

8.2 Reference values 2: Linear-up Log-Down rule; Extravascular

WinNonlin 8.2.0.4383
Subject=1,Formulation=T

Date: 2/11/2020
Time: 22:58:06

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	121.2			0.0000	0.0000	
0.5000	178.9			37.52	5.592	
1.000	190.9			130.0	52.56	
1.500	164.9			218.8	140.8	
2.000	140.0			294.8	254.4	
2.500	129.6			362.2	388.9	
3.000	131.4			427.4	552.1	
4.000	150.9			568.5	1016.	
5.000	121.2			704.0	1589.	
6.000	139.2			834.3	2277.	
8.000	128.5			1102.	4080.	
10.00 *	143.2	144.7	-1.453	1374.	6473.	1.000
12.00 *	145.0	143.7	1.244	1662.	9573.	1.000
24.00 *	133.2	138.0	-4.840	3330.	3.903e+04	1.000
48.00 *	137.3	127.2	10.04	6575.	1.556e+05	1.000
72.00 *	112.8	117.3	-4.460	9567.	3.332e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples 15
Dose 100.0000
Rsqr 0.7861
Rsqr_adjusted 0.7148
Corr_XY -0.8866
No_points_lambda_z 5
Lambda_z 0.0034
Lambda_z_intercept 5.0085
Lambda_z_lower 10.0000
Lambda_z_upper 72.0000
HL_Lambda_z 204.7857

Span	0.3028
Tlag	0.0000
Tmax	1.0000
Cmax	190.8690
Cmax_D	1.9087
Tlast	72.0000
Clast	112.8460
Clast_pred	117.3058
AUClast	9566.5968
AUClast_D	95.6660
AUCall	9566.5968
AUCINF_obs	42906.1941
AUCINF_D_obs	429.0619
AUC_%Extrap_obs	77.7035
AUCINF_pred	44223.8063
AUCINF_D_pred	442.2381
AUC_%Extrap_pred	78.3678
Tmin	5.0000
Cmin	121.2390
Ctau	137.7219
Cavg	140.9195
Swing	0.5743
Swing_Tau	0.3859
Fluctuation%	49.4112
Fluctuation%_Tau	37.7145
CLss_F	0.0788
MRTINF_obs	299.7917
MRTINF_pred	309.1418
Vz_F	23.2949
Accumulation_Index	33.3296
AUC_TAU	1268.2756
AUC_TAU_D	12.6828
AUC_TAU_%Extrap	0.0000
AUMC_TAU	5477.2042

WinNonlin 8.2.0.4383
Subject=2,Formulation=R

Date: 2/11/2020
Time: 22:58:06

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	62.22			0.0000	0.0000	
0.5000	62.22			15.56	1.944	
1.000	261.2			96.41	54.80	
1.500	234.1			220.1	177.9	

2.000	234.1			337.1	353.5	
2.500	222.9			451.4	581.7	
3.000	213.9			560.5	854.5	
4.000	196.0			765.4	1519.	
5.000	199.6			963.2	2360.	
6.000	196.0			1161.	3399.	
8.000	213.4			1570.	6179.	
10.00 *	200.1	197.9	2.174	1984.	9791.	1.000
12.00 *	196.0	192.4	3.626	2380.	1.405e+04	1.000
24.00 *	160.3	162.4	-2.108	4511.	5.145e+04	1.000
48.00 *	110.3	115.8	-5.512	7721.	1.638e+05	1.000
72.00 *	85.24	82.54	2.704	1.005e+04	3.020e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
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	2.6118
Tlast	72.0000
Clast	85.2410
Clast_pred	82.5367
AUClast	10054.2865
AUClast_D	100.5429
AUCall	10054.2865
AUCINF_obs	16097.0411
AUCINF_D_obs	160.9704
AUC_%Extrap_obs	37.5395
AUCINF_pred	15905.3319
AUCINF_D_pred	159.0533
AUC_%Extrap_pred	36.7867
Tmin	0.5000
Cmin	62.2220
Ctau	204.9625
Cavg	203.5356
Swing	3.1975
Swing_Tau	0.2743
Fluctuation%	97.7495
Fluctuation%_Tau	27.6190
CLss_F	0.0546
MRTINF_obs	74.6550
MRTINF_pred	73.7131
Vz_F	3.8699
Accumulation_Index	8.3873
AUC_TAU	1831.8205
AUC_TAU_D	18.3182
AUC_TAU_%Extrap	0.0000
AUMC_TAU	8367.5709

