CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-056

Bioequivalence Review(s)

A2.)

Amoxicillin Tablets
500 mg and 875 mg
ANDA #65-056
Reviewer: Kuldeep R. Dhariwal
File name: 65056SDW.D99

Teva Pharmaceuticals
1510 Delp Drive
Kulpsville
PA 19443
Submission Date:
December 3, 1999
February 14, 2000
February 29, 2000

Review of Fasting Study, Non-fasting Study, Dissolution Data, and Waiver Request

Introduction

First Generic: Yes
Type of Submission: Original ANDA, paper submission
Contents of submission:
Dissolution data and *in vivo* bioequivalence study under fasting and non-fasting conditions on 875 mg strength.
Dissolution data and waiver request for *in vivo* bioequivalence study requirements for 500 mg strength.
Indication: Treatment of infections due to susceptible strains of B-lactamase-negative microorganisms.
RLD: Amoxil® 875 mg as well as Amoxil® 500 mg (SmithKline Beecham) are listed as RLD in The Orange Book. As per Don Hare, the Orange Book will be corrected and only 875 mg strength will be listed as RLD.
Pharmacokinetics: Amoxicillin is stable in the presence of gastric acid and is rapidly absorbed after oral administration. The half-life of amoxicillin is 61.3 minutes. Orally administered doses of 250 mg and 500 mg amoxicillin capsules result in average peak blood levels 1 to 2 hours after administration in the range of 3.5 microgram/mL to 5 microgram/mL and 5.5 microgram/mL to 7.5 microgram/mL respectively.

Bioequivalence Study Under Fasting Conditions:

A. Study Information:

Protocol #:
IRB Approval: Yes
Consent Form Signed: Yes
Clinical Site: Phoenix International
Principal Investigator: Samuel Serfaty, M.D.

Analytical Facility:	Phoenix International
Analytical Team Leader:	
Study Dates:	Period I August 1, 1999 Period II August 8, 1999
Washout Period:	7 days
Analysis Dates:	August 26-September 17, 1999
Storage Period:	47 days
Study Design:	Randomized, single dose, two-way crossover.
Randomization Scheme:	AB: 3,4,8,10,11,12,15,17,18,21,22, 24,25 BA: 1,2,5,6,7,9,13,14,16,19,20,23,26

Treatments:

A: Amoxicillin tablet, 1x875 mg; Teva Pharmaceuticals; Lot #1034-7; Batch size: ablets (theoretical), 129,505 tablets (actual); Manufacture Date: 5/19/1999; Assay: 98.3%

B: Amoxil® tablet, 1x875 mg; SmithKline Beecham; Lot #MB2223; Expiry Date: 05/2000; Assay: 98.1%

Formulation of Test Product:

	ingredients are listed in [illegible].
Subjects:	26 male, 19-44 years old subjects were enrolled according to inclusion/exclusion criteria specified in the protocol.
Housing:	From 12 hours pre-dose until 8 hours post-dose.
Dosing:	After 10 hour fast, with 240 mL of water.
Sample Collection:	Blood samples (5 mL) were collected in Vacutainers containing EDTA at predose (0 h) and at following times after dosing: 0.33,0.67,1,1.33,1.67, 2,2.5,3,4,5,6, and 8 hours.

B. Study Results:

1. Clinical:

Drop-outs:	None
Adverse Events:	One subject complained of dizziness on test drug.
Protocol Deviations:	There were four sampling time deviations of 4 minutes or less. The actual times were used in pharmacokinetic calculations.

2. Analytical:

Within-Study:

Method:	detection.
Internal Standard:	
Linearity:	Std. curve range: 0.10-19.047 mcg/mL. Correlation coefficients were better than 0.9983.
Regression:	1/concentration, linear
QC Samples:	0.300, 8.001, 15.501 mcg/mL
Accuracy:	Standards 94.9-105.1% QC samples 96.7-103.9%
Precision:	Standards 2.2-5.6% QC samples 4.6-5.9%
Reassays:	Some samples were reassayed due to anomalous values, above curve limit, and high/low standard missing.

