

## 2. Drug Product, Continued

### f. Investigational Formulations - continued

The formulas for the clinical batches used in the Pivotal Study #366 are summarized below.

#### Synthetic Conjugated Estrogens Tablets Quantitative Formula for Clinical Batches used in Pivotal Study #366

Component	Amount per Tablet		
	C-0034 0.3 mg	94850 0.625 mg	C-0031 Placebo
<u>Core Tablet:</u>			
Synthetic Conjugated Estrogens <sup>1</sup>	0.3 mg	0.625 mg	N/A
Lactose Monohydrate, NF			
Hydroxypropyl Methylcellulose USP			
Pregelatinized Starch, NF			
Magnesium Stearate, NF			
Alcohol			
Purified Water, USP			
<u>Subcoat Coat:</u>			
Ethylcellulose Aqueous Dispersion, NF			
Triethyl Citrate, NF			
Purified Water, USP			
<u>Color Coat:</u>			
Maroon			
Purified Water, USP			
<u>Clear Coat:</u>			
Clear			
Purified Water, USP	- <sup>2</sup>	- <sup>2</sup>	- <sup>2</sup>

<sup>1</sup> Contains a target 125 g of Synthetic Conjugated Estrogens

<sup>2</sup> Removed during the manufacturing process.

<sup>3</sup> Weights indicate theoretical amount of residue

## 2. Drug Product, Continued

### b. Manufacturer

Duramed Pharmaceuticals, Inc. is the manufacturer for all strengths of Synthetic Conjugated Estrogens Tablets. The full name and address of the drug product manufacturer is:

Duramed Pharmaceuticals, Inc.  
5040 Lester Road  
Cincinnati, Ohio 45213

### c. Specifications and Analytical Methods

The test methods and specifications for Synthetic Conjugated Estrogens Solution are based upon the USP test methods for Conjugated Estrogens Tablets.

### d. Container/Closure System

The market package configurations are summarized as follows:

Synthetic Conjugated Estrogens Tablets  
Proposed Market Package Configurations

Market Package Size	Bottle Description	Cap Description	Liner Description	Desiccant	Stuffer Description
30 count	60 cc white 2X HDPE	33 mm white polypropylene CRC	130 Inner Seal	Two 2 gram canisters	Rayon
100 count	60 cc white 2X HDPE	33 mm white polypropylene	75 Inner Seal	Two 2 gram canisters	Rayon
1000 count (0.3 mg, 0.625 mg & 0.9 mg)	300 cc white 2X HDPE	45 mm white polypropylene	75 Inner Seal	Four 2 gram canisters	Rayon
1000 count (1.25 mg & 2.5 mg)	500 cc white 2X HDPE	45 mm white polypropylene	75 Inner Seal	Four 2 gram canisters	Rayon

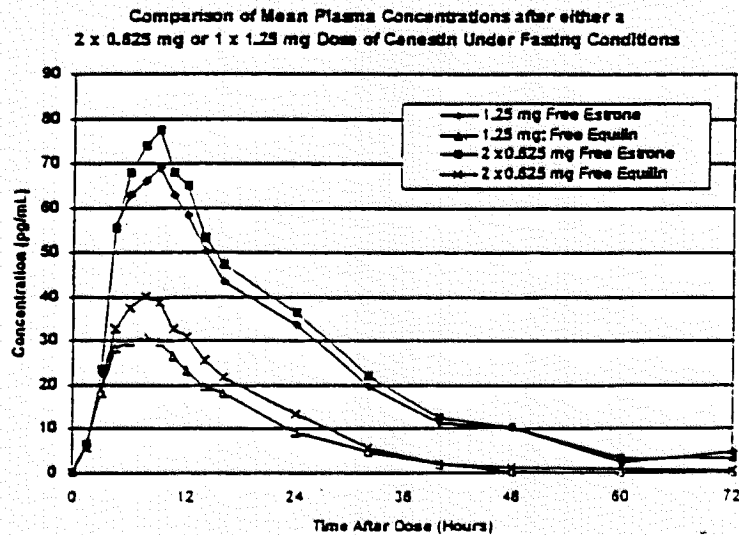
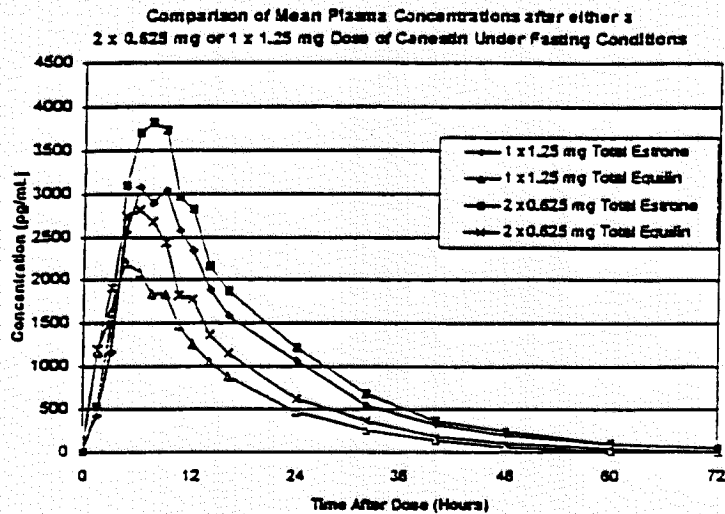
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ATTACHMENT 3

