

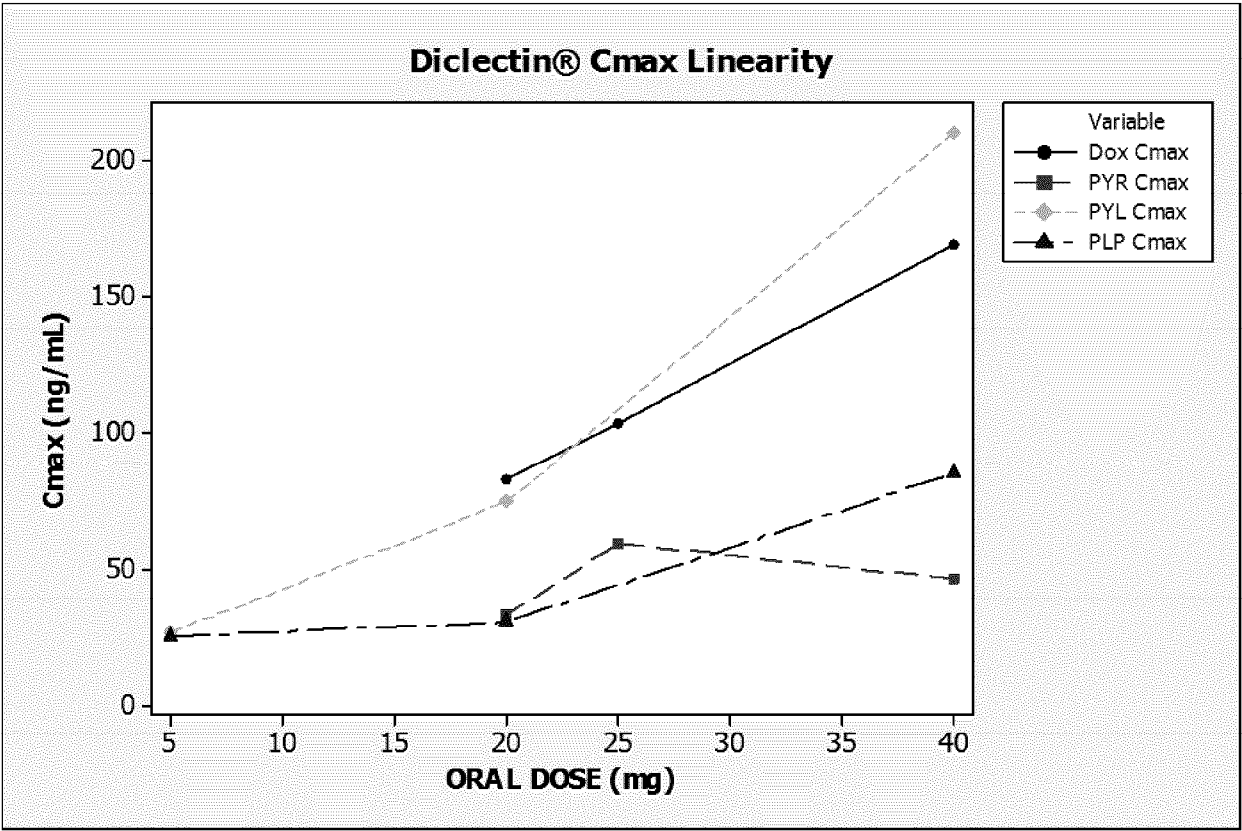


FIG. 1

2/17

			Fasted	Fed	delta	Single dose	Multi dose	delta
			in women	in women		in women	in women	
Pyridoxine								
AUC inf	ng/mL		40	24	-40%	43	64 [†]	+50%
Cmax	ng/mL		35	14	-60%	33	46 [†]	+40%
Tmax	hr		2.5	9.25	+7h	5.5	5.5	=
T1/2	hr		0.4	0.5	=	0.5	0.5	=
Pyridoxal								
AUC inf	ng/mL		231	197	-15%	211	1587 [†]	+650%
Cmax	ng/mL		85	46	-45%	74	210 [†]	+184%
Tmax	hr		3	10	+7h	6	6.8	=
T1/2	hr		2	2	=	1.3	19	+18h
PLP								
AUC inf	ng/mL		2415	2839 [†]	+17%	1536	6100 [†]	+297%
Cmax	ng/mL		30	34	=	30	85 [†]	+183%
Tmax	hr		12	16	+4h	11.5	6	-5h
T1/2	hr		82	95 [†]	+15%	37	54	45%
Doxy								
AUC inf	ng/mL		1448	1579	=	1281	3721 [†]	+190%
Cmax	ng/mL		94.9	75.74	-20%	83.3	168.6 [†]	+104%
Tmax	hr		5	12	+7h	7.2	7.8	=
T1/2	hr		12.64	12.48	=	10.1	11.9	=

FIG. 2

Diclectin® Fed Conditions (B) vs Diclectin® Fasting Conditions (A)

Doxylamine	AUC _{0-t}	AUC _{0-inf} [*]	C _{max}
Ratio ¹	102.86%	108.81%	79.61%
90 % Geometric C.I. ²	96.92 % to 109.15 %	104.33 % to 113.49 %	74.73 % to 84.81 %
Intra-Subject CV	16.24 %	10.57 %	17.31 %

¹ Calculated using least-squares means according to the formula: $e^{\frac{(\text{Diclectin® Fed Conditions (B)} - \text{Diclectin® Fasting Conditions (A)})}{N}} \times 100$

² 90% Geometric Confidence Interval using ln-transformed data

^{*} For this parameter, N = 37.

FIG. 3A

3/17

Diclectin® Fed Conditions (B) vs Diclectin® Fasting Conditions (A)

Pyridoxine	AUC _{0-t} N = 33	AUC _{0-inf} N = 12	C _{max} N = 33
Ratio ¹	44.62%	61.45%	32.39%
90 % Geometric C.I. ²	31.26 % to 63.68 %	40.31 % to 93.67 %	22.79 % to 46.03 %
Intra-Subject CV	102.22 %	58.03 %	100.52 %

¹ Calculated using least-squares means according to the formula: $e^{\frac{(\text{Diclectin® Fed Conditions (B)} - \text{Diclectin® Fasting Conditions (A)})}{N}} \times 100$

² 90% Geometric Confidence Interval using ln-transformed data

FIG. 3B

	AUC ₀₋₂₄ (ng/mL) after 20 mg day 1	AUC ₀₋₂₄ (ng/mL) after 20 mg day 18	Accumulation index AI AUC ₀₋₂₄ day 18 / AUC ₀₋₂₄ day 1
Doxy	911.4	2531.5	2.76
PYR	40.7	62.7	1.59
PYL	195.1	1147.2	3.09
PLP	442	1725	3.98
PYM	0.57	1.79	3.16
PMP	3.504	17.08	4.88

FIG. 4

4/17

Doxylamine

subject	dose	treatment	AUCt (ng/mL)	AUCt intra study % cv	Cmax (ng/mL)	Cmax intra study %cv	Tmax (hr)	Tmax intra study % cv	T1/2 (hr)	T1/2 intra study % cv
18 women	20mg	fasted	1678.19	32.7	90.4	14.5	6.1	29.0	11.8	28.9
24 women	20mg	fasted	1519.79	8.5	85.9	20.6	5.3	29.5	11.7	19.9
42 women	20mg	fasted	1407.20	23.9	94.9	19.4	5.1	66.1	12.6	27.2
18 women	20mg	fasted	911.40	22.6	83.3	24.8	7.2	25.9	10.1	20.8
24 women	20mg	fed	1567.23	23.4	82.0	18.9	10.6	17.0	12.0	15.9
42 women	20mg	fed	1488.03	31.1	75.7	21.9	14.9	49.2	12.5	23.1
18 women	40mg	multidose	3661.27	34.9	168.6	22.8	7.8	20.7	11.9	28.0
average %CV				25.3		20.4		33.9		23.4

