8.4 Reference values 4: Linear/Log Trapezoidal;

WinNonlin 8.0.0.3176 Formulation=R,Subject=2

> Date: 9/09/2019 Time: 18:03:37

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration Number of nonmissing observations: 16

Steady state interval Tau: 12.00

0.00 Dose time: Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal

Weighting for lambda_z calculations: Uniform weighting Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	62.22			15.56	7.778	
1.000	261.2			96.41	80.85	
1.500	234.1			220.1	234.9	
2.000	234.1			337.1	439.7	
2.500	222.9			451.4	696.5	
3.000	213.9			560.5	996.5	
4.000	196.0			765.4	1712.	
5.000	199.6			963.2	2602.	
6.000	196.0			1161.	3690.	
8.000	213.4			1570.	6560.	
10.00 *	200.1	197.9	2.174	1983.	1.028e+04	1.000
12.00 *	196.0	192.4	3.626	2380.	1.463e+04	1.000
24.00 *	160.3	162.4	-2.108	4511.	5.256e+04	1.000
48.00 *	110.3	115.8	-5.512	7721.	1.657e+05	1.000
72.00 *	85.24	82.54	2.704	1.005e+04	3.045e+05	1.000

^{*)} Starred values were included in the estimation of Lambda_z.

N_Samples	16
Dose	120.0000
Rsq	0.9928
Rsq_adjusted	0.9904
Corr_XY	-0.9964
No_points_lambda_z	5
Lambda_z	0.0141
Lambda_z_intercept	5.4289
Lambda_z_lower	10.0000
Lambda_z_upper	72.0000
HL_Lambda_z	49.1374
Span	1.2618
Tlag	0.0000

Tmax	1.0000
Cmax	261.1770
Cmax_D	2.1765
Tlast	72.0000
Clast	85.2410
Clast_pred	82.5367
AUClast	10054.0368
AUClast_D	83.7836
AUCall	10054.0368
AUCINF_obs	16096.7914
AUCINF_D_obs	134.1399
AUC_%Extrap_obs	37.5401
AUCINF_pred	15905.0822
AUCINF_D_pred	132.5424
AUC_%Extrap_pred	36.7873
Tmin	0.0000
Cmin	0.0000
Ctau	196.0350
Cavg	198.2972
Swing	Missing
Swing_Tau	0.3323
Fluctuation%	131.7099
Fluctuation%_Tau	32.8507
CLss_F	0.0504
MRTINF_obs	75.3237
MRTINF_pred	74.3569
Vz_F	3.5749
Accumulation_Index	6.4216
AUC_TAU	2379.5666
AUC_TAU_D	19.8297
AUC_TAU_%Extrap	0.0000
AUMC_TAU	14631.1197

WinNonlin 8.0.0.3176 Formulation=R,Subject=3

> 9/09/2019 Date: 18:03:38 Time:

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: Steady state interval Tau: 12.00

Dose time: 0.00 Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

 ,						
 Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
 0.0000	0.0000			0.0000	0.0000	
0.5000	49.85			12.46	6.231	
1.000	77.37			44.27	31.80	
1.500	105.3			89.94	90.65	
2.000	100.9			141.5	180.8	
2.500	72.75			184.5	277.0	
3.000	69.99			220.2	375.1	

4.000	93.57			301.4	661.3	
5.000	91.98			394.2	1079.	
6.000 *	82.71	83.17	-0.4609	481.5	1558.	1.000
8.000 *	84.21	82.63	1.580	648.4	2727.	1.000
10.00 *	85.34	82.08	3.259	817.9	4253.	1.000
12.00 *	76.03	81.54	-5.518	979.1	6023.	1.000
24.00 *	81.26	78.39	2.872	1922.	2.307e+04	1.000
48.00 *	70.11	72.43	-2.326	3736.	8.780e+04	1.000
72.00 *	67.90	66.93	0.9699	5392.	1.871e+05	1.000