## F. Human Pharmacokinetics and Bioavailability Summary, Continued

Figure 5

### Comparison of Mean Plasma Concentrations of Total and Free Estrone and Equilin After Either a 2 x 0.625 mg or 1 x 1.25 mg Dose of Cenestin™ Under Fasting Conditions



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**Fasting Bioavailability Study - 0.625 mg, Continued**

**Table 13**

**Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Total Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (ng*hr/mL)	46.46 (47.5)	48.82 (45.5)	-	-
AUC <sub>(0-72)</sub> (Geometric) (ng*hr/mL)	41.68	44.67	93.30	89.13 - 97.65
AUC <sub>(0-∞)</sub> (Measured) (ng*hr/mL)	47.25 (47.4)	49.66 (45.2)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (ng*hr/mL)	42.47	45.51	93.32	89.16 - 97.66
C <sub>max</sub> (Measured) (ng/mL)	3.271 (43.5)	3.650 (41.1)	-	-
C <sub>max</sub> (Geometric) (ng/mL)	2.937	3.336	83.04	81.75 - 94.81
k <sub>el</sub> (Measured) (1/hr)	0.0756 (23.1)	0.0729 (21.2)	-	-
t <sub>1/2</sub> (Measured) (hr)	9.66 (23.0)	9.89 (19.4)	-	-
T <sub>max</sub> (Measured) (hr)	5.8 (31.1)	6.7 (28.5)	-	-

**Table 14**

**Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Total Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (ng*hr/mL)	69.89 (39.2)	69.69 (38.8)	-	-
AUC <sub>(0-72)</sub> (Geometric) (ng*hr/mL)	65.01	65.32	99.53	95.16 - 104.10
AUC <sub>(0-∞)</sub> (Measured) (ng*hr/mL)	70.99 (39.3)	71.12 (39.8)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (ng*hr/mL)	66.04	66.21	99.73	95.44 - 104.21
C <sub>max</sub> (Measured) (ng/mL)	4.430 (40.4)	4.535 (38.2)	-	-
C <sub>max</sub> (Geometric) (ng/mL)	4.0576	4.2243	96.05	90.16 - 102.31
k <sub>el</sub> (Measured) (1/hr)	0.0705 (29.3)	0.0728 (28.6)	-	-
t <sub>1/2</sub> (Measured) (hr)	10.55 (25.4)	10.21 (25.1)	-	-
T <sub>max</sub> (Measured) (hr)	7.7 (30.3)	7.5 (24.1)	-	-

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# Fasting Bioavailability Study - 0.625 mg, Continued

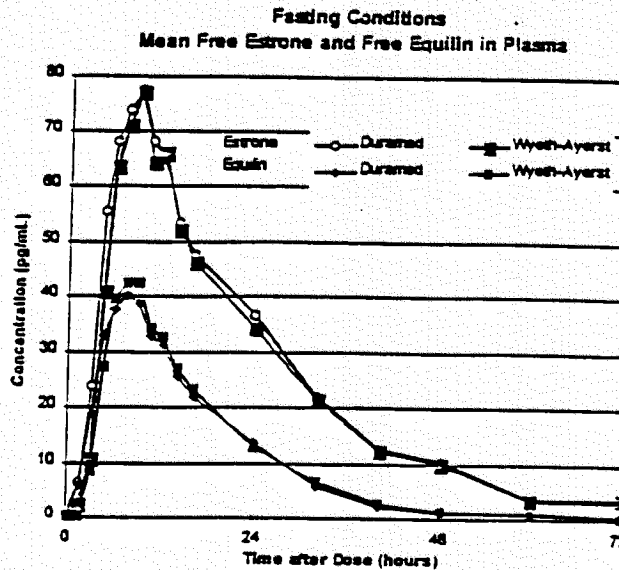


Table 15

Mean Plasma Concentrations of Free Estrone and Equilin after a 2 x 0.625 mg Dose under Fasting Conditions