Pyridoxine

subject	dose	treatment	AUCt (ng/mL)	AUCt intra study % cv	Cmax (ng/mL)	Cmax intra study %cv	Tmax (hr)	Tmax intra study % cv	T1/2 (hr)	T1/2 intra study % cv
18 women	20mg	fasted	39.34	42.0	32.4	46.1	5.7	26.7	0.5	47.4
24 women	20mg	fasted	33.75	40.6	35.5	61.0	2.5	37.7	0.4	42.3
42 women	20mg	fasted			55.1	36.8	2.7	40.2		
18 women	20mg	fasted	51.41	45.2	50.7	61.1	3.8	31.4	0.3	44.5
24 women	20mg	fed			24.0	58.3	7.7	22.5		
42 women	20mg	fed								
18 women	40mg	multidose	59.53	57.2	46.1	61.5	5.6	22.2	0.5	30.0
average %CV				46.2		54.1		30.1		41.1

FIG. 5

5/17

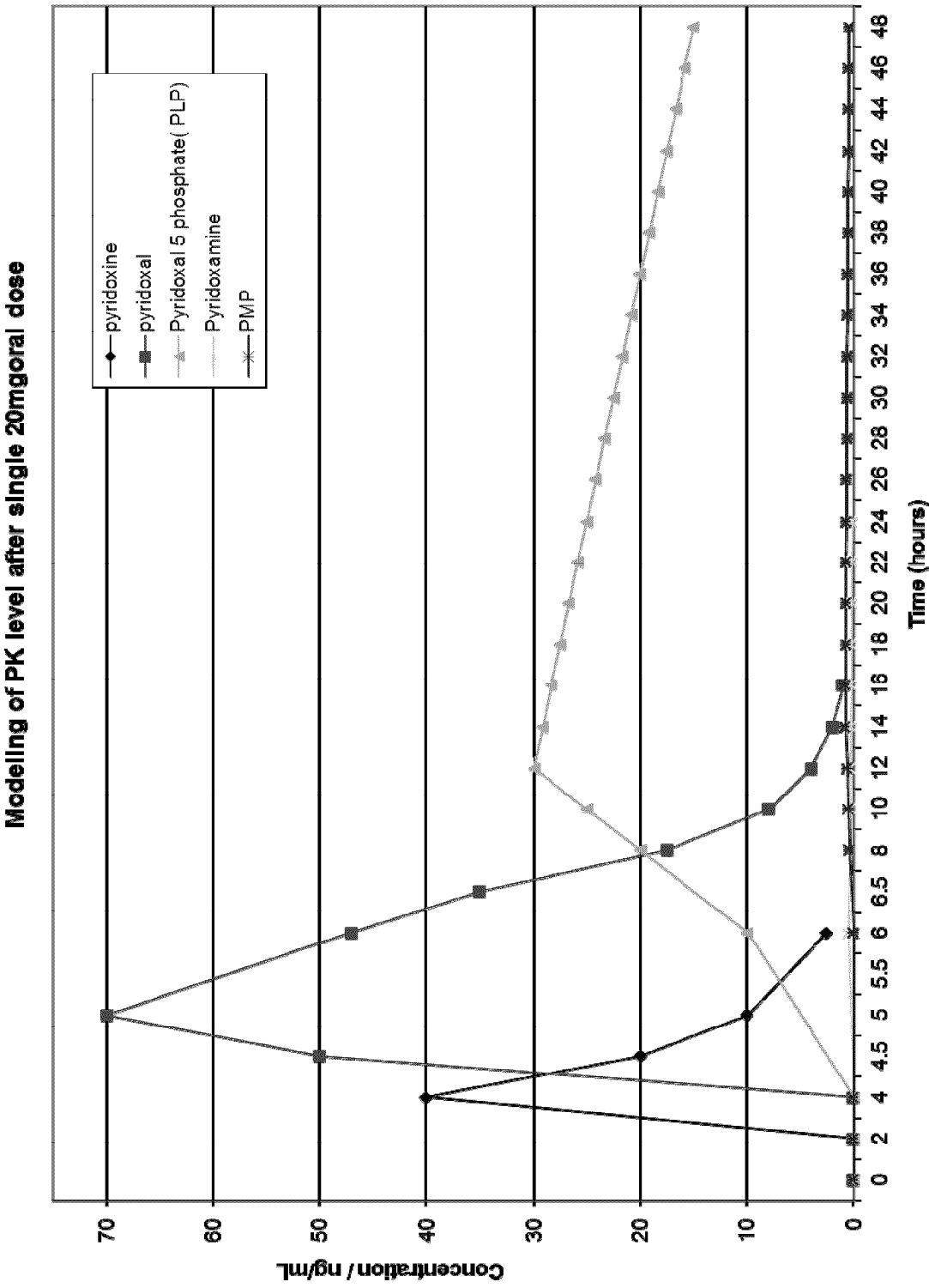


FIG. 6