WinNonlin 8.2.0.4383
Subject=3,Formulation=R

Date: 2/11/2020
Time: 22:58:06

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	49.85			0.0000	0.0000	
0.5000	49.85			12.46	1.558	
1.000	77.37			44.27	19.18	
1.500	105.3			89.94	66.61	
2.000	100.9			141.5	143.9	
2.500	72.75			184.5	229.4	
3.000	69.99			220.2	318.5	
4.000	93.57			302.0	590.2	
5.000	91.98			394.8	984.3	
6.000 *	82.71	83.17	-0.4609	482.0	1442.	1.000
8.000 *	84.21	82.63	1.580	648.9	2570.	1.000
10.00 *	85.34	82.08	3.259	818.5	4055.	1.000
12.00 *	76.03	81.54	-5.518	979.7	5784.	1.000
24.00 *	81.26	78.39	2.872	1923.	2.272e+04	1.000
48.00 *	70.11	72.43	-2.326	3737.	8.701e+04	1.000
72.00 *	67.90	66.93	0.9699	5392.	1.858e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
Rsqr	0.8136
Rsqr_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	1.0535

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Tlast                72.0000
Clast                67.9010
Clast_pred           66.9311
AUClast              5392.4572
AUClast_D            53.9246
AUCall               5392.4572
AUCINF_obs           26022.0900
AUCINF_D_obs         260.2209
AUC_%Extrap_obs     79.2774
AUCINF_pred          25727.4026
AUCINF_D_pred        257.2740
AUC_%Extrap_pred    79.0400
Tmin                 0.5000
Cmin                 49.8490
Ctau                 84.9156
Cavg                 83.8499
Swing                1.1133
Swing_Tau            0.2406
Fluctuation%         66.1849
Fluctuation%_Tau    24.3642
CLss_F               0.1325
MRTINF_obs           305.9200
MRTINF_pred          302.4055
Vz_F                 40.2597
Accumulation_Index  34.2602
AUC_TAU              754.6494
AUC_TAU_D            7.5465
AUC_TAU_%Extrap     0.0000
AUMC_TAU             3455.3464

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WinNonlin 8.2.0.4383
Subject=4, Formulation=R

Date: 2/11/2020
Time: 22:58:06

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

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-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
                    Log Trapezoidal Rule for Decreasing Values
Weighting for lambda_z calculations: Uniform weighting
Lambda_z method: Find best fit for lambda_z, Log regression

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Summary Table

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Time      Conc.    Pred.    Residual    AUC    AUMC    Weight
-----
0.2500 @  52.42
0.5000    52.42
1.000    208.5
1.500    188.9
2.000    165.2
2.500    147.0
3.000    152.7
4.000    154.3
5.000    128.4

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6.000	149.8			852.5	2450.		
8.000	151.1			1153.	4482.		
10.00	136.8			1441.	6995.		
12.00	132.3			1710.	9885.		
24.00 *	141.2	145.8	-4.547	3351.	3.934e+04	1.000	
48.00 *	129.1	121.2	7.930	6594.	1.547e+05	1.000	
72.00 *	97.63	100.8	-3.143	9297.	3.147e+05	1.000	

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
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	2.0854
Tlast	72.0000
Clast	97.6250
Clast_pred	100.7679
AUClast	9297.0963
AUClast_D	92.9710
AUCall	9297.0963
AUCINF_obs	21983.3385
AUCINF_D_obs	219.8334
AUC_%Extrap_obs	57.7084
AUCINF_pred	22391.7586
AUCINF_D_pred	223.9176
AUC_%Extrap_pred	58.4798
Tmin	0.5000
Cmin	52.4210
Ctau	141.9970
Cavg	148.4979
Swing	2.9782
Swing_Tau	0.4686
Fluctuation%	105.1335
Fluctuation%_Tau	44.8121
CLss_F	0.0748
MRTINF_obs	143.5384
MRTINF_pred	146.2888
Vz_F	9.7232
Accumulation_Index	14.9445
AUC_TAU	1336.4809
AUC_TAU_D	13.3648
AUC_TAU_%Extrap	0.0000
AUMC_TAU	6014.6460

