

8 Appendix 2

8.1 Reference values 1: Linear-trapezoidal rule; Extravascular

WinNonlin 8.0.0.3176
Subject=1, Formulation=T

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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			226.1	202.0	
2.000	140.0			302.4	333.8	
2.500	129.6			369.8	484.8	
3.000	131.4			435.0	664.3	
4.000	150.9			576.1	1163.	
5.000	121.2			712.1	1768.	
6.000	139.2			842.4	2489.	
8.000	128.5			1110.	4352.	
10.00 *	143.2	144.7	-1.453	1382.	6813.	1.000
12.00 *	145.0	143.7	1.244	1670.	9985.	1.000
24.00 *	133.2	138.0	-4.840	3339.	3.960e+04	1.000
48.00 *	137.3	127.2	10.04	6584.	1.570e+05	1.000
72.00 *	112.8	117.3	-4.460	9585.	3.336e+05	1.000

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

Final Parameters

N_Samples 16
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             9585.4218
AUClast_D           95.8542
AUCall              9585.4218
AUCINF_obs          42925.0191
AUCINF_D_obs        429.2502
AUC_%Extrap_obs    77.6694
Vz_F_obs            0.6883
Cl_F_obs            0.0023
AUCINF_pred         44242.6313
AUCINF_D_pred       442.4263
AUC_%Extrap_pred   78.3344
Vz_F_pred           0.6678
Cl_F_pred           0.0023
AUMClast            333582.4808
AUMCINF_obs         12583994.9366
AUMC_%Extrap_obs   97.3492
AUMCINF_pred        13068142.7409
AUMC_%Extrap_pred  97.4474
MRTlast             34.8010
MRTINF_obs          293.1622
MRTINF_pred         295.3744

```

WinNonlin 8.0.0.3176
Subject=2, Formulation=R

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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			220.2	233.9	
2.000	234.1			337.3	438.7	
2.500	222.9			451.5	695.1	
3.000	213.9			560.7	994.8	
4.000	196.0			765.7	1708.	
5.000	199.6			963.5	2599.	
6.000	196.0			1161.	3686.	
8.000	213.4			1571.	6569.	
10.00 *	200.1	197.9	2.174	1984.	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	4519.	5.183e+04	1.000
48.00 *	110.3	115.8	-5.512	7766.	1.615e+05	1.000
72.00 *	85.24	82.54	2.704	1.011e+04	2.987e+05	1.000

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

Final Parameters

```

-----
N_Samples                16
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                 10112.1755
AUClast_D               101.1218
AUCall                  10112.1755
AUCINF_obs              16154.9301
AUCINF_D_obs            161.5493
AUC_%Extrap_obs        37.4050
Vz_F_obs                0.4388
Cl_F_obs                0.0062
AUCINF_pred             15963.2209
AUCINF_D_pred           159.6322
AUC_%Extrap_pred       36.6533
Vz_F_pred               0.4441
Cl_F_pred               0.0063
AUMClast                298701.3885
AUMCINF_obs             1162152.0263
AUMC_%Extrap_obs       74.2976
AUMCINF_pred            1134758.6551
AUMC_%Extrap_pred      73.6771
MRTlast                 29.5388
MRTINF_obs              71.9379
MRTINF_pred             71.0858

```

WinNonlin 8.0.0.3176
Subject=3,Formulation=R

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00

```

Dose amount: 100.00
 Calculation method: Linear Trapezoidal with Linear Interpolation
 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	180.6	
2.500	72.75			184.9	276.6	
3.000	69.99			220.6	374.5	
4.000	93.57			302.4	666.6	
5.000	91.98			395.2	1084.	
6.000 *	82.71	83.17	-0.4609	482.5	1562.	1.000
8.000 *	84.21	82.63	1.580	649.4	2732.	1.000
10.00 *	85.34	82.08	3.259	819.0	4259.	1.000
12.00 *	76.03	81.54	-5.518	980.3	6024.	1.000
24.00 *	81.26	78.39	2.872	1924.	2.320e+04	1.000
48.00 *	70.11	72.43	-2.326	3740.	8.698e+04	1.000
72.00 *	67.90	66.93	0.9699	5397.	1.860e+05	1.000