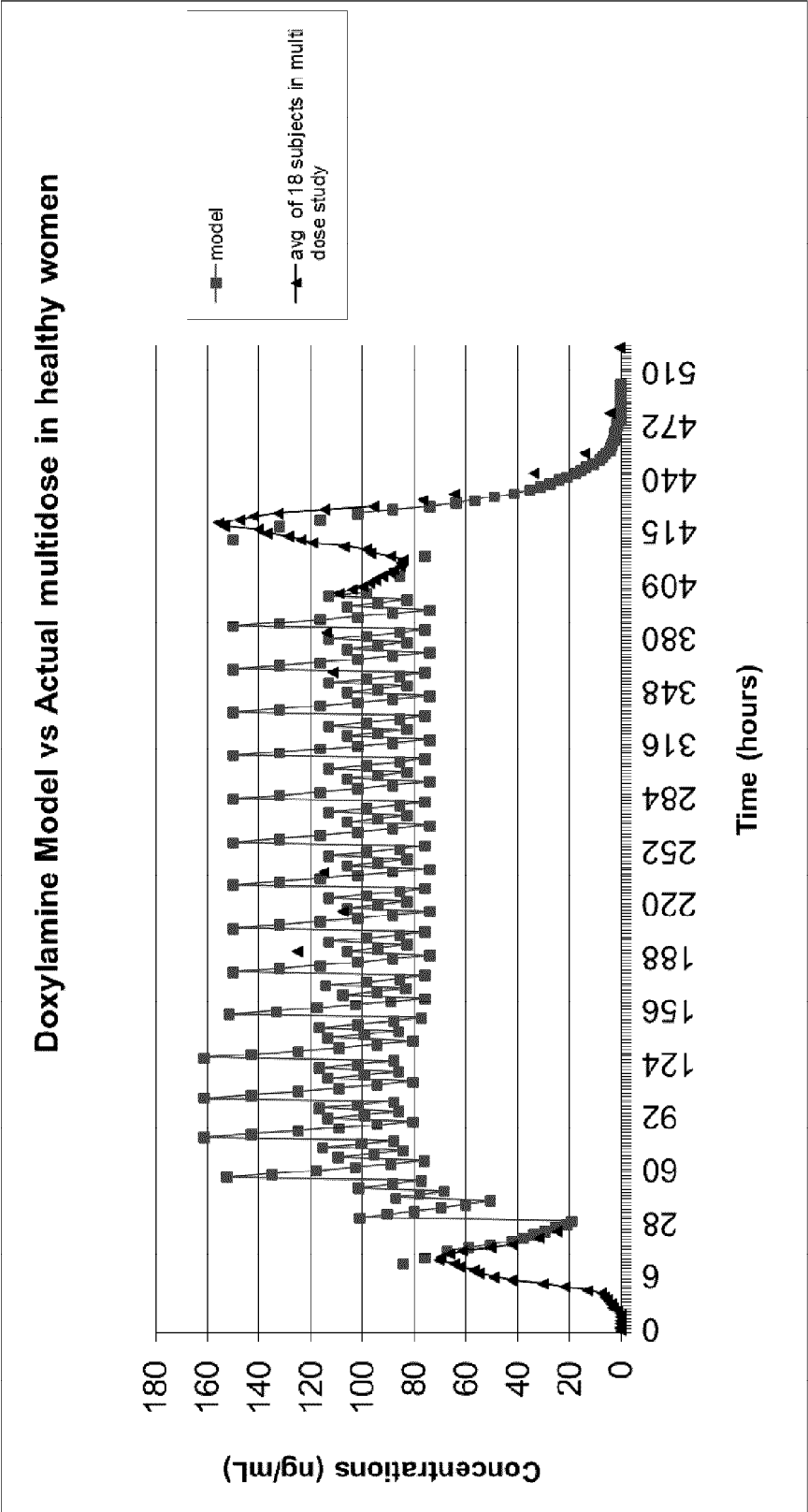


FIG. 7A

7/17

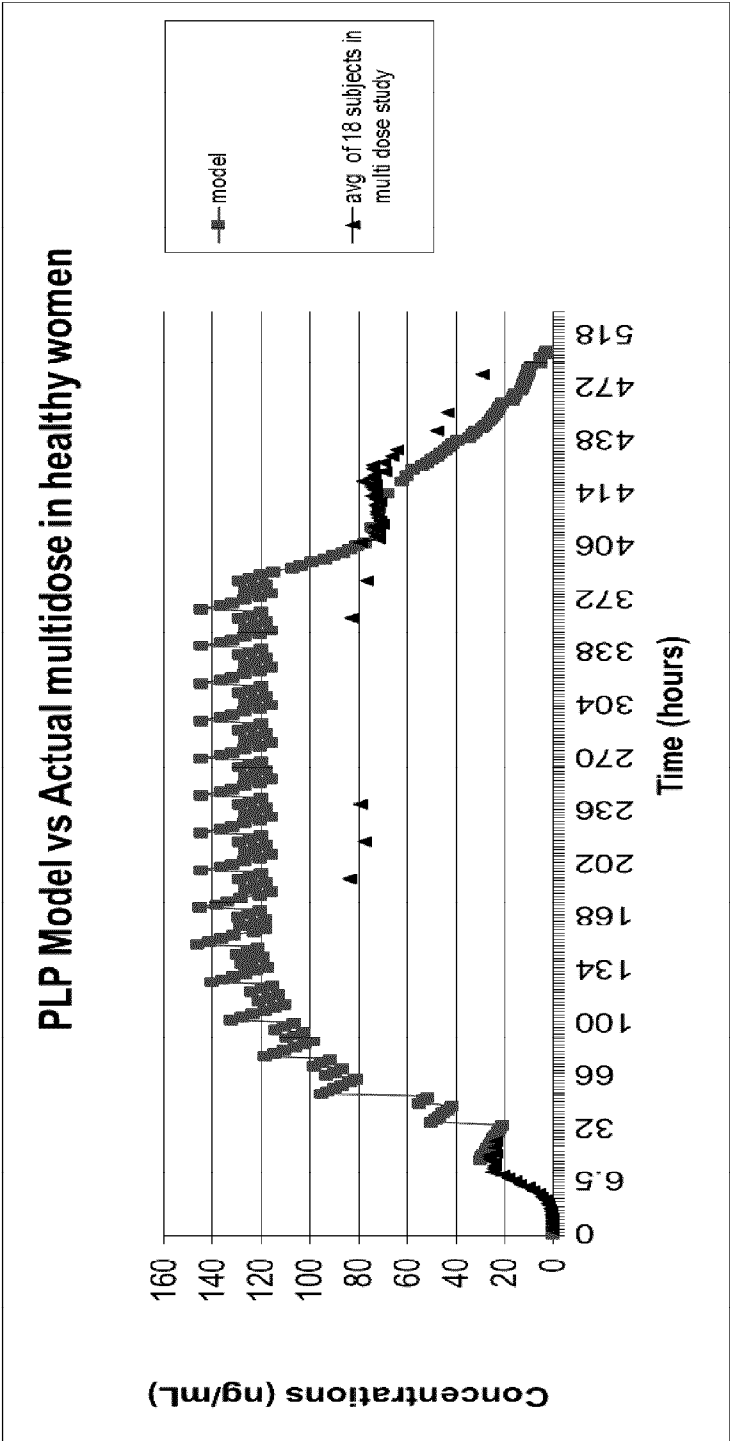


FIG. 7B

8/17

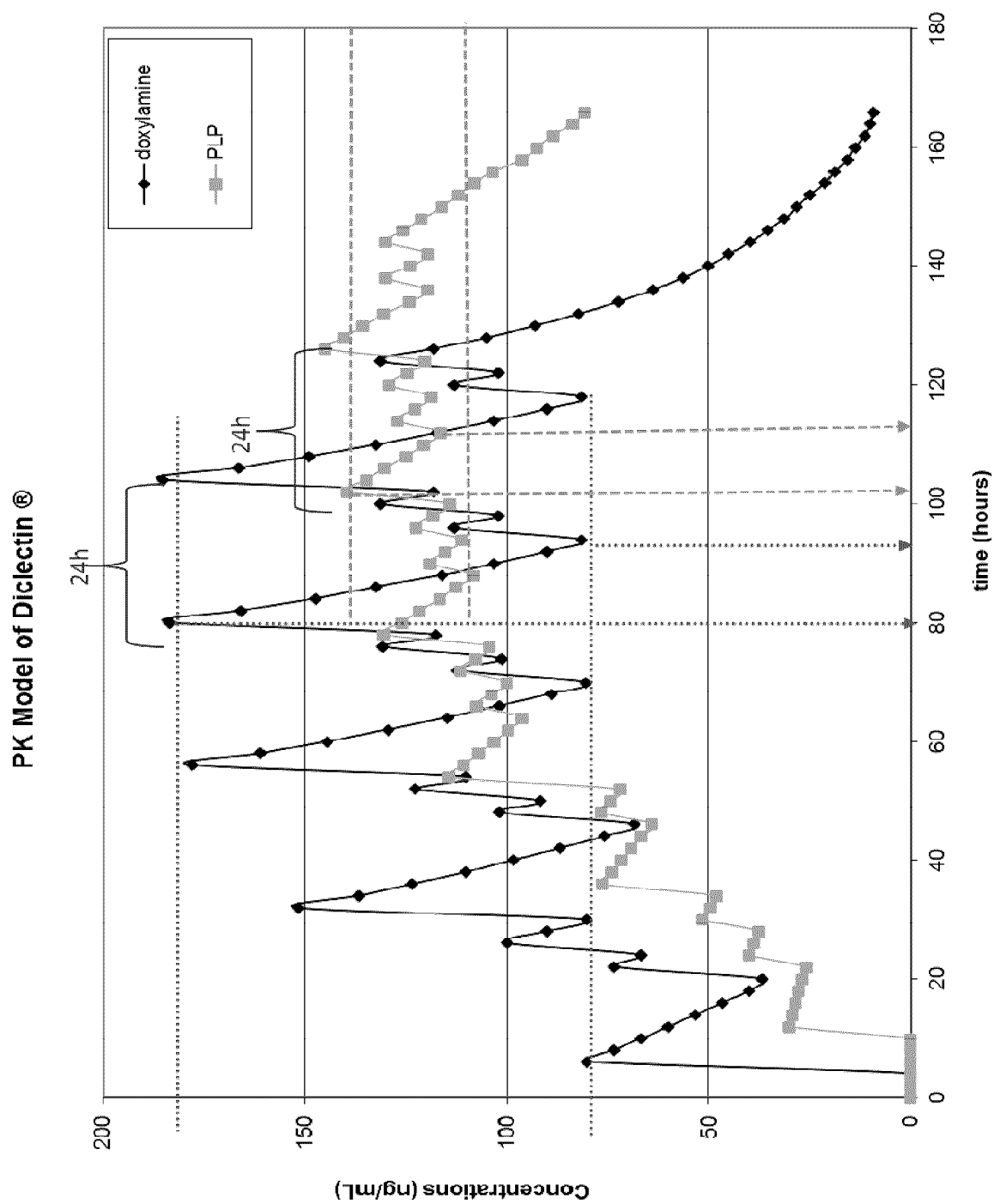


FIG. 7C

9/17

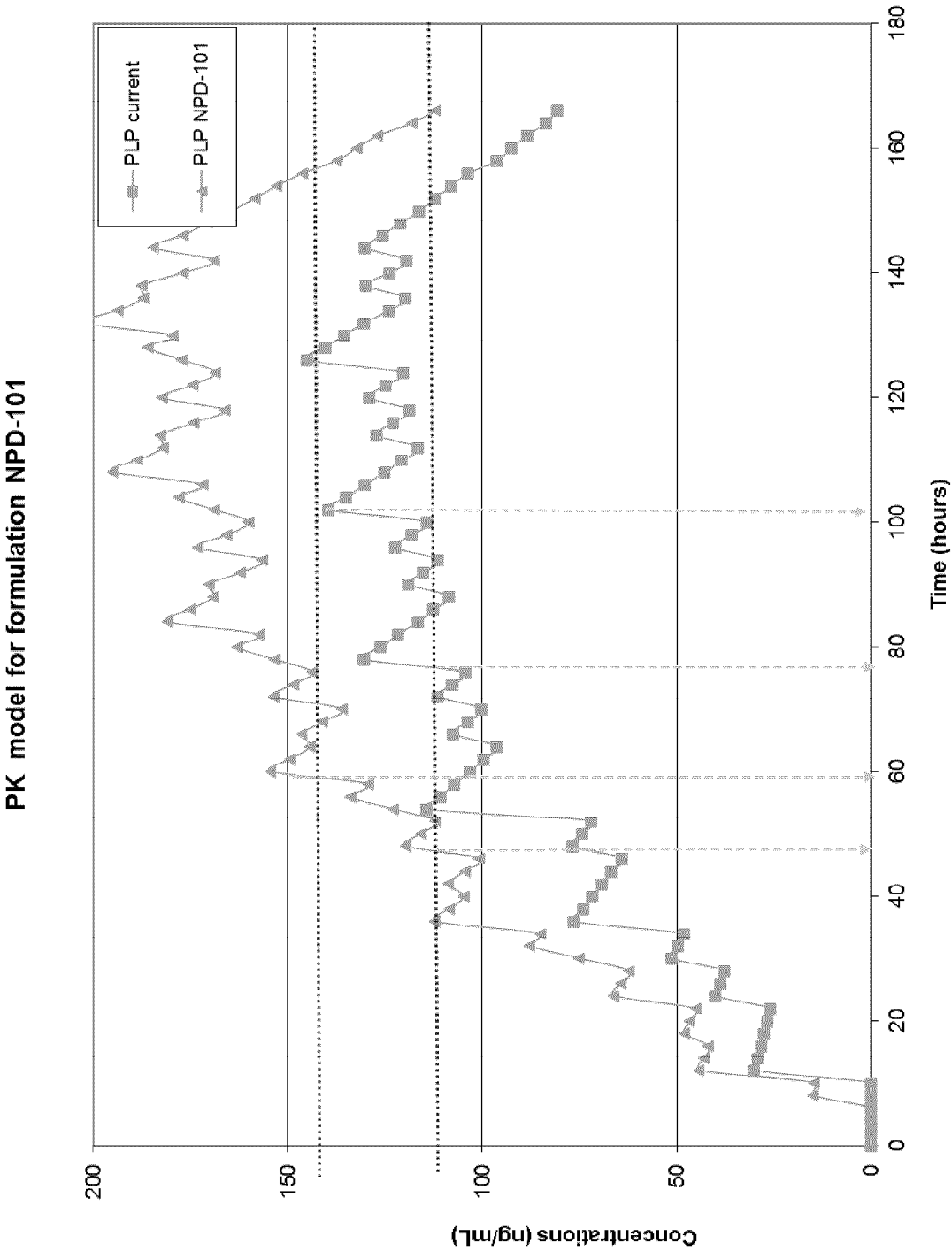


FIG. 8

10/17