Time After Dose (hr)	Free Estrone (Baseline Corrected)		Free Equilin	
	Test Formulation (Cenestin™) Duramed ng/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst ng/mL (CV%)	Test Formulation (Cenestin™) Duramed ng/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst ng/mL (CV%)
0	0.00	0.00	0.35 (578.7)	0.33 (596.2)
1.5	6.47 (75.6)	2.50 (163.3)	5.75 (143.7)	0.39 (597.9)
3.0	23.61 (52.5)	10.55 (86.9)	19.06 (74.6)	8.54 (118.7)
4.5	55.55 (39.7)	40.84 (69.2)	32.77 (41.5)	27.19 (77.8)
6.0	67.98 (41.6)	63.58 (57.7)	37.61 (51.4)	39.36 (65.4)
7.5	73.98 (44.9)	70.87 (45.6)	40.50 (51.9)	42.32 (51.7)
9.0	77.49 (45.2)	77.06 (46.7)	38.80 (53.6)	42.49 (48.1)
10.5	67.89 (47.1)	64.39 (44.9)	32.78 (53.8)	34.22 (47.8)
12	64.85 (44.2)	63.76 (48.3)	31.11 (55.9)	32.63 (48.1)
14	53.34 (42.7)	52.04 (42.9)	25.69 (54.6)	26.89 (45.6)
16	47.35 (43.4)	46.11 (43.5)	21.78 (52.9)	23.29 (50.4)
24	36.48 (43.9)	34.14 (45.4)	13.49 (82.3)	12.90 (73.2)
32	21.92 (59.8)	21.35 (61.7)	5.75 (159.1)	6.56 (126.3)
40	12.44 (75.6)	12.28 (80.0)	2.15 (285.9)	2.79 (221.0)
48	10.37 (71.0)	9.85 (81.4)	1.09 (373.5)	1.33 (330.3)
60	3.39 (143.6)	3.54 (163.3)	0.97 (366.3)	0.70 (410.3)
72	3.32 (132.9)	3.62 (151.9)	0.55 (470.5)	0.23 (848.5)

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**Fasting Bioavailability Study - 1.25 mg, Continued**

**Table 20**  
**Mean Pharmacokinetic Parameters after a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Total Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg <sup>o</sup> hr/mL)	34902 (57.2)	34569 (54.8)	—	—
AUC <sub>(0-72)</sub> (Geometric) (pg <sup>o</sup> hr/mL)	30907	30501	101.33	95.29 - 107.74
AUC <sub>(0-∞)</sub> (Measured) (pg <sup>o</sup> hr/mL)	36220 (55.6)	35667 (53.3)	—	—
AUC <sub>(0-∞)</sub> (Geometric) (pg <sup>o</sup> hr/mL)	31985	31720	100.84	96.45 - 105.41
C <sub>max</sub> (Measured) (pg/mL)	2537.8 (50.6)	2581.2 (57.4)	—	—
C <sub>max</sub> (Geometric) (pg/mL)	2302.5	2247.5	102.45	93.68 - 112.05
k <sub>el</sub> (Measured) (1/hr)	0.0796 (29.1)	0.0775 (22.3)	—	—
t <sub>1/2</sub> (Measured) (hr)	9.34 (25.4)	9.42 (23.5)	—	—
T <sub>max</sub> (Measured) (hr)	5.433 (35.1)	7.947 (35.2)	—	—