Pre-Study Method Validation:

Specificity:	Ten blank plasma samples did not show any interference near the retention times of amoxicillin or internal standard.
Linearity:	Std. curve range: 0.10-19.047 mcg/mL. Correlation coefficients were better than 0.998.
QC samples:	0.300, 8.001, and 15.501 mcg/mL
Accuracy:	Inter-day Standards 95.5-106.6% QC samples 96.5-99.2% Intra-day

	QC samples	94.6-102.9%
Precision:	Inter-day	
	Standards	0.6-5.1%
	QC samples	5.8-6.5%
	Intra-day	
	QC samples	1.1-2.2%
Recovery:	0.300 mcg/mL	100.3% (9.1%CV)
	8.001 mcg/mL	90.2% (2.9%CV)
	15.501 mcg/mL	90.4% (0.9%CV)
	Internal std.	77.7% (4.7%CV)

Stability:

a) Amoxicillin was stable at room temperature for at least 4.56 hours in unextracted samples.
b) Amoxicillin was stable at 4^0C for at least 96.5 hours in extracted samples.
c) Freeze-thaw: stable over 2 cycles.
d) Long-term: stability demonstrated for 77 days.

Comment: Method validation is acceptable.

3. Pharmacokinetics/Statistics:

Mean Plasma Concentrations:	Table 2 and Figure 1	
Pharmacokinetic Parameters:	Table 2	
90% Confidence Intervals:	$LAUC_{0-t}$	97.23-108.51%
	$LAUC_{0-inf}$	96.83-107.67%
	LC_{max}	96.26-114.57%
Test/Reference Ratios:	AUC_{0-t}	1.04 (0.70-1.52)
	AUC_{0-inf}	1.03 (0.70-1.40)
	C_{max}	1.09 (0.72-2.21)
AUC_{0-t}/AUC_{0-inf} Ratios:	Test	0.98 (0.96-0.99)
	Reference	0.98 (0.91-0.99)
Root MSE:	$LAUC_{0-t}$	0.11561
	$LAUC_{0-inf}$	0.11178
	LC_{max}	0.18346

Comments:

1. The pharmacokinetic parameters and 90% confidence intervals were recalculated by the reviewer. The reported values are in good agreement with those obtained by the reviewer.
2. The 90% confidence intervals for log transformed AUC_{0-t}, AUC_{0-inf}, and C_{max} are within acceptable limits. There was no statistically significant sequence, treatment or period effect for any of these parameters.
3. The fasting study is acceptable.

Bioavailability Study Under Non-Fasting Conditions:

A. Study Information:

Protocol #:	
IRB Approval:	Yes
Consent Form Signed:	Yes
Clinical Site:	Phoenix International
Principal Investigator:	Samuel Serfaty, M.D.
Analytical Facility:	Phoenix International
Analytical Team Leader:	
Study Dates:	Period I August 2, 1999 Period II August 4, 1999 Period III August 6, 1999
Washout Period:	2 days
Analysis Dates:	August 31-September 17, 1999
Storage Period:	46 days
Study Design:	Randomized, single dose, three-way crossover.
Randomization Scheme:	BAC: 1,7,18 CBA: 2,4,10 BCA: 3,5,17 ACB: 6,9,14 CAB: 8,11,12 ABC: 13,15,16

Treatments:

A: Amoxicillin tablet, 1x875 mg; Teva Pharmaceuticals; Lot #1034-7; administered after a 10 hour fast

B: Amoxicillin tablet, 1x875 mg; Teva Pharmaceuticals; Lot #1034-7; administered after a standard high-fat breakfast

C: Amoxil® tablet, 1x875 mg; SmithKline Beecham; Lot #MB2223; administered after a standard high-fat breakfast

Lot numbers of the drug products administered in this study are the same as those for the fasting study.

Subjects:	18 male, 20-39 years old subjects were enrolled according to inclusion/exclusion criteria specified in the protocol.
Housing:	From 12 hours pre-dose until 8 hours post-dose.