Doxylamine PK Model for formulation NPD-102

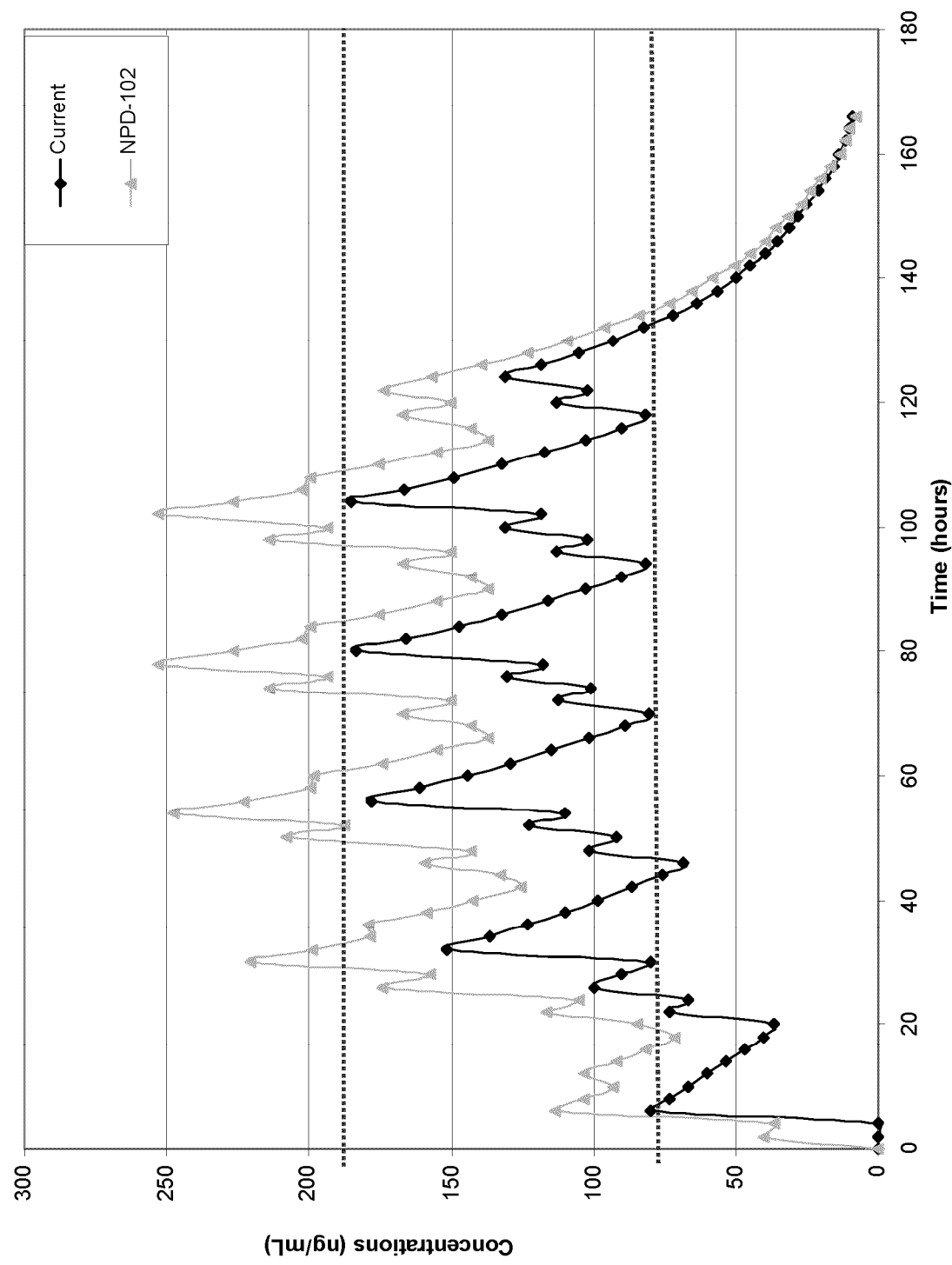


FIG. 9

11/17

Doxylamine PK Model for formulation NPD 102

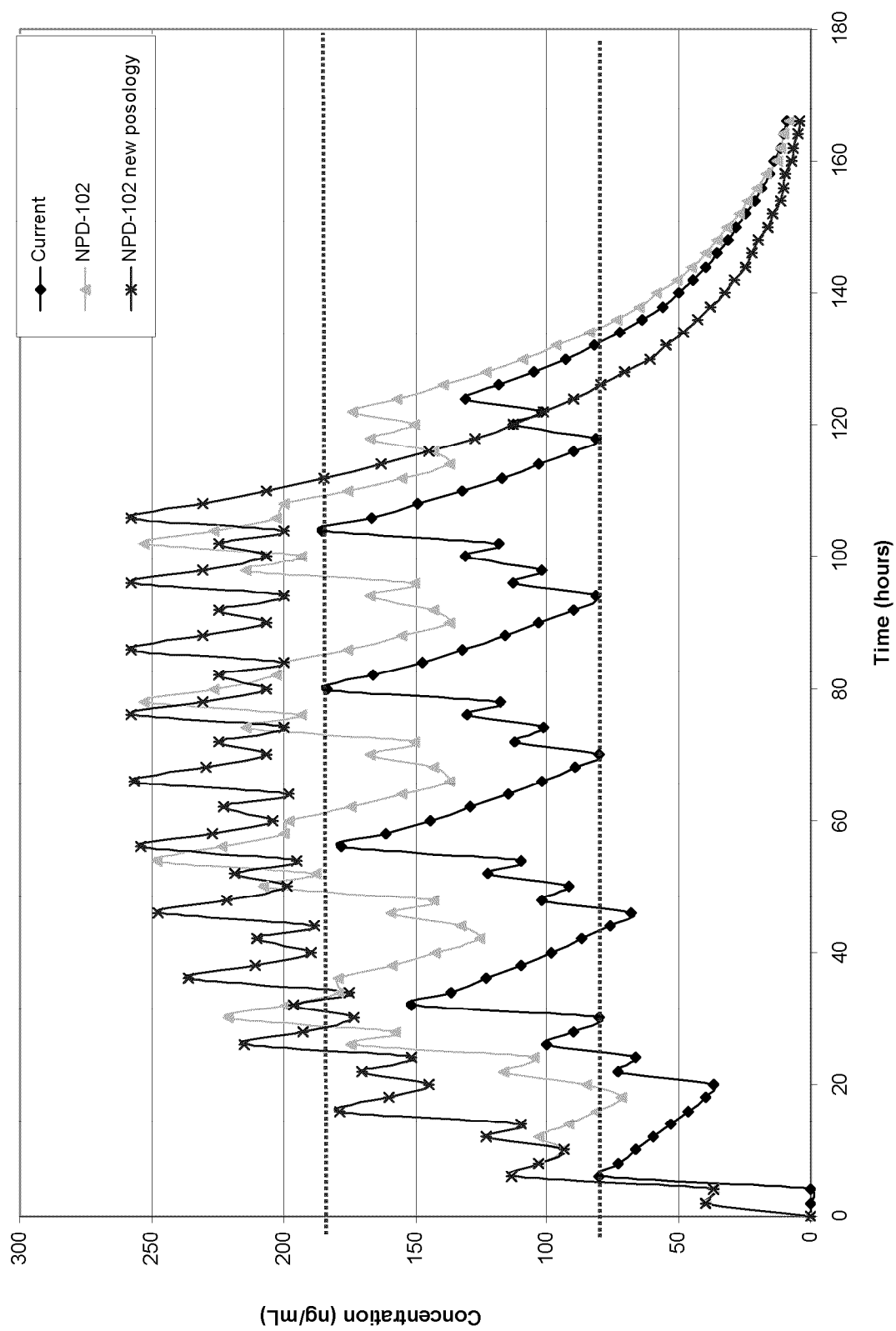


FIG. 10A

12/17