**Table 21**  
**Mean Pharmacokinetic Parameters after a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Total Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg <sup>o</sup> hr/mL)	58229 (42.6)	56727 (39.3)	—	—
AUC <sub>(0-72)</sub> (Geometric) (pg <sup>o</sup> hr/mL)	53690	53149	101.02	95.38 - 106.97
AUC <sub>(0-∞)</sub> (Measured) (pg <sup>o</sup> hr/mL)	59513 (44.3)	57881 (40.3)	—	—
AUC <sub>(0-∞)</sub> (Geometric) (pg <sup>o</sup> hr/mL)	54576	54089	100.90	95.13 - 107.01
C <sub>max</sub> (Measured) (pg/mL)	3695.1 (39.8)	3617.5 (38.3)	—	—
C <sub>max</sub> (Geometric) (pg/mL)	3428.3	3400.5	100.82	93.50 - 108.70
k <sub>el</sub> (Measured) (1/hr)	0.0732 (30.9)	0.0732 (29.9)	—	—
t <sub>1/2</sub> (Measured) (hr)	10.33 (30.1)	10.26 (27.7)	—	—
T <sub>max</sub> (Measured) (hr)	7.168 (30.5)	8.333 (30.3)	—	—

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## Fasting Bioavailability Study - 1.25 mg, Continued

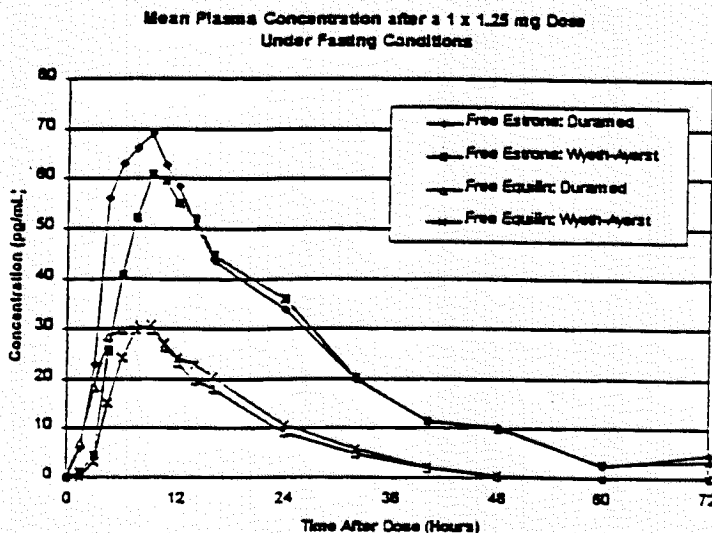


Table 22

Mean Plasma Concentrations of Free Estrone and Equilin after a 1 x 1.25 mg Dose Under Fasting Conditions

Time After Dose (hr)	Free Estrone (Baseline Corrected)		Free Equilin	
	Test Formulation (Cenesun™) Duramed pg/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst pg/mL (CV%)	Test Formulation (Cenesun™) Duramed pg/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst pg/mL (CV%)
0	0.00	0.00	0.00	0.00
1.5	6.07 (112.0)	0.99 (158.0)	7.23 (80.5)	0.00
3.0	22.76 (59.3)	4.54 (110.5)	18.23 (53.1)	3.32 (188.8)
4.5	56.13 (46.9)	25.60 (81.4)	28.42 (44.9)	15.06 (105.6)
6.0	62.88 (45.7)	40.64 (61.7)	29.70 (42.6)	24.23 (61.4)
7.5	66.15 (42.9)	52.20 (58.1)	30.90 (45.3)	29.77 (51.9)
9.0	69.06 (42.1)	60.95 (53.6)	29.81 (43.8)	30.89 (46.9)
10.5	62.84 (43.8)	59.63 (52.5)	26.40 (42.7)	27.16 (40.6)
12	58.43 (43.4)	55.03 (50.9)	23.21 (45.6)	24.31 (44.9)
14	50.50 (40.3)	51.75 (46.9)	19.61 (42.3)	22.81 (47.8)
16	43.57 (45.7)	44.77 (48.7)	18.07 (47.1)	20.59 (49.0)
24	33.70 (45.1)	35.92 (46.9)	9.11 (81.7)	10.75 (69.5)
32	19.71 (58.3)	20.21 (57.1)	4.87 (120.4)	5.81 (98.3)
40	11.41 (72.0)	11.36 (75.7)	1.87 (203.8)	2.18 (168.2)
48	10.28 (61.5)	9.85 (66.9)	0.38 (475.5)	0.60 (349.2)
60	2.32 (162.3)	2.76 (148.6)	0.10 (793.7)	0.08 (800.0)
72	4.72 (142.7)	3.38 (98.8)	0.00	0.00