Dosing:	Treatment A: Subjects were given a single oral dose of the assigned formulation with 240 mL of water after a 10.5 hour fast. Treatments B and C: Subjects were given OGD approved standardized breakfast 30 minutes before dosing after a fast lasting at least 10 hours. All subjects completed their breakfast. The dose was given with 240 mL of water.
Sample Collection:	Blood samples (5 mL) were collected in Vacutainers containing EDTA at predose (0 h) and at following times after dosing: 0.33,0.67,1,1.33,1.67, 2,2.5,3,4,5,6, and 8 hours.

B. Study Results:

1. Clinical:

Drop-outs:	Subject #15 was withdrawn prior to dosing in period II due to a positive drug screen for cannabinoids.
Adverse Events:	Two subjects reported that they feel tired.
Protocol Deviations:	There were four sampling time deviations. The actual times were used in pharmacokinetic calculations.

2. Analytical:

Within-Study:

Method:	
Internal Standard:	
Linearity:	Std. curve range: 0.10-19.047 mcg/mL. Correlation coefficients were better than 0.9983.
Regression:	1/concentration, linear
QC Samples:	0.300, 8.001, 15.501 mcg/mL
Accuracy:	Standards 93.5-105.8% QC samples 97.9-102.7%

Precision:	Standards	1.4-4.7%
	QC samples	2.7-5.5%
Reassays:	Some samples were reassayed due to anomalous values and high/low standard missing.	

3. Pharmacokinetics/Statistics:

Mean Plasma Concentrations:	Table 3, Figure 2	
Pharmacokinetic Parameters:	Table 4	
AUC_{0-t}/AUC_{0-inf} Ratios:	Test fasting:	0.97 (0.87-0.99)
	Test non-fasting:	0.98 (0.95-0.99)
	Ref non-fasting:	0.98 (0.96-0.99)

Comments:

1. The pharmacokinetic parameters and ratios of means were recalculated by the reviewer. The reported values are in good agreement with those obtained by the reviewer. The firm in its analysis of variance model included subject, period, treatment and first order carryover as factors. The reviewer did not use first order carryover in the model. The least squares means obtained by the reviewer therefore differ slightly from those reported by the firm. The ratios of means are within acceptable limits by either method.
2. The non-fasting study is acceptable.
3. The non-fasting study is not required for this drug product.

In Vitro Dissolution Testing:

The dissolution testing was conducted in 900 mL of water using apparatus II (paddle) at 75 rpm (USP method, Pharmacopeial Forum, volume 25, number 4). The test products dissolve more than in 90 minutes and meet USP specifications.

F_2 Test:

Test 875 mg vs. Test 500 mg	96.30
Ref 875 mg vs. Ref 500 mg	75.87
Test 875 mg vs. Ref 875 mg	82.32
Test 500 mg vs. Ref 500 mg	82.05

Waiver Request:

The firm is requesting a waiver of *in vivo* bioequivalence study requirements for 500 mg tablet. The 500 mg and 875 mg tablets are proportionally similar in their active and inactive

ingredients. The dissolution data are acceptable. The waiver can be granted.

Recommendations:

1. The bioequivalence study conducted under fasting conditions by Teva Pharmaceuticals on its Amoxicillin 875 mg tablet, lot #1034-7 comparing it to Amoxil® 875 mg tablet, lot #MB2223 manufactured by SmithKline Beecham is acceptable to the Division of Bioequivalence. The study demonstrates that Teva's Amoxicillin 875 mg tablet is bioequivalent to the reference product, Amoxil® 875 mg tablet manufactured by SmithKline Beecham.
2. The bioequivalence study conducted under non-fasting conditions by Teva Pharmaceuticals on its Amoxicillin 875 mg tablet, lot #1034-7 comparing it to Amoxil® 875 mg tablet, lot #MB2223 manufactured by SmithKline Beecham is acceptable to the Division of Bioequivalence. The study demonstrates that under non-fasting conditions, the bioavailability of Teva's Amoxicillin 875 mg tablet is similar to that of the reference product, Amoxil® 875 mg tablet manufactured by SmithKline Beecham. However, the non-fasting study is not required.
3. The dissolution testing conducted by the firm on its 500 mg and 875 mg tablets is acceptable. The formulation for 500 mg test tablet is proportionally similar to the 875 mg strength of the test product which underwent bioequivalency testing. The waiver of the *in vivo* bioequivalence study requirements for 500 mg tablet of the test product is granted. The 500 mg test tablet is therefore deemed bioequivalent to Amoxil® 500 mg tablet manufactured by SmithKline Beecham.
4. The dissolution testing should be incorporated into firm's manufacturing controls and stability programs. The dissolution testing should be conducted in 900 mL of water at 37°C using apparatus II (paddle) at 75 rpm. The test product should meet the following specifications:

   Not less than of the labeled amount of amoxicillin in the dosage form is dissolved in 90 minutes.
5. From bioequivalence point of view, the firm has met the requirements for *in vivo* bioequivalence and *in vitro* dissolution testing and the application is acceptable.

Kuldeep R. Dhariwal, Ph.D.
Review Branch II
Division of Bioequivalence

RD INITIALED S.NERURKAR
FT INITIALED S.NERURKAR _____ Date 3/6/00

Concur: _____ Date 3/7/00
Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

Table 1

Comparative Quantitative Composition of Amoxicillin Tablets

Ingredient	500 mg		875 mg	
	mg/tab	w/w %	mg/tab	w/w %
Amoxicillin Trihydrate				
Microcrystalline Cellulose				
Sodium Starch				
Crospovidone				
Colloidal Silicon				
Magnesium Stearate				
Coating:				
	-		-	
Total				

Test 500 mg tablet: Film-coated, capsule shaped, off-white tablet, debossed "93" on one side and "2263" on the other side.

Test 875 mg tablet: Film-coated, capsule shaped, off-white tablet, scored on one side, debossed "93" on one side of the score and "2264" on the other side of the score.

Reference tablets: Each film-coated, capsule shaped, pink tablet is debossed with Amoxil centered over 500 or 875, respectively. The 875 mg tablet is scored on the reverse side.

Table 2

MEAN PLASMA AMOXICILLIN LEVELS (microgram/mL) FOR TEST (1) AND REFERENCE (2) PRODUCTS IN FASTING STUDY, n=26
Dose= 1x875 mg

	MEAN1	SD1	MEAN2	SD2	RMEAN12
TIME HR					
0	0.00	0.00	0.00	0.00	.
0.33	1.50	1.74	1.61	1.60	0.93
0.67	5.83	4.77	6.21	3.64	0.94
1	8.98	4.52	8.88	4.34	1.01
1.33	10.66	4.17	10.44	4.04	1.02
1.67	11.20	3.44	10.43	3.49	1.07
2	10.98	3.23	10.47	3.38	1.05
2.5	9.46	2.80	8.90	2.23	1.06
3	7.98	2.22	7.07	1.80	1.13
4	5.01	2.16	5.09	2.56	0.98
5	2.73	1.29	2.82	1.96	0.97
6	1.48	0.70	1.63	0.98	0.90
8	0.44	0.16	0.51	0.28	0.87

UNIT: PLASMA LEVEL=MICROGRAM/ML TIME=HRS
ARITHMETIC MEANS AND RATIOS

	MEAN1	SD1	MEAN2	SD2	RMEAN12
PARAMETER					
AUCI	39.16	8.54	38.44	8.62	1.02
AUCT	38.42	8.41	37.49	8.46	1.02
CMAX	12.79	3.31	12.21	3.28	1.05
KE	0.61	0.08	0.58	0.09	1.05
LAUCI	38.28	0.22	37.49	0.23	1.02
LAUCT	37.55	0.22	36.56	0.23	1.03
LCMAX	12.38	0.26	11.79	0.27	1.05
THALF	1.16	0.15	1.23	0.21	0.95
TMAX	1.98	0.73	1.85	0.74	1.07

UNIT: AUC=MICROGRAM HR/ML CMAX=MICROGRAM/ML TMAX=HR
LOG-TRANSFORMED DATA WERE CONVERTED TO ANTI-LOG IN THE TABLE
LSMEANS AND 90% CONFIDENCE INTERVALS