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

Final Parameters

N_Samples	16
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
Tlast	72.0000
Clast	67.9010
Clast_pred	66.9311
AUClast	5396.5498
AUClast_D	53.9655
AUCall	5396.5498
AUCINF_obs	26026.1826
AUCINF_D_obs	260.2618
AUC_%Extrap_obs	79.2649
Vz_F_obs	1.1674
Cl_F_obs	0.0038
AUCINF_pred	25731.4952
AUCINF_D_pred	257.3150
AUC_%Extrap_pred	79.0275
Vz_F_pred	1.1807
Cl_F_pred	0.0039
AUMClast	186032.0553
AUMCINF_obs	7939045.7669
AUMC_%Extrap_obs	97.6567
AUMCINF_pred	7828296.5609

AUMC_%Extrap_pred 97.6236
MRTlast 34.4724
MRTINF_obs 305.0407
MRTINF_pred 304.2301

WinNonlin 8.0.0.3176
Subject=4,Formulation=R

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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			177.7	188.2	
2.000	165.2			266.2	341.7	
2.500	147.0			344.3	516.1	
3.000	152.7			419.2	722.5	
4.000	154.3			572.7	1260.	
5.000	128.4			714.1	1890.	
6.000	149.8			853.2	2660.	
8.000	151.1			1154.	4768.	
10.00	136.8			1442.	7344.	
12.00	132.3			1711.	1.030e+04	
24.00 *	141.2	145.8	-4.547	3352.	4.016e+04	1.000
48.00 *	129.1	121.2	7.930	6597.	1.552e+05	1.000
72.00 *	97.63	100.8	-3.143	9318.	3.140e+05	1.000

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

Final Parameters

N_Samples	16
Dose	100.0000
Rsqr	0.9189
Rsqr_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             9317.8358
AUClast_D           93.1784
AUCall              9317.8358
AUCINF_obs          22004.0779
AUCINF_D_obs        220.0408
AUC_%Extrap_obs    57.6541
Vz_F_obs            0.5906
Cl_F_obs            0.0045
AUCINF_pred         22412.4980
AUCINF_D_pred       224.1250
AUC_%Extrap_pred   58.4257
Vz_F_pred           0.5798
Cl_F_pred           0.0045
AUMClast            313955.9048
AUMCINF_obs         2875926.0451
AUMC_%Extrap_obs   89.0833
AUMCINF_pred        2958405.9609
AUMC_%Extrap_pred  89.3877
MRTlast             33.6941
MRTINF_obs          130.6997
MRTINF_pred         131.9980

```

WinNonlin 8.0.0.3176
Subject=5,Formulation=T

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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
0.5000        0.0000
1.000         9.545
1.500         154.0
2.000         152.3
2.500         151.5
3.000         161.3
4.000         169.3
5.000 *       162.9          166.2         -3.309          605.4          1909.          1.000
6.000 *       166.7          165.1          1.563          770.2          2817.          1.000
8.000 *       168.7          162.9          5.815          1106.          5166.          1.000
10.00 *       155.1          160.6         -5.546          1429.          8066.          1.000
12.00 *       154.1          158.5         -4.409          1738.          1.147e+04      1.000

```

24.00 *	163.0	146.0	16.94	3641.	4.603e+04	1.000
48.00 *	109.8	124.0	-14.19	6914.	1.562e+05	1.000
72.00 *	110.8	105.3	5.480	9561.	3.152e+05	1.000

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

Final Parameters

```

-----
N_Samples                16
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                    0.5000
Tmax                    4.0000
Cmax                    169.3340
Cmax_D                  1.6933
Tlast                   72.0000
Clast                   110.7780
Clast_pred              105.2983
AUClast                 9561.2600
AUClast_D              95.6126
AUCall                  9561.2600
AUCINF_obs             25820.2749
AUCINF_D_obs           258.2027
AUC_%Extrap_obs        62.9700
Vz_F_obs                0.5684
Cl_F_obs                0.0039
AUCINF_pred            25016.0160
AUCINF_D_pred          250.1602
AUC_%Extrap_pred       61.7794
Vz_F_pred               0.5867
Cl_F_pred               0.0040
AUMClast               315181.5625
AUMCINF_obs            3872185.0137
AUMC_%Extrap_obs       91.8604
AUMCINF_pred           3696236.3722
AUMC_%Extrap_pred      91.4729
MRTlast                32.9644
MRTINF_obs             149.9668
MRTINF_pred            147.7548