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**Fasting Bioavailability Study - 1.25 mg, Continued**

**Table 23**  
**Mean Pharmacokinetic Parameters After a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Free Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	1609.5 (43.9)	1483.3 (46.8)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	1369.9	1318.9	103.86	93.18 - 115.77
C <sub>max</sub> (Measured) (pg/mL)	75.69 (40.4)	67.54 (43.2)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	68.31	59.72	114.38	105.13 - 124.43
T <sub>max</sub> (Measured) (hr)	7.844 (30.9)	11.250 (32.8)	-	-

**Table 24**  
**Mean Pharmacokinetic Parameters After a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Free Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	556.5 (52.6)	543.4 (48.7)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	483.7	479.0	100.99	93.35 - 109.24
C <sub>max</sub> (Measured) (pg/mL)	35.142 (40.9)	36.211 (44.7)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	32.160	32.621	98.59	90.46 - 107.43
T <sub>max</sub> (Measured) (hr)	6.954 (31.5)	9.406 (34.3)	-	-

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~~INDICATIONS:~~

Comparison of Baseline Adjusted Pharmacokinetic Parameters for 2x0.625 mg Tablets and 1x1.25 mg Tablets from Different Studies:

Study BN038 (2x0.625), Study BN037 (1x1.25), Parameters under Fasted Conditions

Ratio 1.25/2x0.625	Total Estrone	Total Equilin	Free Estrone	Free Equilin
AUC 0-72	0.833	0.75	0.92	0.77
Cmax	0.83	0.78	0.90	0.77

Study BN038 (2x0.625), Study 941817 (1x1.25), Parameters under Fasted Conditions

Ratio 1.25/2x0.625	Total Estrone	Total Equilin	Free Estrone	Free Equilin
AUC 0-72	1.04	0.95	1.46	1.12
Cmax	1.04	0.92	1.38	1.18

Study 930125 (2x0.625), Study 941817 (1x1.25), Parameters under Fed Conditions

Ratio 1.25/2x0.625	Total Estrone	Total Equilin	Free Estrone	Free Equilin
AUC 0-72	0.96	1.01	1.04	0.90
Cmax	0.84	0.92	0.94	0.91

**ATTACHMENT 4**

BNC39

**Fasting Bioavailability Study - 0.625 mg, Continued**

**Table 13**

**Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Total Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (ng*hr/mL)	46.46 (47.5)	48.82 (45.5)	-	-
AUC <sub>(0-72)</sub> (Geometric) (ng*hr/mL)	41.68	44.67	93.30	89.13 - 97.65
AUC <sub>(0-∞)</sub> (Measured) (ng*hr/mL)	47.25 (47.4)	49.66 (45.2)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (ng*hr/mL)	42.47	45.51	93.32	89.16 - 97.66
C <sub>max</sub> (Measured) (ng/mL)	3.271 (43.5)	3.650 (41.1)	-	-
C <sub>max</sub> (Geometric) (ng/mL)	2.937	3.336	88.04	81.75 - 94.81
k <sub>el</sub> (Measured) (1/hr)	0.0756 (23.1)	0.0729 (21.2)	-	-
t <sub>1/2</sub> (Measured) (hr)	9.66 (25.0)	9.89 (19.4)	-	-
T <sub>max</sub> (Measured) (hr)	5.8 (31.1)	6.7 (23.5)	-	-

**Table 14**

**Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Total Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (ng*hr/mL)	69.89 (39.2)	69.69 (38.8)	-	-
AUC <sub>(0-72)</sub> (Geometric) (ng*hr/mL)	65.01	65.32	99.53	95.16 - 104.10
AUC <sub>(0-∞)</sub> (Measured) (ng*hr/mL)	70.99 (39.3)	71.12 (39.8)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (ng*hr/mL)	66.04	66.21	99.73	95.44 - 104.21
C <sub>max</sub> (Measured) (ng/mL)	4.430 (40.4)	4.535 (38.2)	-	-
C <sub>max</sub> (Geometric) (ng/mL)	4.0576	4.2243	96.05	90.16 - 102.31
k <sub>el</sub> (Measured) (1/hr)	0.0705 (29.3)	0.0728 (28.6)	-	-
t <sub>1/2</sub> (Measured) (hr)	10.55 (25.4)	10.21 (25.1)	-	-
T <sub>max</sub> (Measured) (hr)	7.7 (30.3)	7.5 (24.1)	-	-