	LSM1	LSM2	RLSM12	LOWCI12	UPPCI12
PARAMETER					
AUCI	39.16	38.44	1.02	96.93	106.81
AUCT	38.42	37.49	1.02	97.39	107.55
CMAX	12.79	12.21	1.05	96.53	113.01
LAUCI	38.28	37.49	1.02	96.83	107.67
LAUCT	37.55	36.56	1.03	97.23	108.51
LCMAX	12.38	11.79	1.05	96.26	114.57

Table 3

MEAN PLASMA AMOXICILLIN LEVELS (MICROGRAM/ML) FOR TEST AND REFERENCE PRODUCTS IN NON-FASTING STUDY, N=17
Dose= 1x875 mg

	MEAN1	SD1	MEAN2	SD2	MEAN3	SD3	RMEAN12
TIME HR							
0	0.00	0.00	0.00	0.00	0.00	0.00	.
0.33	1.03	1.04	0.36	0.48	0.09	0.23	2.84
0.67	4.78	2.52	3.42	2.58	1.30	1.19	1.40
1	8.14	3.83	7.35	4.50	3.83	2.89	1.11
1.33	9.46	3.66	9.73	4.43	6.79	3.95	0.97
1.67	9.78	3.39	10.65	3.21	9.11	3.73	0.92
2	9.69	2.64	10.34	2.24	10.07	2.85	0.94
2.5	7.92	2.27	8.74	1.83	9.60	1.93	0.91
3	6.08	1.83	6.95	1.89	8.28	2.18	0.87
4	3.87	1.41	4.05	1.45	4.71	1.64	0.96
5	2.19	1.06	2.14	0.72	2.55	0.88	1.03
6	1.25	0.75	1.21	0.45	1.39	0.51	1.03
8	0.46	0.40	0.42	0.13	0.46	0.15	1.09

(CONTINUED)

UNIT: PLASMA LEVEL=MICROGRAM/ML TIME=HRS
MEAN PLASMA AMOXICILLIN LEVELS FOR TEST AND REFERENCE PRODUCTS

	RMEAN13	RMEAN23
TIME HR		
0	.	.
0.33	11.79	4.15
0.67	3.66	2.62
1	2.12	1.92
1.33	1.39	1.43
1.67	1.07	1.17
2	0.96	1.03
2.5	0.82	0.91
3	0.73	0.84
4	0.82	0.86
5	0.86	0.84
6	0.90	0.87
8	1.00	0.92

1= TEST FASTING
2= TEST NON-FASTING
3= REF NON-FASTING

Table 4

AMOXICILLIN PHARMACOKINETIC PARAMETERS IN NON-FASTING STUDY, N=17
Dose= 1x875 mg

UNIT: PLASMA LEVEL=MICROGRAM/ML TIME=HRS
ARITHMETIC MEANS AND RATIOS

	MEAN1	SD1	MEAN2	SD2	MEAN3	SD3	RMEAN12
PARAMETER							
AUCI	32.96	7.48	33.61	4.81	32.83	4.33	0.98
AUCT	32.01	7.00	32.82	4.81	32.04	4.24	0.98
CMAX	11.02	3.20	12.23	2.88	11.62	2.64	0.90
KE	0.55	0.10	0.55	0.08	0.59	0.06	1.00
LAUCI	31.92	0.28	33.30	0.14	32.58	0.13	0.96
LAUCT	31.04	0.28	32.51	0.14	31.79	0.13	0.95
LCMAX	10.39	0.40	11.93	0.22	11.36	0.21	0.87
THALF	1.30	0.27	1.28	0.21	1.19	0.11	1.02
TMAX	1.81	0.45	1.78	0.41	2.20	0.51	1.02

(CONTINUED)

UNIT: AUC=MICROGRAM HR/ML CMAX=MICROGRAM/ML TMAX=HR
LOG-TRANSFORMED DATA WERE CONVERTED TO ANTI-LOG IN THE TABLE
ARITHMETIC MEANS AND RATIOS