N_Samples	16
Dose	120.0000
Rsq	0.8136
Rsq_adjusted	0.7763
Corr_XY	-0.9020
No_points_lambda_z	7
Lambda z	0.0033
Lambda_z_intercept	4.4406
Lambda_z_lower	6.0000
Lambda_z_upper	72.0000
HL_Lambda_z	210.5915
Span	0.3134
Tlag	0.0000
Tmax	1.5000
Cmax	105.3450
Cmax D	0.8779
Tlast	72.0000
Clast	67.9010
Clast_pred	66.9311
AUClast	5391.5322
AUClast D	44.9294
AUCall	5391.5322
AUCINF obs	26021.1651
AUCINF_D_obs	216.8430
AUC %Extrap obs	79.2802
AUCINF_pred	25726.4777
AUCINF_D_pred	214.3873
AUC_%Extrap_pred	79.0429
Tmin	0.0000
Cmin	0.0000
Ctau	76.0270
Cavg	81.5924
Swing	Missing
Swing_Tau	0.3856
Fluctuation%	129.1113
Fluctuation% Tau	35.9323
CLss_F	0.1226
MRTINF_obs	313.0680
MRTINF_pred	309.4563
Vz F	37.2362
Accumulation_Index	25.8216
AUC TAU	979.1088
AUC TAU D	8.1592
AUC_TAU_%Extrap	0.0000
AUMC TAU	6022.9286
701C_170	0022.3200

WinNonlin 8.0.0.3176 Formulation=R,Subject=4

> Date: 9/09/2019 Time: 18:03:37

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration Number of nonmissing observations: 16 Steady state interval Tau: 12.00

0.00 Dose time: 120.00 Dose amount:

Calculation method: Linear/Log Trapezoidal
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	52.42			13.11	6.553	
1.000	208.5			78.35	65.24	
1.500	188.9			177.6	188.9	
2.000	165.2			266.0	343.1	
2.500	147.0			344.0	518.2	
3.000	152.7			418.9	724.3	
4.000	154.3			572.4	1262.	
5.000	128.4			713.4	1894.	
6.000	149.8			852.2	2659.	
8.000	151.1			1153.	4766.	
10.00	136.8			1441.	7350.	
12.00	132.3			1710.	1.031e+04	
24.00 *	141.2	145.8	-4.547	3350.	3.994e+04	1.000
48.00 *	129.1	121.2	7.930	6593.	1.561e+05	1.000
72.00 *	97.63	100.8	-3.143	9296.	3.168e+05	1.000

*) Starred values were included in the estimation of Lambda_z.

N_Samples	16
Dose	120.0000
Rsq	0.9189
Rsq_adjusted	0.8377
Corr_XY	-0.9586
No_points_lambda_z	3
Lambda_z	0.0077
Lambda_z_intercept	5.1669
Lambda_z_lower	24.0000
Lambda_z_upper	72.0000
HL_Lambda_z	90.0736
Span	0.5329
Tlag	0.0000
Tmax	1.0000
Cmax	208.5420
Cmax_D	1.7379
Tlast	72.0000
Clast	97.6250
Clast_pred	100.7679
AUClast	9296.2179
AUClast_D	77.4685
AUCall	9296.2179
AUCINF_obs	21982.4600
AUCINF_D_obs	183.1872

AUC_%Extrap_obs AUCINF_pred	57.7107 22390.8801
AUCINF_D_pred	186.5907
AUC_%Extrap_pred	58.4821
Tmin	0.0000
Cmin	0.0000
Ctau	132.2570
Cavg	142.4823
Swing _	Missing
Swing_Tau	0.5768
Fluctuation%	146.3634
Fluctuation%_Tau	53.5400
CLss_F	0.0702
MRTINF_obs	148.3108
MRTINF_pred	151.1773
Vz F	9.1203
Accumulation_Index	11.3368
AUC TAU	1709.7878
AUC ^T AU D	14.2482
AUC TAU %Extrap	0.0000
AUMC_TAU	10307.9543

WinNonlin 8.0.0.3176 Formulation=R,Subject=7

> 9/09/2019 Date: Time: 18:03:38

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration Number of nonmissing observations: 16 Steady state interval Tau: 12.00

Dose time: 0.00 Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal

Weighting for lambda_z calculations: Uniform weighting Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	19.95			4.988	2.494	
1.000	128.4			42.08	37.09	
1.500	136.8			108.4	120.5	
2.000	113.1			170.9	228.3	
2.500	153.3			237.4	380.7	
3.000	123.6			306.4	569.7	
4.000	142.7			439.3	1036.	
5.000	112.3			566.2	1605.	
6.000	139.9			691.8	2298.	
8.000	105.5			935.6	3993.	
10.00 *	134.4	132.4	1.964	1174.	6152.	1.000
12.00 *	123.4	129.2	-5.814	1432.	8982.	1.000
24.00 *	110.5	111.2	-0.7336	2834.	3.406e+04	1.000
48.00 *	90.29	82.49	7.798	5235.	1.195e+05	1.000
72.00 *	58.05	61.17	-3.122	6987.	2.231e+05	1.000