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## Fasting Bioavailability Study - 0.625 mg, Continued

Table 16

Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Free Estrone (Baseline Corrected)

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	1749.0 (43.8)	1650.4 (47.3)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	1621.8	1482.0	109.44	101.74 - 117.71
C <sub>max</sub> (Measured) (pg/mL)	84.54 (41.4)	83.06 (45.0)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	78.87	75.17	104.92	98.08 - 112.22
T <sub>max</sub> (Measured) (hr)	8.250 (35.6)	8.938 (23.7)	-	-

Table 17

Mean Pharmacokinetic Parameters after a 2 x 0.625 mg Dose under Fasting Conditions  
 Free Equilin

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC(0-72) (Measured) (pg*hr/mL)	723.2 (67.9)	719.5 (57.6)	-	-
AUC(0-72) (Geometric) (pg*hr/mL)	606.3	610.6	99.30	91.80 - 107.40
C <sub>max</sub> (Measured) (pg/mL)	45.58 (47.3)	48.72 (52.9)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	41.58	43.34	95.93	86.05 - 100.04
T <sub>max</sub> (Measured) (hr)	7.779 (28.8)	8.313 (28.2)	-	-

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## Fasting Bioavailability Study - 0.625 mg, Continued

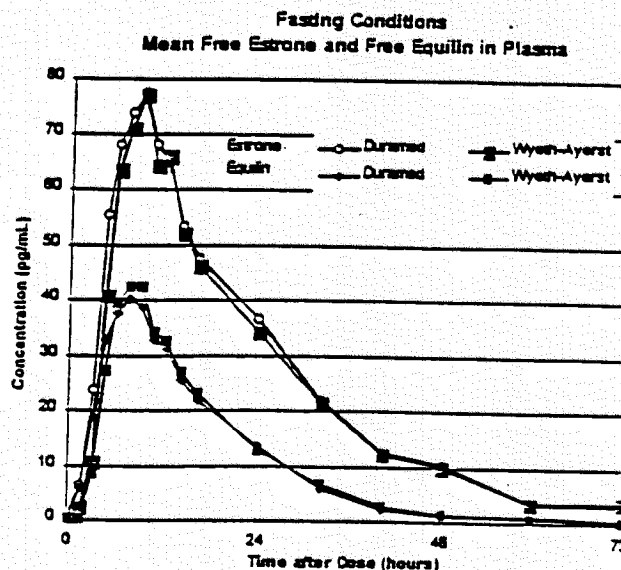


Table 15

Mean Plasma Concentrations of Free Estrone and Equilin after a 2 x 0.625 mg Dose under Fasting Conditions

Time After Dose (hr)	Free Estrone (Baseline Corrected)		Free Equilin	
	Test Formulation (Cenestin™) Duramed ng/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst ng/mL (CV%)	Test Formulation (Cenestin™) Duramed ng/mL (CV%)	Reference Formulation (Premarin®) Wyeth-Ayerst ng/mL (CV%)
0	0.00	0.00	0.35 (578.7)	0.33 (596.2)
1.5	6.47 (75.6)	2.50 (163.3)	5.75 (143.7)	0.39 (597.9)
3.0	23.61 (52.5)	10.55 (86.9)	19.06 (74.6)	8.54 (118.7)
4.5	55.55 (39.7)	40.84 (69.2)	32.77 (41.5)	27.19 (77.8)
6.0	67.98 (41.6)	63.58 (57.7)	37.61 (51.4)	39.36 (65.4)
7.5	73.98 (44.9)	70.87 (45.6)	40.30 (51.9)	42.32 (51.7)
9.0	77.49 (45.2)	77.06 (46.7)	38.80 (53.6)	42.49 (48.1)
10.5	67.89 (47.1)	64.39 (44.9)	32.78 (53.8)	34.22 (47.8)
12	64.85 (44.2)	65.76 (48.3)	31.11 (55.9)	32.63 (48.1)
14	53.34 (42.7)	52.04 (42.9)	25.69 (54.6)	26.89 (45.6)
16	47.35 (43.4)	46.11 (43.5)	21.78 (52.9)	23.29 (50.4)
24	36.48 (43.9)	34.14 (45.4)	15.49 (82.3)	12.90 (73.2)
32	21.92 (59.3)	21.33 (61.7)	5.75 (159.1)	6.56 (126.3)
40	12.44 (75.6)	12.28 (80.0)	2.15 (285.9)	2.79 (221.0)
48	10.37 (71.0)	9.85 (81.4)	1.09 (373.5)	1.33 (330.3)
60	3.39 (143.6)	3.54 (163.8)	0.97 (366.3)	0.70 (410.3)
72	3.32 (132.9)	3.62 (151.9)	0.55 (470.5)	0.25 (848.5)