	RMEAN13	RMEAN23
PARAMETER		
AUCI	1.00	1.02
AUCT	1.00	1.02
CMAX	0.95	1.05
KE	0.94	0.94
LAUCI	0.98	1.02
LAUCT	0.98	1.02
LCMAX	0.91	1.05
THALF	1.09	1.08
TMAX	0.83	0.81

UNIT: AUC=MICROGRAM HR/ML CMAX=MICROGRAM/ML TMAX=HR
LOG-TRANSFORMED DATA WERE CONVERTED TO ANTI-LOG IN THE TABLE
LSMEANS AND RATIOS

	LSM1	LSM2	LSM3	RLSM12	RLSM13	RLSM23
PARAMETER						
AUCI	32.76	33.37	32.75	0.98	1.00	1.02
AUCT	31.81	32.58	31.95	0.98	1.00	1.02
CMAX	10.93	12.15	11.55	0.90	0.95	1.05
LAUCI	31.75	33.05	32.52	0.96	0.98	1.02
LAUCT	30.87	32.25	31.72	0.96	0.97	1.02
LCMAX	10.32	11.84	11.32	0.87	0.91	1.05

1= TEST FASTING
2= TEST NON-FASTING
3= REF NON-FASTING

Table 5. In Vitro Dissolution Testing

Drug (Generic Name): Amoxicillin Tablets
Dose Strength: 500 mg and 875 mg
ANDA No.: 65-056
Firm: Teva
Submission Date: December 3, 1999
File Name: 65056SDW.D99

I. Conditions for Dissolution Testing: USP method

USP XXIII Basket: Paddle: x RPM: 75
No. Units Tested: 12
Medium: Water Volume: 900 mL
Specifications: NLT 90 minutes
Reference Drug: Amoxil® (SmithKline)
Assay Methodology

II. Results of *In Vitro* Dissolution Testing:

Sampling Times (Minutes)	Test Product Lot #1034-58 Strength(mg) 500			Reference Product Lot #KK1681 Strength(mg) 500		
	Mean %	Range	%CV	Mean %	Range	%CV
10	96.6		3.33	95.7		1.22
20	98.6		2.03	97.1		0.77
90	100.2		2.27	97.1		0.66

Sampling Times (Minutes)	Test Product Lot #1034-7 Strength(mg) 875			Reference Product Lot #MB2223 Strength(mg) 875		
	Mean %	Range	%CV	Mean %	Range	%CV
10	95.5		2.18	98.7		0.86
20	98.5		1.93	99.9		0.84
90	100.2		1.08	99.9		0.80

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 65-056 APPLICANT: Teva Pharmaceuticals

DRUG PRODUCT: Amoxicillin Tablets, 500 mg and 875 mg

The Division of Bioequivalence has completed its review and has no further questions at this time.

We acknowledge that the following dissolution testing has been incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900 mL of water at 37°C using USP Apparatus II (paddle) at 75 rpm. The test product should meet the following specifications:
>
> Not less than of the labeled amount of the drug in the dosage form is dissolved in 90 minutes.

Please note that a food-effect study is not required for drug products (tablets, capsules, chewable tablets and suspensions) containing only amoxicillin.