Tillat Talameters	
N. C. 1	16
N_Samples	16
Dose	120.0000
Rsq	0.9703
Rsq_adjusted	0.9604
Corr_XY	-0.9850
No_points_lambda_z	5
Lambda_z	0.0125
Lambda_z_intercept	5.0107
Lambda_z_lower	10.0000
Lambda_z_upper	72.0000
HL_Lambda_z	55.6345
Span	1.1144
Tlag	0.0000
Tmax	2.5000
Cmax	153.2540
Cmax D	1.2771
Tlast	72.0000
Clast	58.0510
Clast_pred	61.1727
AUClast	6987.0645
AUClast D	58.2255
AUCall	6987.0645
AUCINF obs	11646.4437
AUCINF_D_obs	97.0537
AUC_%Extrap_obs	40.0069
AUCINF_pred	11897.0026
AUCINF D pred	99.1417
AUC_%Extrap_pred	41.2704
Tmin	0.0000
Cmin	0.0000
Ctau	123.3700
Cavg	119.3351
Swing	Missing
Swing_Tau	0.2422
Fluctuation%	128.4232
Fluctuation%_Tau	25.0421
CLSS_F	0.0838
MRTINF_obs	91.8667
MRTINF_pred	93.9663
Vz_F	6.7259
Accumulation_Index	7.2011
AUC_TAU	1432.0218
AUC_TAU_D	11.9335
AUC_TAU_%Extrap	0.0000
AUMC_TAU	8982.0378

WinNonlin 8.0.0.3176 Formulation=R,Subject=8

> Date: 9/09/2019 Time: 18:03:37

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: 16 Steady state interval Tau: 12.00 Dose time: 0.00
Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	136.9			34.23	17.11	
1.000	126.6			100.1	65.89	
1.500	118.5			161.4	142.0	
2.000	134.9			224.8	253.9	
2.500	113.2			286.8	392.1	
3.000	130.9			347.8	561.0	
4.000	138.3			482.4	1034.	
5.000	22.72			546.4	1313.	
6.000	53.77			582.5	1514.	
8.000	55.11			691.4	2276.	
10.00	102.9			844.4	3669.	
12.00 *	134.1	129.2	4.939	1080.	6272.	1.000
24.00 *	108.0	116.1	-8.045	2527.	3.201e+04	1.000
48.00 *	98.47	93.68	4.791	5003.	1.207e+05	1.000
72.00 *	74.44	75.60	-1.167	7065.	2.432e+05	1.000

*) Starred values were included in the estimation of Lambda_z.

N_Samples	16
Dose	120.0000
Rsq	0.9480
Rsq_adjusted	0.9220
Corr XÝ	-0.9736
No_points_lambda_z	4
Lambda_z	0.0089
Lambda_z_intercept	4.9685
Lambda_z_lower	12.0000
Lambda_z_upper	72.0000
HL_Lambda_z	77.6194
Span	0.7730
Tlag	0.0000
Tmax	4.0000
Cmax	138.3270
Cmax_D	1.1527
Tlast	72.0000
Clast	74.4370
Clast_pred	75.6043
AUClast	7064.7816
AUClast_D	58.8732
AUCall	7064.7816
AUCINF_obs	15400.3174
AUCINF_D_obs	128.3360
AUC_%Extrap_obs	54.1257
AUCINF_pred	15531.0303
AUCINF_D_pred	129.4253
AUC_%Extrap_pred	54.5118
Tmin	0.0000
Cmin	0.0000
Ctau	134.1330
Cavg	90.0019
Swing _	Missing
Swing_Tau	0.0313
Fluctuation%	153.6934

Fluctuation%_Tau	4.6599
CLss_F	0.1111
MRTINF_obs	164.9180
MRTINF_pred	166.3703
Vz_F	12.4421
Accumulation_Index	9.8407
AUC_TAU	1080.0233
AUC_TAU_D	9.0002
AUC_TAU_%Extrap	0.0000
AUMC_TAU	6271.7444

WinNonlin 8.0.0.3176 Formulation=R,Subject=10

> Date: 9/09/2019 Time: 18:03:38

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: 16 Steady state interval Tau: 12.00