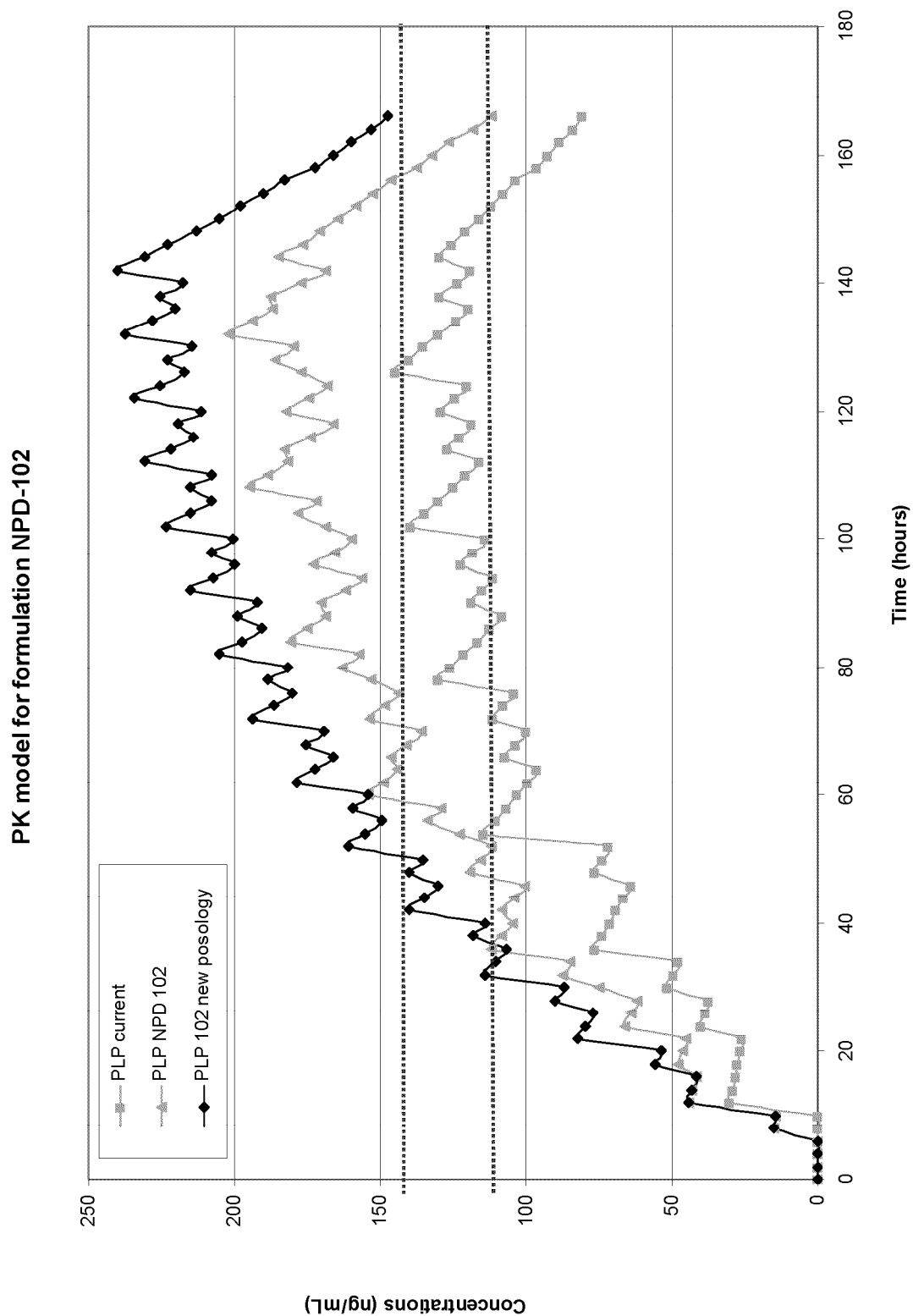


FIG. 10B

13/17

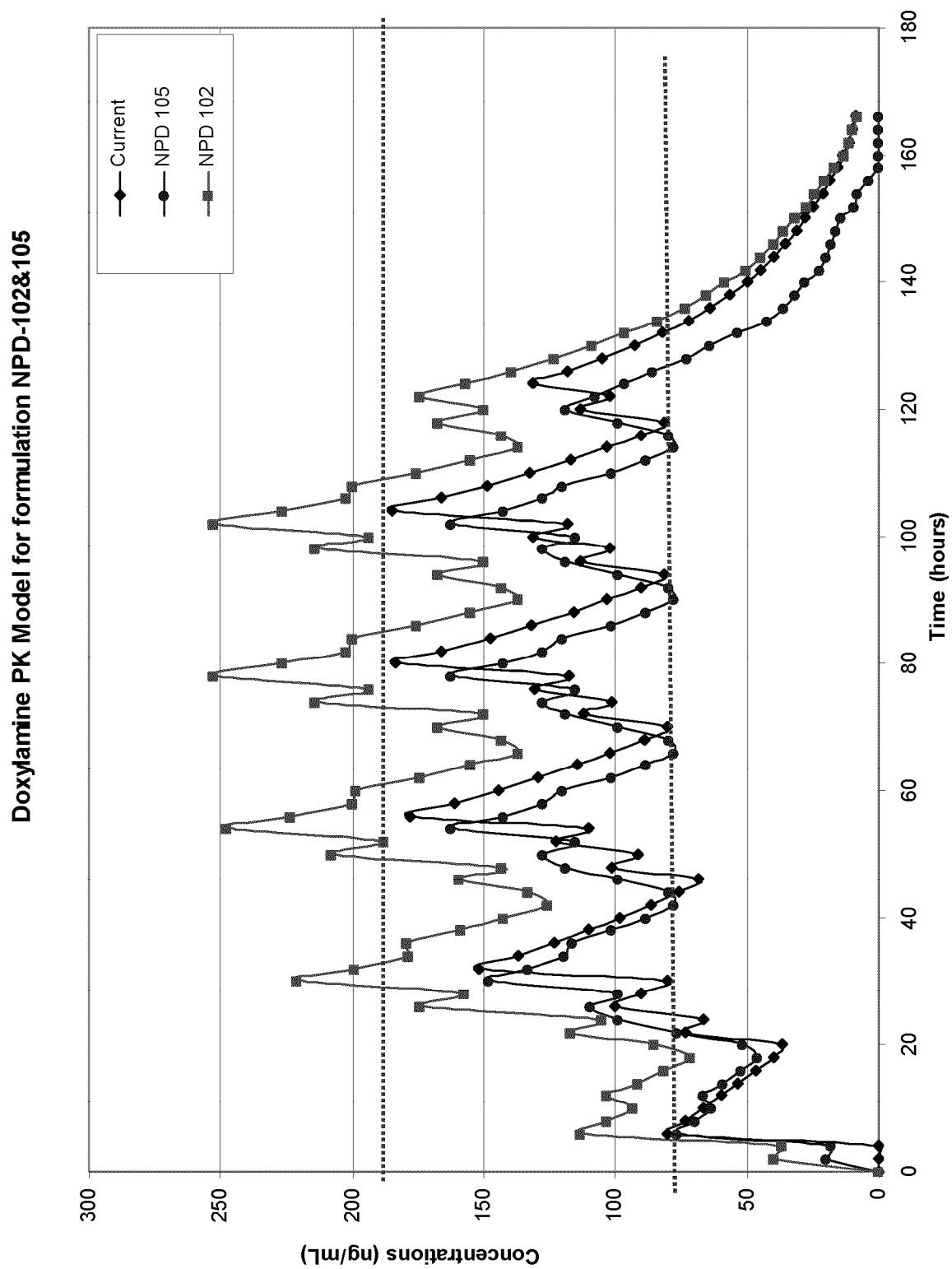


FIG. 11A

14/17

PLP PK Model for formulation NDP-102 & 105

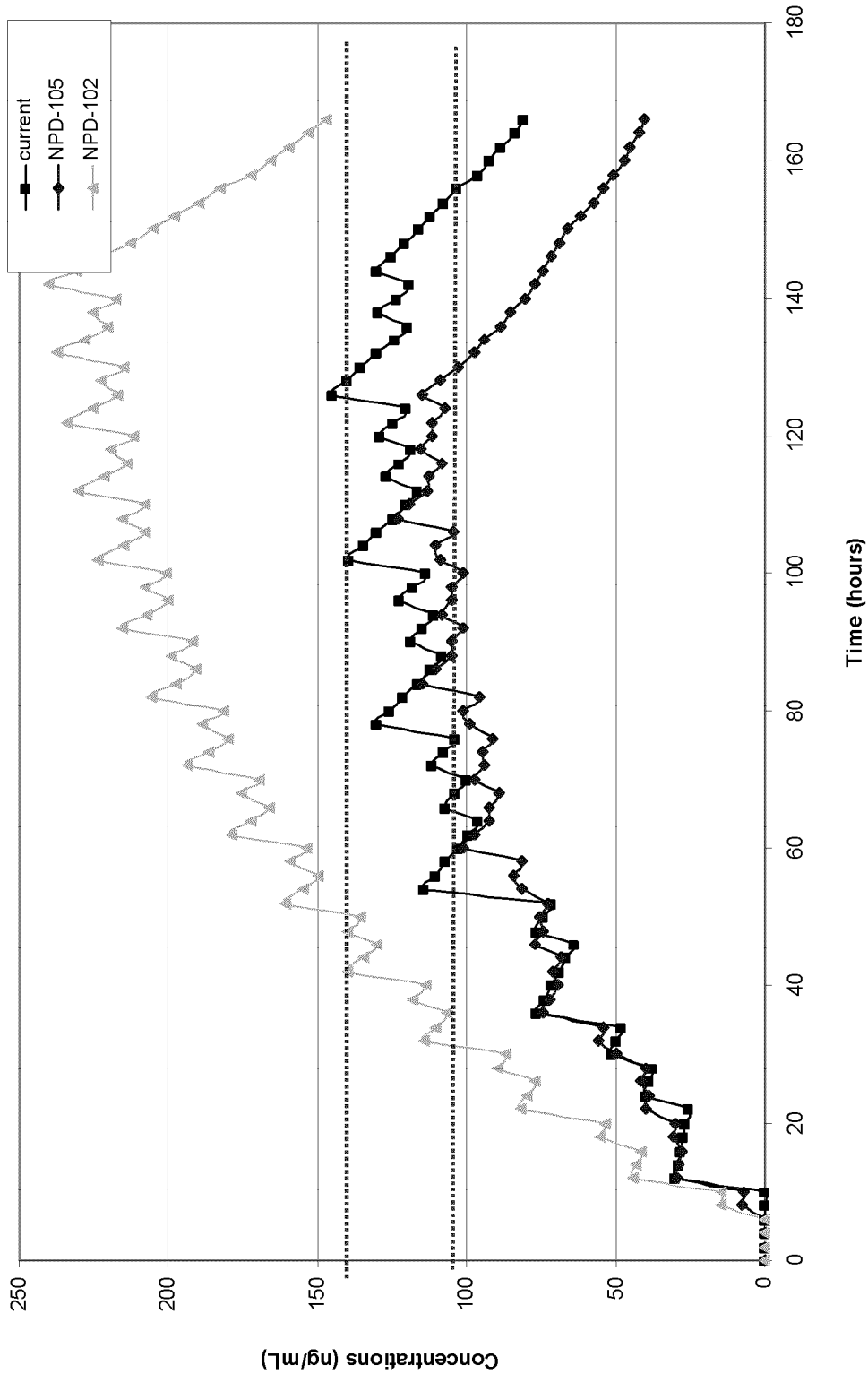


FIG. 11B