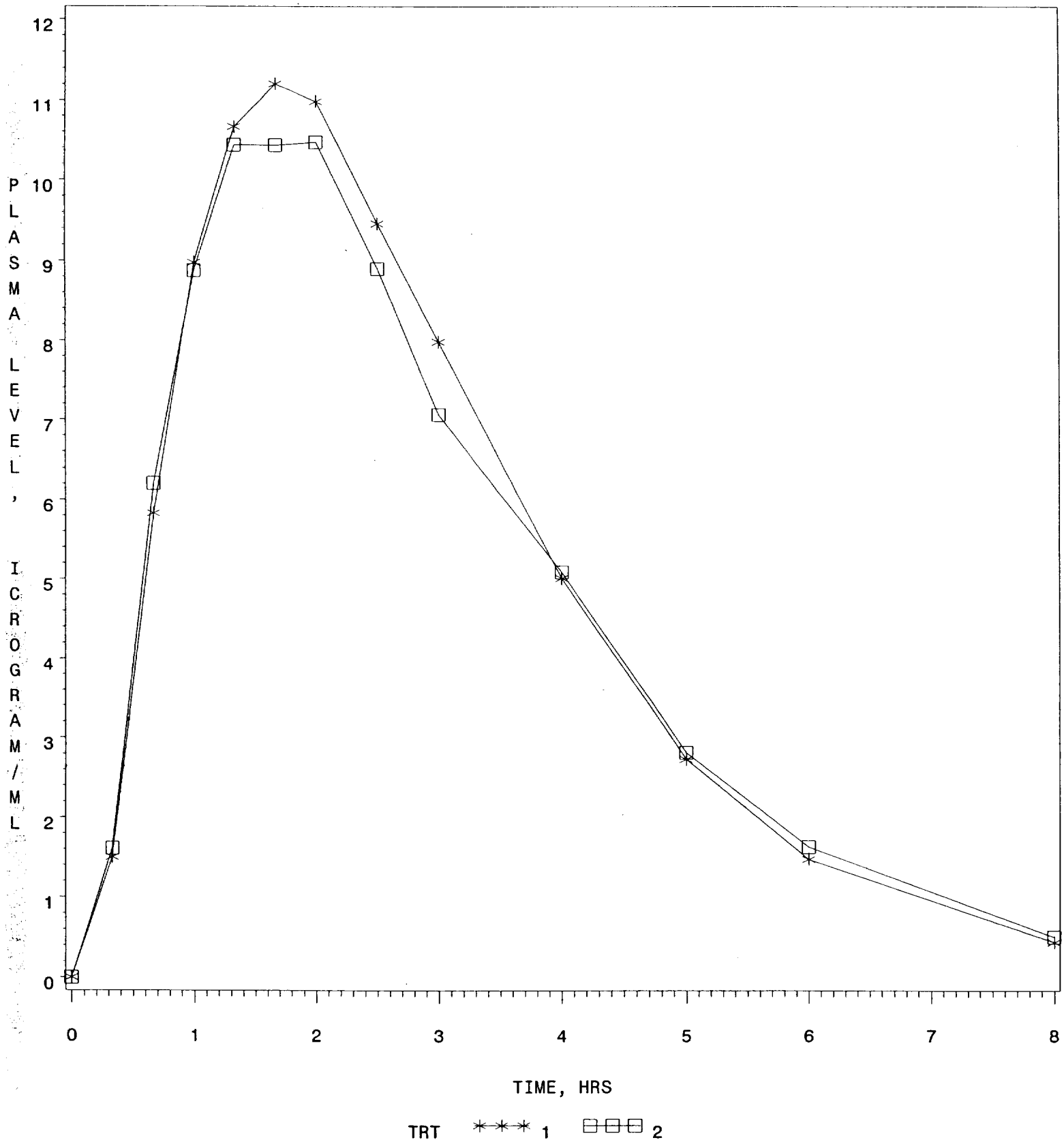
Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. 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,