Dose time: 0.00 Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal

Weighting for lambda_z calculations: Uniform weighting Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

-----Conc. Pred. Residual AUC AUMC Time Weight ______ 0.0000 0.0000 0.5000 13.63 0.0000 0.0000 3.409 1.704 1.704 1.000 62.56 22.46 19.05 76.93 1.500 112.7 66.26 2.000 125.5 125.8 181.9 116.3 2.500 186.2 317.6 474.9 3.000 112.7 243.4
 112.7

 117.0
 124.9
 -7.925

 119.8
 122.8
 -2.972

 107.6
 120.7
 -13.13

 120.5
 116.6
 3.868

 124.2
 112.7
 11.50

 106.5
 108.9
 -2.386

 116.5
 88.57
 27.94

 45.20
 58.63
 -13.43
 -7.925 -2.972 -13.13 3.868 11.50 -2.386 27.94 -13.43 3.380 4.000 * 877.2 358.2 1.000 5.000 * 476.6 1410. 1.000 6.000 * 590.2 2034. 1.000 * 000.8 818.0 1.000 3633. 1063. 10.00 * 5836. 1.000 1293. 8362. 2630. 3.255e+04 4437. 9.425e+04 5486. 1.570e+05 12.00 * 1.000 24.00 * 1.000 48.00 * 1.000 3.380 72.00 * 42.19 38.81 1.000

*) Starred values were included in the estimation of Lambda_z.

Final Parameters

N_Samples 16
Dose 120.0000
Rsq 0.8809
Rsq_adjusted 0.8639
Corr_XY -0.9386
No_points_lambda_z 9

Lambda z 0.0172 Lambda z intercept 4.8964 Lambda_z_lower 4.0000 Lambda_z_upper 72.0000 HL Lambda z 40.3233 Span 1.6864 Tlag 0.0000 Tmax 2.0000 Cmax 125.4820 Cmax_D 1.0457 72.0000 Tlast 42.1910 Clast Clast pred 38.8109 AUClast 5485.6538 AUClast_D 45.7138 AUCall 5485.6538 AUCINF_obs AUCINF_D_obs 7940.0834 66.1674 AUC %Extrap obs 30.9119 AUCINF_pred 7743.4462 AUCINF D pred 64.5287 AUC_%Extrap_pred 29.1575 Tmin 0.0000 Cmin 0.0000 106.4760 Ctau Cavg 107.7356 Swing Missing Swing Tau 0.1785 Fluctuation% 116.4722 Fluctuation%_Tau 17.6413 CLss F 0.0928 MRTINF_obs 68.1676 MRTINF_pred 66.3424 Vz F 5.3997 Accumulation_Index 5.3650 AUC_TAU AUC_TAU_D AUC_TAU_%Extrap AUMC_TAU 1292.8271 10.7736 0.0000 8361.7894

WinNonlin 8.0.0.3176 Formulation=T,Subject=1

> Date: 9/09/2019 Time: 18:03:38

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: 16 Steady state interval Tau: 12.00

Dose time: 0.00 Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal

Weighting for lambda_z calculations: Uniform weighting Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time Conc. Pred. Residual AUC AUMC Weight

0.0000	0.0000			0.0000	0.0000	
0.5000	178.9			44.74	22.37	
1.000	190.9			137.2	92.45	
1.500	164.9			226.0	202.9	
2.000	140.0			302.0	335.5	
2.500	129.6			369.4	486.8	
3.000	131.4			434.6	666.2	
4.000	150.9			575.5	1161.	
5.000	121.2			711.0	1768.	
6.000	139.2			841.0	2485.	
8.000	128.5			1109.	4355.	
10.00 *	143.2	144.7	-1.453	1380.	6803.	1.000
12.00 *	145.0	143.7	1.244	1668.	9974.	1.000
24.00 *	133.2	138.0	-4.840	3336.	3.985e+04	1.000
48.00 *	137.3	127.2	10.04	6581.	1.569e+05	1.000
72.00 *	112.8	117.3	-4.460	9573.	3.352e+05	1.000
. = . • •	===:0	==,.0		30.0.		