WinNonlin 8.2.0.4383
Subject=5,Formulation=T

Date: 2/11/2020
Time: 22:58:07

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
                    Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	0.0000			0.0000	0.0000	
0.5000	0.0000			0.0000	0.0000	
1.000	9.545			2.386	1.790	
1.500	154.0			43.26	51.69	
2.000	152.3			119.8	166.5	
2.500	151.5			195.8	318.4	
3.000	161.3			274.0	514.5	
4.000	169.3			439.3	1054.	
5.000 *	162.9	166.2	-3.309	605.4	1759.	1.000
6.000 *	166.7	165.1	1.563	770.2	2625.	1.000
8.000 *	168.7	162.9	5.815	1105.	4891.	1.000
10.00 *	155.1	160.6	-5.546	1429.	7717.	1.000
12.00 *	154.1	158.5	-4.409	1738.	1.104e+04	1.000
24.00 *	163.0	146.0	16.94	3640.	4.513e+04	1.000
48.00 *	109.8	124.0	-14.19	6872.	1.581e+05	1.000
72.00 *	110.8	105.3	5.480	9519.	3.164e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

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N_Samples                15
Dose                     100.0000
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                     0.2500
Tmax                     4.0000
Cmax                     169.3340
Cmax_D                   1.6933
Tlast                    72.0000
Clast                    110.7780
Clast_pred               105.2983
AUClast                  9519.1809
AUClast_D                95.1918
  
```

```

AUCall                      9519.1809
AUCINF_obs                   25778.1958
AUCINF_D_obs                 257.7820
AUC_%Extrap_obs             63.0727
AUCINF_pred                  24973.9369
AUCINF_D_pred                249.7394
AUC_%Extrap_pred            61.8835
Tmin                          0.5000
Cmin                          0.0000
Ctau                          160.0571
Cavg                          145.6561
Swing                          Missing
Swing_Tau                     0.0580
Fluctuation%                 116.2561
Fluctuation%_Tau             6.3691
CLss_F                        0.0763
MRTINF_obs                   173.0221
MRTINF_pred                  167.5004
Vz_F                          11.1962
Accumulation_Index           16.8130
AUC_TAU                      1310.9045
AUC_TAU_D                    13.1090
AUC_TAU_%Extrap              0.0000
AUMC_TAU                     6609.7883

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WinNonlin 8.2.0.4383
Subject=6, Formulation=T

Date: 2/11/2020
Time: 22:58:07

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
                    Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	57.88			0.0000	0.0000	
0.5000	57.88			14.47	1.809	
1.000	100.5			54.07	24.27	
1.500	138.7			113.9	86.44	
2.000	147.3			185.3	194.2	
2.500	154.6			260.8	345.6	
3.000	122.3			329.7	517.3	
4.000	132.9			457.3	934.6	
5.000	126.1			586.8	1484.	
6.000	140.5			720.0	2187.	
8.000	115.5			975.2	3902.	
10.00	102.2			1193.	5800.	
12.00 *	113.8	114.1	-0.3825	1409.	8132.	1.000
24.00 *	101.0	104.1	-3.021	2696.	3.083e+04	1.000

48.00 *	92.55	86.53	6.024	5018.	1.134e+05	1.000
72.00 *	69.50	71.94	-2.439	6949.	2.277e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
Rsqr	0.9501
Rsqr_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	0.6659
Tlag	0.0000
Tmax	2.5000
Cmax	154.6480
Cmax_D	1.5465
Tlast	72.0000
Clast	69.5010
Clast_pred	71.9399
AUClast	6948.9856
AUClast_D	69.4899
AUCall	6948.9856
AUCINF_obs	15984.1474
AUCINF_D_obs	159.8415
AUC_%Extrap_obs	56.5258
AUCINF_pred	16301.2109
AUCINF_D_pred	163.0121
AUC_%Extrap_pred	57.3714
Tmin	0.5000
Cmin	57.8820
Ctau	106.9863
Cavg	123.8045
Swing	1.6718
Swing_Tau	0.4455
Fluctuation%	78.1603
Fluctuation%_Tau	38.4976
CLss_F	0.0897
MRTINF_obs	124.6534
MRTINF_pred	127.2144
Vz_F	11.6672
Accumulation_Index	14.9503
AUC_TAU	1114.2404
AUC_TAU_D	11.1424
AUC_TAU_%Extrap	0.0000
AUMC_TAU	5064.7238