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

FIG 1. PLASMA AMOXICILLIN LEVELS

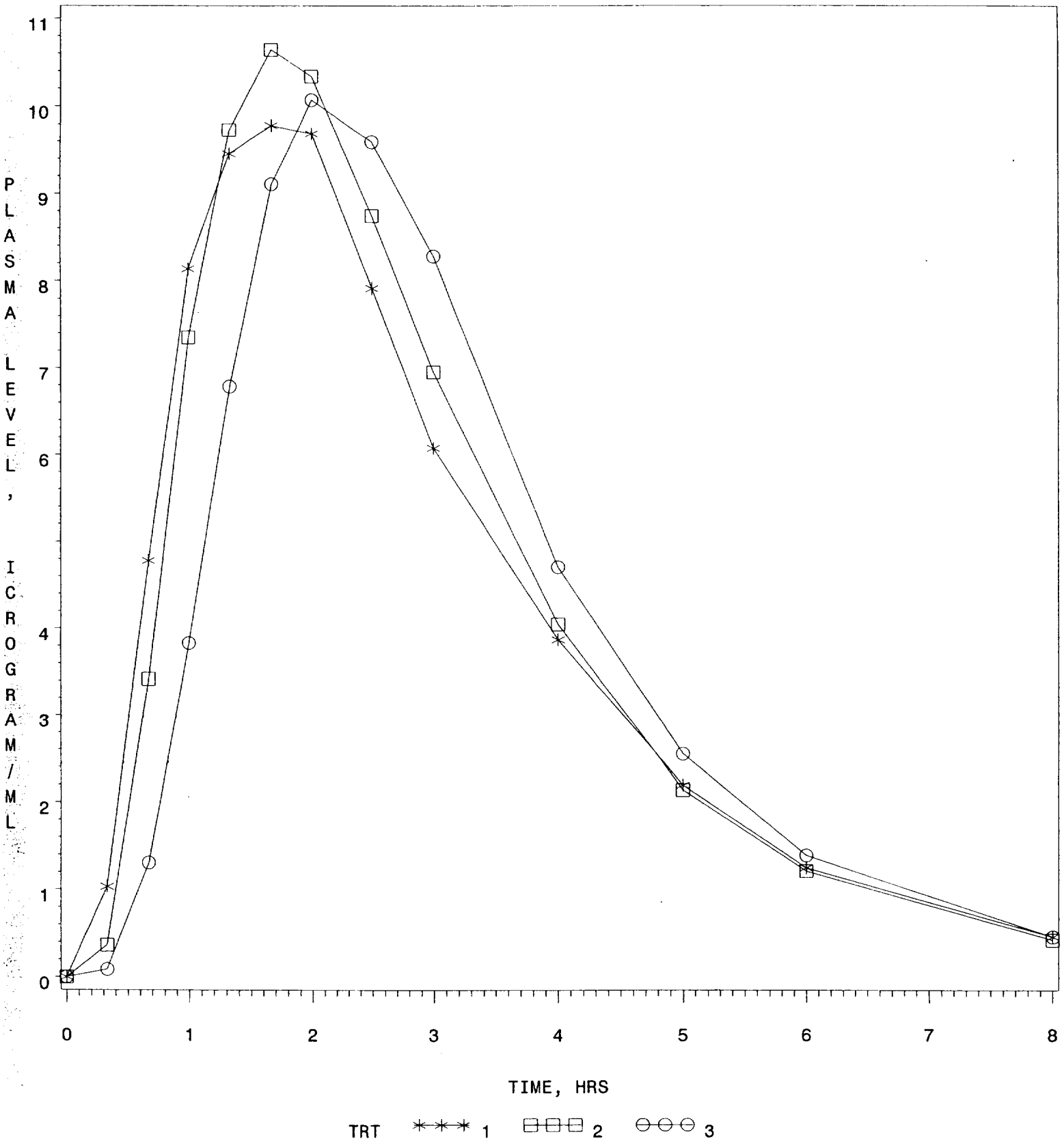
AMOXICILLIN TABLETS, 875 MG, ANDA #65-056
UNDER FASTING CONDITIONS
DOSE=1 X 875 MG



1=TEST(TEVA) 2=REF(SMITH-KLINE)

FIG 2. PLASMA AMOXICILLIN LEVELS

AMOXICILLIN TABLETS, 875 MG, ANDA #65-056
UNDER FASTING/NONFASTING CONDITIONS
DOSE=1 X 875 MG



1=TEST(FAST) 2=TEST(FED) 3=REF(FED)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 65-056 APPLICANT: Teva Pharmaceuticals

DRUG PRODUCT: Amoxicillin Tablets, 500 mg and 875 mg

The Division of Bioequivalence has completed its review and has no further questions at this time.

We acknowledge that the following dissolution testing has been incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900 mL of water at 37°C using USP Apparatus II (paddle) at 75 rpm. The test product should meet the following specifications:
>
> Not less than of the labeled amount of the drug in the dosage form is dissolved in 90 minutes.

Please note that a food-effect study is not required for drug products (tablets, capsules, chewable tablets and suspensions) containing only amoxicillin.

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,

Dale P. Conner

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