods or the two treatments for any of the following pharmacokinetic parameters: AUC_{0-t} , $LN AUC_{0-t}$, AUC_{0-inf} , $LN AUC_{0-inf}$, C_{max} and $LN C_{max}$. The LS means of AUC_{0-t} , $LN AUC_{0-t}$, AUC_{0-inf} , $LN AUC_{0-inf}$, C_{max} and $LN C_{max}$, ratio of these means and the 90% confidence interval of test product versus reference product are presented in Tables 2.

Table 1

Mean (C.V.%) Plasma Terazosin Concentrations (ng/ml) at Each Sampling Time Point and Arithmetic Means of Pharmacokinetic Parameters (n = 35)

Time (hour)	Treatment A (Zenith)	Treatment B (Abbott)
0	0	0
0.17		
0.33		
0.50		
0.75		
1.00		
1.50		
2.00		
3.00		
5.00		
8.00		
10.00		
12.00		
16.00		
24.00		
36.00		
48.00		
60.00		
AUC _{0-t} (ng*hr/mL)	1111.34 (28)	1125.06 (22)
AUC _{0-inf} (ng*hr/mL)	1160.71 (30)	1175.37 (23)
C _{max} (ng/mL)	101.09 (23)	101.19 (26)
LNAUC _{0-t}	6.984 (3.3)	7.004 (3.0)
LNAUC _{0-inf}	7.025 (3.4)	7.046 (3.1)
LNC _{max}	4.591 (4.9)	4.585 (5.5)
T _{max} (hour)	1.190 (68)	1.262 (54)
T _{1/2} (hour)	13.335 (14)	13.147 (18)

Table 2: Statistical Analysis

<u>Parameter</u>	<u>LS Means (Zenith)</u>	<u>LS Means (Abbott)</u>	<u>Ratio (T/R)</u>	<u>90% Confidence Interval</u>
AUC _{0-t}	1109.55	1123.96	0.987	(93.4; 104)
AUC _{0-inf}	1158.90	1174.42	0.987	(93.0; 104)
C _{max}	100.88	101.00	0.999	(92.3; 107)
LNAUC _{0-t}	6.98268	7.00336	0.980	(93.5; 103)
LNAUC _{0-inf}	7.02393	7.04493	0.979	(93.4; 103)
LNC _{max}	4.58919	4.58366	1.010	(93.5; 108)

Comment:

The conduct and results of the bioequivalence study under fasting condition are satisfactory.

Dissolution Testing:

The firm has submitted dissolution data on its Terazosin Tablet, 5 mg, batch #ND-193, compared to the reference product, Hytrin 5 mg Tablet, batch #82-449-AA-21. The method used and results are presented in Table 3.

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Table 3. In-Vitro Dissolution Testing - 5 mg Tablets

I. Conditions for Dissolution Testing:

USP XXII Basket Paddle xx RPM 50 No. Units Tested: 12
 Medium: 0.1 N HCL Volume: 900 ml
 Reference Drug: (Manuf.) Hytrin^R 5 mg Tablets (Abbott)
 Assay Methodology:

II. Results of In-Vitro Dissolution Testing:

<u>Sampling Times (min)</u>	<u>Test Product</u>			<u>Reference Product</u>		
	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>
		<u>Lot # ND-193</u>			<u>Lot # 82-449-AA-21</u>	
		<u>Strength: 5 mg</u>			<u>Strength: 5 mg</u>	
<u>10</u>	<u>96.0</u>	<u>-</u>	<u>(1.7)</u>	<u>88.0</u>	<u>-</u>	<u>(3.3)</u>
<u>20</u>	<u>97.4</u>	<u>-</u>	<u>(0.9)</u>	<u>94.0</u>	<u>-</u>	<u>(2.4)</u>
<u>30</u>	<u>97.9</u>	<u>-</u>	<u>(1.0)</u>	<u>94.7</u>	<u>-</u>	<u>(2.0)</u>
<u>45</u>	<u>97.4</u>	<u>-</u>	<u>(1.1)</u>	<u>96.0</u>	<u>-</u>	<u>(2.1)</u>
<u>60</u>	<u>97.8</u>	<u>-</u>	<u>(1.0)</u>	<u>97.0</u>	<u>-</u>	<u>(1.9)</u>

Comment:

The FDA dissolution specification for terazosin hydrochloride tablets recommends employing water as the dissolution medium, instead of 0.1 N HCL used by the firm.

Waiver Request for Terazosin Tablets, 1 mg, 2 mg and 10 mg:

The firm is requesting a waiver of requirement for in vivo bioequivalence study on the 1 mg, 2 mg and 10 mg products. Comparative dissolution tests were conducted by the firm on its Terazosin tablets, 1 mg, 2 mg and 10 mg, compared to Hytrin^R tablets, 1 mg, 2 mg, and 10 mg, respectively, manufactured by Abbott Laboratories. The method and results are presented in Tables 4, 5 and 6 respectively.