WinNonlin 8.2.0.4383
Subject=7, Formulation=R

Date: 2/11/2020
Time: 22:58:07

Settings

 Model: Plasma Data, Extravascular Administration
 Number of nonmissing observations: 15
 Steady state interval Tau: 9.00
 Dose time: 0.25
 Dose amount: 100.00
 Calculation method: Linear Trapezoidal Rule for for Increasing Values,
 Log Trapezoidal Rule for Decreasing Values
 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
0.2500 @	19.95			0.0000	0.0000	
0.5000	19.95			4.988	0.6234	
1.000	128.4			42.08	25.95	
1.500	136.8			108.4	92.77	
2.000	113.1			170.7	185.7	
2.500	153.3			237.3	321.4	
3.000	123.6			306.2	493.2	
4.000	142.7			439.3	930.6	
5.000	112.3			566.2	1467.	
6.000	139.9			692.4	2136.	
8.000	105.5			936.2	3771.	
10.00 *	134.4	132.4	1.964	1176.	5899.	1.000
12.00 *	123.4	129.2	-5.814	1434.	8665.	1.000
24.00 *	110.5	111.2	-0.7336	2836.	3.339e+04	1.000
48.00 *	90.29	82.49	7.798	5237.	1.183e+05	1.000
72.00 *	58.05	61.17	-3.122	6989.	2.214e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
Rsqr	0.9703
Rsqr_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	1.5325
Tlast	72.0000
Clast	58.0510
Clast_pred	61.1727
AUClast	6988.7726
AUClast_D	69.8877
AUCall	6988.7726
AUCINF_obs	11648.1518
AUCINF_D_obs	116.4815
AUC_%Extrap_obs	40.0010
AUCINF_pred	11898.7107

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AUCINF_D_pred          118.9871
AUC_%Extrap_pred      41.2645
Tmin                   0.5000
Cmin                   19.9500
Ctau                   123.5724
Cavg                   119.9297
Swing                  6.6819
Swing_Tau              0.2402
Fluctuation%          111.1518
Fluctuation%_Tau      24.7492
CLss_F                0.0926
MRTINF_obs            92.7359
MRTINF_pred           94.8251
Vz_F                  7.4362
Accumulation_Index    9.4275
AUC_TAU               1079.3669
AUC_TAU_D             10.7937
AUC_TAU_%Extrap      0.0000
AUMC_TAU              4976.9637

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WinNonlin 8.2.0.4383
Subject=8,Formulation=R

Date: 2/11/2020
Time: 22:58:07

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

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-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
                    Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	22.72			0.0000	0.0000	
0.5000	136.9			19.95	4.278	
1.000	126.6			85.81	36.99	
1.500	118.5			147.1	98.09	
2.000	134.9			210.4	194.1	
2.500	113.2			272.3	317.4	
3.000	130.9			333.3	471.1	
4.000	138.3			467.9	910.5	
5.000	22.72			531.9	1173.	
6.000	53.77			570.2	1382.	
8.000	55.11			679.1	2118.	
10.00	102.9			837.1	3548.	
12.00 *	134.1	129.2	4.939	1074.	6127.	1.000
24.00 *	108.0	116.1	-8.045	2521.	3.150e+04	1.000
48.00 *	98.47	93.68	4.791	4997.	1.196e+05	1.000
72.00 *	74.44	75.60	-1.167	7059.	2.416e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
Rsq	0.9480
Rsq_adjusted	0.9220
Corr_XY	-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	1.3833
Tlast	72.0000
Clast	74.4370
Clast_pred	75.6043
AUClast	7058.8190
AUClast_D	70.5882
AUCall	7058.8190
AUCINF_obs	15394.3548
AUCINF_D_obs	153.9435
AUC_%Extrap_obs	54.1467
AUCINF_pred	15525.0677
AUCINF_D_pred	155.2507
AUC_%Extrap_pred	54.5328
Tmin	5.0000
Cmin	22.7240
Ctau	84.9595
Cavg	85.1800
Swing	5.0873
Swing_Tau	0.6282
Fluctuation%	135.7161
Fluctuation%_Tau	62.6526
CLss_F	0.1304
MRTINF_obs	175.4619
MRTINF_pred	176.9964
Vz_F	14.6071
Accumulation_Index	12.9490
AUC_TAU	766.6202
AUC_TAU_D	7.6662
AUC_TAU_%Extrap	0.0000
AUMC_TAU	2863.0052