```

WinNonlin 8.0.0.3176
Subject=6,Formulation=T

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00

```

Dose amount: 100.00
 Calculation method: Linear Trapezoidal with Linear Interpolation
 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	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			330.1	601.0	
4.000	132.9			457.6	1050.	
5.000	126.1			587.1	1631.	
6.000	140.5			720.4	2368.	
8.000	115.5			976.4	4135.	
10.00	102.2			1194.	6081.	
12.00 *	113.8	114.1	-0.3825	1410.	8467.	1.000
24.00 *	101.0	104.1	-3.021	2699.	3.121e+04	1.000
48.00 *	92.55	86.53	6.024	5022.	1.136e+05	1.000
72.00 *	69.50	71.94	-2.439	6967.	2.270e+05	1.000

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

Final Parameters

N_Samples	16
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	6966.5980
AUClast_D	69.6660
AUCall	6966.5980
AUCINF_obs	16001.7597
AUCINF_D_obs	160.0176
AUC_%Extrap_obs	56.4636
Vz_F_obs	0.8124
Cl_F_obs	0.0062
AUCINF_pred	16318.8233
AUCINF_D_pred	163.1882
AUC_%Extrap_pred	57.3094
Vz_F_pred	0.7966
Cl_F_pred	0.0061
AUMClast	226977.0608
AUMCINF_obs	2052083.8596
AUMC_%Extrap_obs	88.9392
AUMCINF_pred	2116130.8466

AUMC_%Extrap_pred 89.2740
MRTlast 32.5808
MRTINF_obs 128.2411
MRTINF_pred 129.6742

WinNonlin 8.0.0.3176
Subject=7,Formulation=R

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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			306.7	569.2	
4.000	142.7			439.8	1040.	
5.000	112.3			567.3	1606.	
6.000	139.9			693.4	2307.	
8.000	105.5			938.9	3990.	
10.00 *	134.4	132.4	1.964	1179.	6178.	1.000
12.00 *	123.4	129.2	-5.814	1437.	9003.	1.000
24.00 *	110.5	111.2	-0.7336	2840.	3.380e+04	1.000
48.00 *	90.29	82.49	7.798	5249.	1.176e+05	1.000
72.00 *	58.05	61.17	-3.122	7030.	2.198e+05	1.000

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

Final Parameters

N_Samples	16
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             7029.5735
AUClast_D           70.2957
AUCall              7029.5735
AUCINF_obs          11688.9527
AUCINF_D_obs        116.8895
AUC_%Extrap_obs    39.8614
Vz_F_obs            0.6867
Cl_F_obs            0.0086
AUCINF_pred         11939.5116
AUCINF_D_pred       119.3951
AUC_%Extrap_pred   41.1234
Vz_F_pred           0.6723
Cl_F_pred           0.0084
AUMClast            219797.7073
AUMCINF_obs         929251.3075
AUMC_%Extrap_obs   76.3468
AUMCINF_pred        967402.2944
AUMC_%Extrap_pred  77.2796
MRTlast             31.2676
MRTINF_obs          79.4983
MRTINF_pred         81.0253

```

WinNonlin 8.0.0.3176
Subject=8,Formulation=R

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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			563.0	1368.	
6.000	53.77			601.2	1586.	
8.000	55.11			710.1	2349.	
10.00	102.9			868.1	3819.	
12.00 *	134.1	129.2	4.939	1105.	6457.	1.000

24.00 *	108.0	116.1	-8.045	2558.	3.167e+04	1.000
48.00 *	98.47	93.68	4.791	5036.	1.195e+05	1.000
72.00 *	74.44	75.60	-1.167	7111.	2.405e+05	1.000