Table 4. In-Vitro Dissolution Testing - 1 mg Tablets

Conditions for Dissolution Testing:

USP XXII Basket ___ Paddle XX RPM 50 No. Units Tested: 12
 Medium: 0.1 N HCL Volume: 900 ml
 Reference Drug: (Manuf.) Hytrin^K 1 mg Tablets (Abbott)
 Assay Methodology:

II. Results of In-Vitro Dissolution Testing:

<u>Sampling Times (min)</u>	<u>Test Product</u>			<u>Reference Product</u>		
	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>
		<u>Lot # ND-190</u>			<u>Lot # 57-486-AA-21</u>	
		<u>Strength: 1 mg</u>			<u>Strength: 1 mg</u>	
<u>10</u>	<u>96.0</u>		<u>(1.1)</u>	<u>86.5</u>		<u>(4.8)</u>
<u>20</u>	<u>96.2</u>		<u>(1.0)</u>	<u>92.3</u>		<u>(2.6)</u>
<u>30</u>	<u>96.3</u>		<u>(1.1)</u>	<u>94.4</u>		<u>(2.0)</u>
<u>45</u>	<u>96.1</u>		<u>(1.2)</u>	<u>95.8</u>		<u>(1.9)</u>
<u>60</u>	<u>96.2</u>		<u>(1.2)</u>	<u>96.6</u>		<u>(1.6)</u>

Table 5. In-Vitro Dissolution Testing - 2 mg Tablets

I. Conditions for Dissolution Testing:

USP XXII Basket ___ Paddle XX RPM 50 No. Units Tested: 12
 Medium: 0.1 N HCL Volume: 900 ml
 Reference Drug: (Manuf.) Hytrin^K 2 mg Tablets (Abbott)
 Assay Methodology:

II. Results of In-Vitro Dissolution Testing:

<u>Sampling Times (min)</u>	<u>Test Product</u>			<u>Reference Product</u>		
	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>
		<u>Lot # ND-4351-2A</u>			<u>Lot # 58-747-AA-21</u>	
		<u>Strength: 2 mg</u>			<u>Strength: 2 mg</u>	
<u>10</u>	<u>97.0</u>		<u>(1.2)</u>	<u>77.6</u>		<u>(6.5)</u>
<u>20</u>	<u>98.1</u>		<u>(1.2)</u>	<u>86.1</u>		<u>(5.5)</u>
<u>30</u>	<u>98.1</u>		<u>(1.0)</u>	<u>90.2</u>		<u>(3.9)</u>
<u>45</u>	<u>98.2</u>		<u>(0.9)</u>	<u>93.6</u>		<u>(2.4)</u>
<u>60</u>	<u>98.2</u>		<u>(1.0)</u>	<u>95.6</u>		<u>(2.5)</u>

Table 6. In-Vitro Dissolution Testing -10 mg Tablets

I. Conditions for Dissolution Testing:

USP XXII Basket Paddle XX RPM 50 No. Units Tested: 12
 Medium: 0.1 N HCL Volume: 900 ml
 Reference Drug: (Manuf.) Hytrin^K 10 mg Tablets (Abbott)
 Assay Methodology:

II. Results of In-Vitro Dissolution Testing:

<u>Sampling Times (min)</u>	<u>Test Product</u>			<u>Reference Product</u>		
	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>	<u>Mean % Dissolved</u>	<u>Range</u>	<u>(%CV)</u>
			<u>Lot # ND-194</u>			<u>Lot # 62-908-AA-21</u>
			<u>Strength: 10 mg</u>			<u>Strength: 10 mg</u>
<u>10</u>	<u>97.3</u>			<u>87.4</u>		<u>(4.9)</u>
<u>20</u>	<u>98.6</u>			<u>92.6</u>		<u>(3.8)</u>
<u>30</u>	<u>99.1</u>			<u>94.1</u>		<u>(3.9)</u>
<u>45</u>	<u>99.1</u>			<u>95.1</u>		<u>(3.8)</u>
<u>60</u>	<u>98.9</u>			<u>95.9</u>		<u>(3.7)</u>

Comment:

The FDA dissolution specification for terazosin hydrochloride tablets recommends employing water as the dissolution medium, instead of 0.1 N HCL used by the firm.

The comparative formulation of the firm's Terazosin Tablet, 1 mg, 2 mg, 5 mg and 10 mg are presented below in Table 7.

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Table 7: Comparative Formulations

<u>Component</u>	1 mg		2 mg		5 mg		10 mg	
	mg/ Tab	w/w%	mg/ Tab	w/w%	mg/ Tab	w/w%	mg/ Tab	w/w%
Terazosin HCl								
Lactose Monohydrate								
Starch (Corn, 400L)								
Croscrovidone, (polyplasdone XL)								
Colloidal Silicon Dioxide								
Talc								
Magnesium Stearate								
Pink Titanium Blend								
Yellow Pigment Blend								
FD&C Blue #2 Aluminum Lke								
Total Weight								

* NP = Not Present

Comment:

The ratios of the weight of each inactive ingredient to the total tablet weight are the same among the 4 strengths of products for each inactive ingredient except that of lactose monohydrate varies from %.

However, this minute difference is acceptable.

Deficiency:

The firm is advised to conduct all dissolution testing for the test product in water instead of 0.1 N HCl.

Recommendation:

1. The bioequivalence study conducted by Zenith Laboratories, Inc. on its Terazosin tablet, 5 mg, Lot #ND-193, comparing to Hytrin^R tablet, 5 mg, manufactured by Abbott Laboratories, in fasting volunteers, has been found acceptable by the Division of Bioequivalence. The study demonstrates that Zenith's Terazosin tablet, 5 mg, is bioequivalent to the reference product, Hytrin^R, 100 mg, manufactured by Abbott Laboratories, under fasting condition. However, the study is incomplete.
2. The dissolution testing conducted by Zenith Laboratories, Inc. on its Terazosin tablet are not acceptable due to the deficiency described in the Deficiency section.
3. The waiver of in vivo bioequivalence study requirements for the firm's Terazosin tablets, 1 mg, 2 mg and 10 mg, can not be granted at present until acceptable dissolution data are submitted.

The firm should be informed of the deficiency and the recommendations.

/S/

Lin-whei Chuang
Division of Bioequivalence
Review Branch I

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Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence

Date:

12/9/94

cc: ANDA 74-530 (original, duplicate), HFD-600 (Hare), HFD-630, HFC-130 (JAllen, HFD-344 (CViswanathan),) HFD-652 (Chuang, Mhatre), Drug File, Division File.