WinNonlin 8.2.0.4383
Subject=9, Formulation=T

Date: 2/11/2020
Time: 22:58:08

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15

Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
Log Trapezoidal Rule for Decreasing Values
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
0.2500 @	105.4			0.0000	0.0000	
0.5000	113.4			27.35	3.543	
1.000	128.3			87.76	34.68	
1.500	125.4			151.2	98.03	
2.000	146.9			219.3	201.5	
2.500	140.6			291.1	345.1	
3.000	167.3			368.1	539.2	
4.000	157.5			530.5	1066.	
5.000	141.4			679.7	1699.	
6.000	140.3			820.6	2438.	
8.000	105.4			1065.	4074.	
10.00	164.8			1335.	6499.	
12.00 *	135.6	131.6	4.014	1634.	9708.	1.000
24.00 *	117.1	122.9	-5.823	3148.	3.635e+04	1.000
48.00 *	109.7	107.4	2.377	5869.	1.333e+05	1.000
72.00 *	93.44	93.76	-0.3218	8302.	2.779e+05	1.000

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

N_Samples	15
Dose	100.0000
Rsqr	0.9475
Rsqr_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	1.6735
Tlast	72.0000
Clast	93.4400
Clast_pred	93.7618
AUClast	8302.3681
AUClast_D	83.0237
AUCall	8302.3681
AUCINF_obs	24852.5338
AUCINF_D_obs	248.5253
AUC_%Extrap_obs	66.5935
AUCINF_pred	24909.5245
AUCINF_D_pred	249.0952
AUC_%Extrap_pred	66.6699
Tmin	8.0000
Cmin	105.4380
Ctau	142.5661

```

Cavg                135.5147
Swing               0.5872
Swing_Tau           0.1738
Fluctuation%        45.6844
Fluctuation%_Tau    18.2865
CLss_F              0.0820
MRTINF_obs          178.8105
MRTINF_pred         179.2311
Vz_F                14.5225
Accumulation_Index  20.1843
AUC_TAU             1219.6319
AUC_TAU_D           12.1963
AUC_TAU_%Extrap    0.0000
AUMC_TAU            5386.8832

```

WinNonlin 8.2.0.4383
Subject=10,Formulation=R

Date: 2/11/2020
Time: 22:58:08

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.2.0.4383
Core Version 110ct2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 15
Steady state interval Tau: 9.00
Dose time: 0.25
Dose amount: 100.00
Calculation method: Linear Trapezoidal Rule for for Increasing Values,
                   Log Trapezoidal Rule for Decreasing Values
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
-----
0.2500 @      13.63
0.5000          13.63          3.409      0.4261
1.000          62.56          22.46      13.01
1.500          112.7          66.26      59.94
2.000          125.5          125.8      150.0
2.500          116.3          186.2      270.7
3.000          112.7          243.4      413.7
4.000 *          117.0          124.9      -7.925      358.3      787.9      1.000
5.000 *          119.8          122.8      -2.972      476.7      1292.      1.000
6.000 *          107.6          120.7      -13.13      590.2      1887.      1.000
8.000 *          120.5          116.6       3.868      818.3      3439.      1.000
10.00 *          124.2          112.7      11.50      1063.      5584.      1.000
12.00 *          106.5          108.9      -2.386      1293.      8052.      1.000
24.00 *          116.5          88.57      27.94      2631.      3.216e+04      1.000
48.00 *          45.20          58.63      -13.43      4439.      9.341e+04      1.000
72.00 *          42.19          38.81       3.380      5487.      1.559e+05      1.000

```

@) Note - the concentration at dose time was added for extrapolation purposes.

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

Final Parameters

```

-----
N_Samples                15
Dose                    100.0000
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                  1.2548
Tlast                   72.0000
Clast                   42.1910
Clast_pred              38.8109
AUClast                 5486.8389
AUClast_D               54.8684
AUCall                  5486.8389
AUCINF_obs              7941.2686
AUCINF_D_obs            79.4127
AUC_%Extrap_obs        30.9073
AUCINF_pred             7744.6313
AUCINF_D_pred           77.4463
AUC_%Extrap_pred       29.1530
Tmin                    0.5000
Cmin                    13.6340
Ctau                    122.7865
Cavg                    107.8118
Swing                   8.2036
Swing_Tau               0.0220
Fluctuation%            103.7437
Fluctuation%_Tau       2.5002
CLss_F                  0.1031
MRTINF_obs              69.5163
MRTINF_pred             67.6924
Vz_F                    5.9955
Accumulation_Index      6.9767
AUC_TAU                 970.3063
AUC_TAU_D               9.7031
AUC_TAU_%Extrap        0.0000
AUMC_TAU                4713.4797

```