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

Final Parameters

```

-----
N_Samples                16
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                 7110.6745
AUClast_D               71.1067
AUCall                  7110.6745
AUCINF_obs              15446.2103
AUCINF_D_obs            154.4621
AUC_%Extrap_obs        53.9649
Vz_F_obs                0.7250
Cl_F_obs                0.0065
AUCINF_pred             15576.9232
AUCINF_D_pred           155.7692
AUC_%Extrap_pred       54.3512
Vz_F_pred               0.7189
Cl_F_pred               0.0064
AUMClast                240526.0538
AUMCINF_obs             1774106.9508
AUMC_%Extrap_obs       86.4424
AUMCINF_pred            1798155.6519
AUMC_%Extrap_pred      86.6237
MRTlast                 33.8261
MRTINF_obs              114.8571
MRTINF_pred             115.4372

```

WinNonlin 8.0.0.3176
Subject=9,Formulation=T

Date: 9/09/2019
Time: 18:03:23

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00

```

Dose amount: 100.00
 Calculation method: Linear Trapezoidal with Linear Interpolation
 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	1201.	
5.000	141.4			681.0	1869.	
6.000	140.3			821.8	2643.	
8.000	105.4			1067.	4328.	
10.00	164.8			1338.	6820.	
12.00 *	135.6	131.6	4.014	1638.	1.010e+04	1.000
24.00 *	117.1	122.9	-5.823	3154.	3.672e+04	1.000
48.00 *	109.7	107.4	2.377	5877.	1.337e+05	1.000
72.00 *	93.44	93.76	-0.3218	8315.	2.776e+05	1.000

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

Final Parameters

N_Samples	16
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	8315.0803
AUClast_D	83.1508
AUCall	8315.0803
AUCINF_obs	24865.2460
AUCINF_D_obs	248.6525
AUC_%Extrap_obs	66.5594
Vz_F_obs	0.7123
Cl_F_obs	0.0040
AUCINF_pred	24922.2366
AUCINF_D_pred	249.2224
AUC_%Extrap_pred	66.6359
Vz_F_pred	0.7107
Cl_F_pred	0.0040
AUMClast	277613.9778
AUMCINF_obs	4400604.1747
AUMC_%Extrap_obs	93.6915
AUMCINF_pred	4414801.7328

AUMC_%Extrap_pred 93.7117
MRTlast 33.3868
MRTINF_obs 176.9781
MRTINF_pred 177.1431

WinNonlin 8.0.0.3176
Subject=10,Formulation=R

Date: 9/09/2019
Time: 18:03:24

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Extravascular Administration
Number of nonmissing observations: 16
Dose time: 0.00
Dose amount: 100.00
Calculation method: Linear Trapezoidal with Linear Interpolation
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	13.63			3.409	1.704	
1.000	62.56			22.46	19.05	
1.500	112.7			66.26	76.93	
2.000	125.5			125.8	181.9	
2.500	116.3			186.2	317.3	
3.000	112.7			243.5	474.5	
4.000 *	117.0	124.9	-7.925	358.3	877.5	1.000
5.000 *	119.8	122.8	-2.972	476.7	1411.	1.000
6.000 *	107.6	120.7	-13.13	590.4	2033.	1.000
8.000 *	120.5	116.6	3.868	818.4	3642.	1.000
10.00 *	124.2	112.7	11.50	1063.	5848.	1.000
12.00 *	106.5	108.9	-2.386	1294.	8367.	1.000
24.00 *	116.5	88.57	27.94	2632.	3.281e+04	1.000
48.00 *	45.20	58.63	-13.43	4572.	9.240e+04	1.000
72.00 *	42.19	38.81	3.380	5621.	1.549e+05	1.000

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

Final Parameters

N_Samples	16
Dose	100.0000
Rsqr	0.8809
Rsqr_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	5620.8945
AUClast_D	56.2089
AUCall	5620.8945
AUCINF_obs	8075.3242
AUCINF_D_obs	80.7532
AUC_%Extrap_obs	30.3942
Vz_F_obs	0.7204
Cl_F_obs	0.0124
AUCINF_pred	7878.6869
AUCINF_D_pred	78.7869
AUC_%Extrap_pred	28.6570
Vz_F_pred	0.7384
Cl_F_pred	0.0127
AUMClast	154893.0605
AUMCINF_obs	474396.5944
AUMC_%Extrap_obs	67.3495
AUMCINF_pred	448799.4879
AUMC_%Extrap_pred	65.4872
MRTlast	27.5567
MRTINF_obs	58.7464
MRTINF_pred	56.9637