15/17

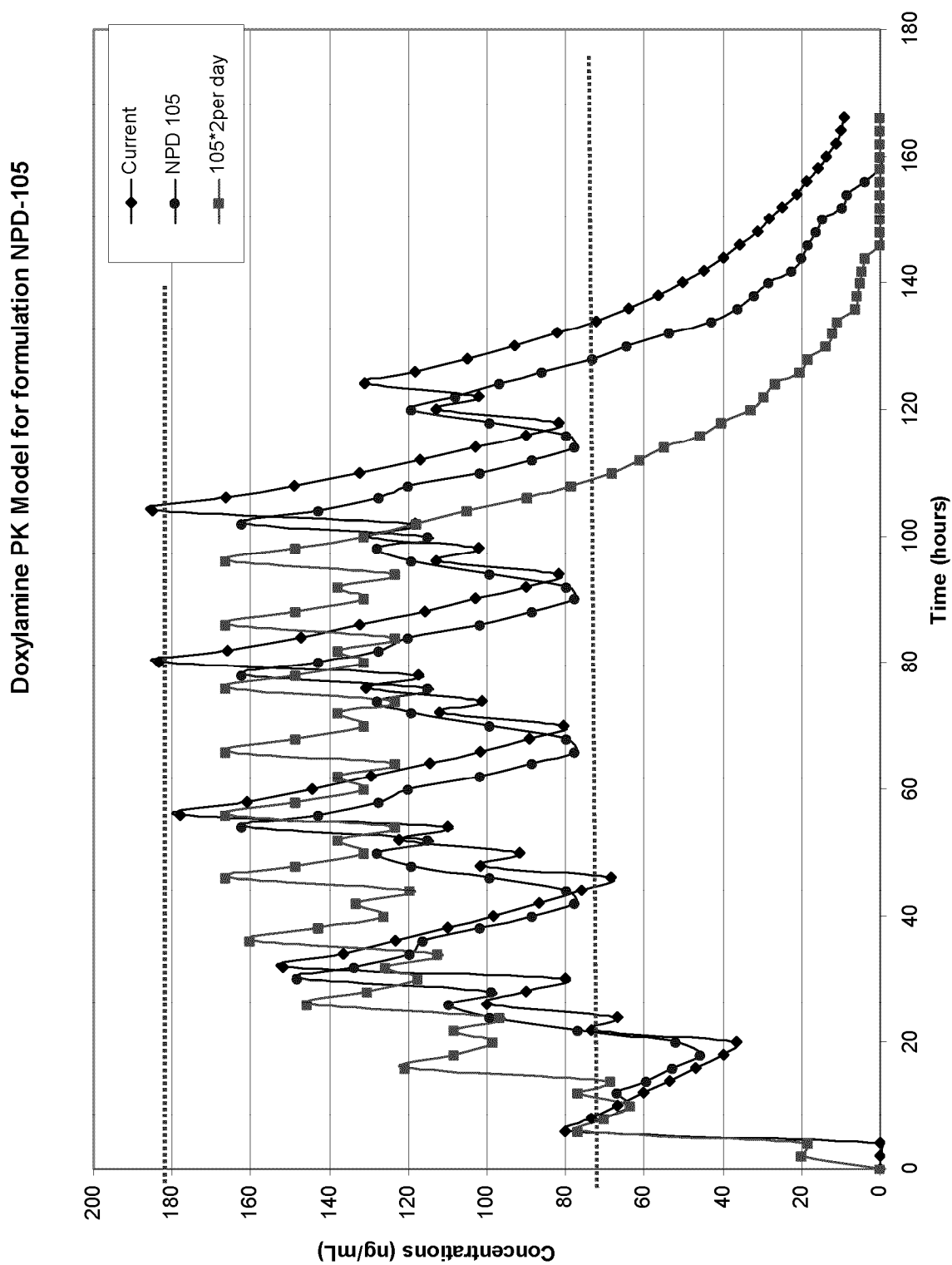


FIG. 11C

16/17

PLP PK Model for formulation NPD-105

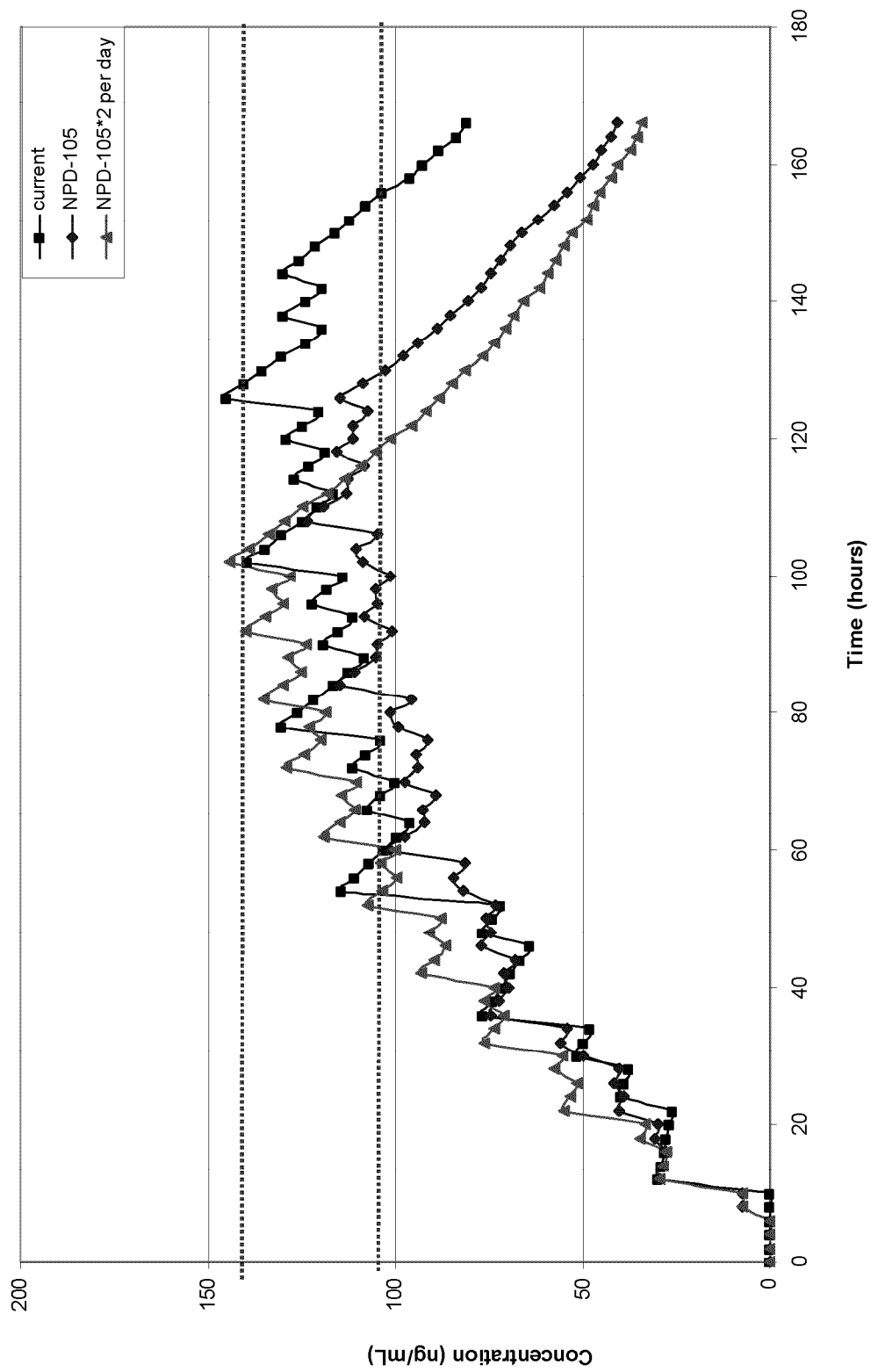


FIG. 11D

17/17

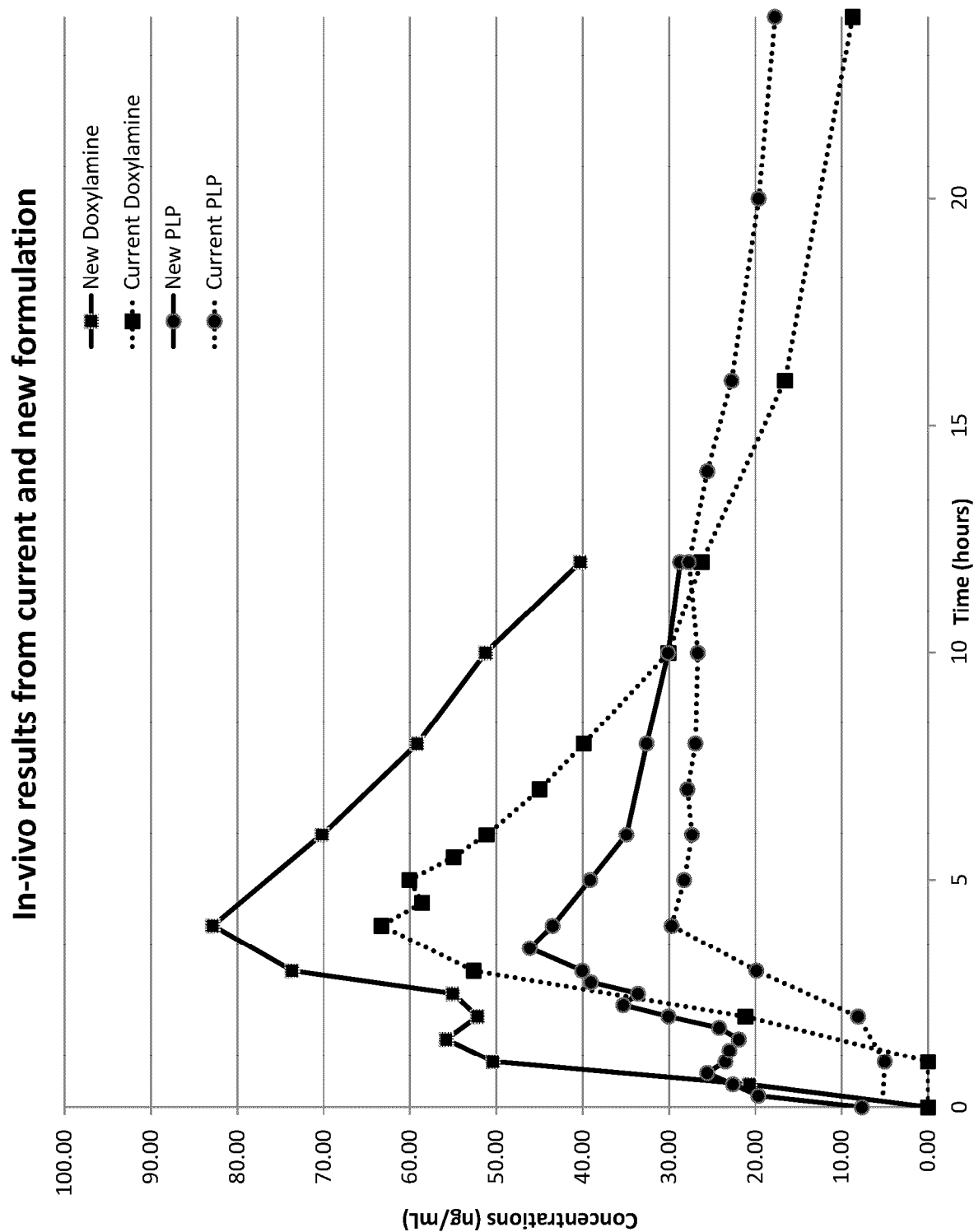


FIG.12