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**Fasting Bioavailability Study - 1.25 mg, Continued**

**Table 20**

**Mean Pharmacokinetic Parameters after a 1 x 1.25 mg Dose Under Fasting Conditions  
 Total Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	34902 (57.2)	34569 (54.3)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	30907	30501	101.33	95.29 - 107.74
AUC <sub>(0-∞)</sub> (Measured) (pg*hr/mL)	36220 (55.6)	35667 (53.3)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (pg*hr/mL)	31985	31720	100.84	96.45 - 105.41
C <sub>max</sub> (Measured) (pg/mL)	2537.8 (50.6)	2581.2 (57.4)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	2302.5	2247.5	102.45	93.68 - 112.03
k <sub>el</sub> (Measured) (1/hr)	0.0796 (29.1)	0.0775 (22.3)	-	-
t <sub>1/2</sub> (Measured) (hr)	9.34 (25.4)	9.42 (23.5)	-	-
T <sub>max</sub> (Measured) (hr)	5.433 (35.1)	7.947 (35.2)	-	-

**Table 21**

**Mean Pharmacokinetic Parameters after a 1 x 1.25 mg Dose Under Fasting Conditions  
 Total Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	58229 (42.6)	56727 (39.3)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	53690	53149	101.02	95.38 - 106.97
AUC <sub>(0-∞)</sub> (Measured) (pg*hr/mL)	59513 (44.3)	57881 (40.3)	-	-
AUC <sub>(0-∞)</sub> (Geometric) (pg*hr/mL)	54576	54089	100.90	95.13 - 107.01
C <sub>max</sub> (Measured) (pg/mL)	3695.1 (39.8)	3617.5 (38.3)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	3428.3	3400.5	100.82	93.50 - 108.70
k <sub>el</sub> (Measured) (1/hr)	0.0732 (30.9)	0.0732 (29.9)	-	-
t <sub>1/2</sub> (Measured) (hr)	10.33 (30.1)	10.26 (27.7)	-	-
T <sub>max</sub> (Measured) (hr)	7.168 (30.5)	8.333 (30.3)	-	-

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**Fasting Bioavailability Study - 1.25 mg, Continued**

**Table 23**  
**Mean Pharmacokinetic Parameters After a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Free Estrone (Baseline Corrected)**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	1609.5 (43.9)	1483.3 (46.8)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	1369.9	1318.9	103.86	93.18 - 115.77
C <sub>max</sub> (Measured) (pg/mL)	75.69 (40.4)	67.54 (48.2)	-	-
C <sub>max</sub> (Geometric) (pg/mL)	68.31	59.72	114.38	105.13 - 124.43
T <sub>max</sub> (Measured) (hr)	7.844 (30.9)	11.250 (32.8)	-	-

**Table 24**  
**Mean Pharmacokinetic Parameters After a 1 x 1.25 mg Dose Under Fasting Conditions**  
**Free Equilin**

Pharmacokinetic Parameter	Test Formulation (Cenestin™) Duramed Mean (CV%)	Reference Formulation (Premarin) Wyeth-Ayerst Mean (CV%)	Ratio of Least Square Means (%)	Confidence Interval (%)
AUC <sub>(0-72)</sub> (Measured) (pg*hr/mL)	556.5 (52.6)	543.4 (48.7)	-	-
AUC <sub>(0-72)</sub> (Geometric) (pg*hr/mL)	483.7	479.0	100.99	93.35 - 109.24
C <sub>max</sub> (Measured) (pg/mL)	35.142 (40.9)	36.211 (44.7)	-	-
C <sub>max</sub> (Geometric) (pg/mL) -	32.160	32.621	98.59	90.46 - 107.43
T <sub>max</sub> (Measured) (hr)	6.954 (31.5)	9.406 (34.3)	-	-

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