N Samples	16
N_Samples Dose	120.0000
Rsq	0.7861
	0.7301
Rsq_adjusted	
Corr_XY	-0.8866 5
No_points_lambda_z	
Lambda_z	0.0034
Lambda_z_intercept	5.0085
Lambda_z_lower	10.0000 72.0000
Lambda_z_upper	
HL_Lambda_z	204.7857
Span	0.3028
Tlag Tmax	0.0000
	1.0000
Cmax	190.8690
Cmax_D	1.5906
Tlast	72.0000
Clast	112.8460 117.3058
Clast_pred AUClast	
_	9572.8582 79.7738
AUClast_D AUCall	9572.8582
AUCINF obs	42912.4555
AUCINF_D_obs	357.6038
AUC_%Extrap_obs	77.6921
AUCINF pred	44230.0677
AUCINF D pred	368.5839
AUC_%Extrap_pred	78.3567
Tmin	0.0000
Cmin	0.0000
Ctau	144.9640
Cavg	139.0297
Swing	Missing
Swing_Tau	0.3167
Fluctuation%	137.2865
Fluctuation% Tau	33.0181
CLss_F	0.0719
MRTINF obs	302.6351
MRTINF_pred	312.1123
Vz_F	21.2504
Accumulation_Index	25.1237
AUC_TAU	1668.3558
AUC_TAU_D	13.9030
AUC_TAU_%Extrap	0.0000
AUMC_TAU	9973.8062

9/09/2019 Date: Time: 18:03:39

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration Number of nonmissing observations: 16

Steady state interval Tau: Dose time: 0.00 12.00

Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	0.0000			0.0000	0.0000	
1.000	9.545			2.386	2.386	
1.500	154.0			43.26	62.51	
2.000	152.3			119.8	196.4	
2.500	151.5			195.8	367.2	
3.000	161.3			274.0	582.9	
4.000	169.3			439.3	1164.	
5.000 *	162.9	166.2	-3.309	605.4	1910.	1.000
6.000 *	166.7	165.1	1.563	770.2	2817.	1.000
8.000 *	168.7	162.9	5.815	1105.	5165.	1.000
10.00 *	155.1	160.6	-5.546	1429.	8073.	1.000
12.00 *	154.1	158.5	-4.409	1738.	1.147e+04	1.000
24.00 *	163.0	146.0	16.94	3640.	4.581e+04	1.000
48.00 *	109.8	124.0	-14.19	6872.	1.596e+05	1.000
72.00 *	110.8	105.3	5.480	9519.	3.185e+05	1.000

^{*)} Starred values were included in the estimation of Lambda_z.

N_Samples	16
Dose	120.0000
Rsq	0.8534
Rsq_adjusted	0.8289
Corr_XY	-0.9238
No_points_lambda_z	8
Lambda_z	0.0068
Lambda_z_intercept	5.1474
Lambda_z_lower	5.0000
Lambda_z_upper	72.0000
HL_Lambda_z	101.7340
Span	0.6586
Tlag	0.5000
Tmax	4.0000
Cmax	169.3340
Cmax_D	1.4111
Tlast	72.0000

Clast_pred AUClast AUClast AUClast_D AUCall AUCINF_obs AUCINF_D_obs AUC_%Extrap_obs AUCINF_pred AUCINF_D_pred AUCINF_D_pred TMIN Cmin Ctau Cavg Swing Swing_Tau Fluctuation% Fluctuation%_Tau CLss_F	110.7780 105.2983 9518.6531 79.3221 9518.6531 25777.6680 214.8139 63.0740 24973.4092 208.1117 61.8848 0.0000 0.0000 154.0660 144.8531 Missing 0.0991 116.9005 10.5403 0.0690
Fluctuation%_Tau	10.5403
MRTINF_obs MRTINF_pred Vz_F Accumulation_Index AUC_TAU AUC_TAU_D AUC_TAU_%Extrap AUMC_TAU	0.0690 172.5577 167.0055 10.1324 12.7377 1738.2375 14.4853 0.0000

WinNonlin 8.0.0.3176 Formulation=T,Subject=6

> Date: 9/09/2019 Time: 18:03:39

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM 8.0.0.3176 Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: 16 Steady state interval Tau: 12.00 Dose time: 0.00

Dose amount: 120.00

Calculation method: Linear/Log Trapezoidal

Weighting for lambda_z calculations: Uniform weighting Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Juli	illary rabte						
	Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
	0.0000	0.0000			0.0000	0.0000	
	0.5000	57.88			14.47	7.235	
	1.000	100.5			54.07	39.60	
	1.500	138.7			113.9	116.7	
	2.000	147.3			185.3	242.4	
	2.500	154.6			260.8	412.6	
	3.000	122.3			329.7	601.5	
	4.000	132.9			457.3	1049.	
	5.000	126.1			586.7	1631.	
	6.000	140.5			719.8	2364.	
	8.000	115.5			975.0	4142.	

10.00	102.2			1192.	6094.	
12.00 *	113.8	114.1	-0.3825	1408.	8471.	1.000
24.00 *	101.0	104.1	-3.021	2695.	3.149e+04	1.000
48.00 *	92.55	86.53	6.024	5017.	1.147e+05	1.000
72.00 *	69.50	71.94	-2.439	6949.	2.294e+05	1.000

Final Parameters

N_Samples	16
Dose	120.0000
Rsq	0.9501
Rsq_adjusted	0.9252
Corr_XY	-0.9747
No_points_lambda_z	4
Lambda z	0.0077
Lambda_z_intercept	4.8297
Lambda_z_lower	12.0000
Lambda_z_upper	72.0000
HL_Lambda_z	90.1095
Span Span	0.6659
Tlag	0.0000
Tmax	2.5000
Cmax	154.6480
Cmax D	1.2887
Tlast	72.0000
Clast	69.5010
Clast_pred	71.9399
AUClast	6948.5757
AUCall	57.9048
AUCINE obs	6948.5757
AUCINF_obs	15983.7374
AUCINF_D_obs	133.1978
AUCTNE a mad	56.5272
AUCINF_pred	16300.8010
AUCINF_D_pred	135.8400
AUC_%Extrap_pred	57.3728
Tmin	0.0000
Cmin	0.0000
Ctau	113.7510
Cavg	117.3464
Swing	Missing
Swing_Tau	0.3595
Fluctuation%	131.7875
Fluctuation%_Tau	34.8515
CLss_F	0.0852
MRTINF_obs	130.2255
MRTINF_pred	132.9275
Vz_F	11.0783
Accumulation_Index	11.3411
AUC_TAU	1408.1573
AUC_TAU_D	11.7346
AUC_TAU_%Extrap	0.0000
AUMC_TAU	8471.0956

WinNonlin 8.0.0.3176 Formulation=T,Subject=9

> Date: 9/09/2019 Time: 18:03:39

Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration

Number of nonmissing observations: Steady state interval Tau: 12.00

0.00 Dose time: 120.00 Dose amount:

Calculation method: Linear/Log Trapezoidal
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

Summary Table

Time	Conc.	Pred.	Residual	AUC	AUMC	Weight
0.0000	0.0000			0.0000	0.0000	
0.5000	113.4			28.34	14.17	
1.000	128.3			88.75	60.41	
1.500	125.4			152.2	139.5	
2.000	146.9			220.2	260.0	
2.500	140.6			292.1	421.3	
3.000	167.3			369.1	634.7	
4.000	157.5			531.5	1202.	
5.000	141.4			680.8	1873.	
6.000	140.3			821.6	2647.	
8.000	105.4			1066.	4344.	
10.00	164.8			1332.	6756.	
12.00 *	135.6	131.6	4.014	1631.	1.004e+04	1.000
24.00 *	117.1	122.9	-5.823	3145.	3.706e+04	1.000
48.00 *	109.7	107.4	2.377	5866.	1.347e+05	1.000
72.00 *	93.44	93.76	-0.3218	8299.	2.799e+05	1.000

*) Starred values were included in the estimation of Lambda_z.

N_Samples	16
Dose	120.0000
Rsq	0.9475
Rsq_adjusted	0.9213
Corr_XY	-0.9734
No_points_lambda_z	4
Lambda_z	0.0056
Lambda_z_intercept	4.9473
Lambda_z_lower	12.0000
Lambda_z_upper	72.0000
HL_Lambda_z	122.7708
Span	0.4887
Tlag	0.0000
Tmax	3.0000
Cmax	167.3470
Cmax_D	1.3946
Tlast	72.0000
Clast	93.4400
Clast_pred	93.7618
AUClast	8298.9634
AUClast_D	69.1580
AUCall	8298.9634
AUCINF_obs	24849.1291
AUCINF_D_obs	207.0761
AUC_%Extrap_obs	66.6026
AUCINF_pred	24906.1197
AUCINF_D_pred	207.5510
AUC_%Extrap_pred	66.6790