

8.3 Reference values 3: Linear Trapezoidal Linear Interpolation rule; IV

WinNonlin 8.0.0.3176
 Formulation=R,Subject=2

Date: 9/09/2019
 Time: 18:03:33

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
 8.0.0.3176
 Core Version 22August2017

Settings

 Model: Plasma Data, Bolus IV Administration
 Number of nonmissing observations: 16
 Steady state interval Tau: 12.00
 Dose time: 0.00
 Dose amount: 120.00
 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 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
 Tmax 1.0000
 Cmax 261.1770

Cmax_D	2.1765
C0	0.0000
Tlast	72.0000
Clast	85.2410
Clast_pred	82.5367
AUClast	10112.1755
AUClast_D	84.2681
AUCall	10112.1755
AUCINF_obs	16154.9301
AUCINF_D_obs	134.6244
AUC_%Extrap_obs	37.4050
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	15963.2209
AUCINF_D_pred	133.0268
AUC_%Extrap_pred	36.6533
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	196.0350
Cavg	198.3558
Swing	Missing
Swing_Tau	0.3323
Fluctuation%	131.6710
Fluctuation%_Tau	32.8410
CLss	0.0504
MRTINF_obs	75.5906
MRTINF_pred	74.6241
Vz	3.5739
Vss_obs	3.8109
Vss_pred	3.7621
Accumulation_Index	6.4216
AUC_TAU	2380.2695
AUC_TAU_D	19.8356
AUC_TAU_%Extrap	0.0000
AUMC_TAU	14630.0685

WinNonlin 8.0.0.3176
Formulation=R,Subject=3

Date: 9/09/2019
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WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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	120.0000
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
Tmax	1.5000
Cmax	105.3450
Cmax_D	0.8779
C0	0.0000
Tlast	72.0000
Clast	67.9010
Clast_pred	66.9311
AUClast	5396.5498
AUClast_D	44.9712
AUCall	5396.5498
AUCINF_obs	26026.1826
AUCINF_D_obs	216.8849
AUC_%Extrap_obs	79.2649
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	25731.4952
AUCINF_D_pred	214.4291
AUC_%Extrap_pred	79.0275
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	76.0270
Cavg	81.6955
Swing	Missing
Swing_Tau	0.3856
Fluctuation%	128.9484
Fluctuation%_Tau	35.8869
CLss	0.1224
MRTINF_obs	312.7208
MRTINF_pred	309.1137
Vz	37.1892
Vss_obs	38.2788
Vss_pred	37.8373
Accumulation_Index	25.8216
AUC_TAU	980.3458
AUC_TAU_D	8.1695
AUC_TAU_%Extrap	0.0000
AUMC_TAU	6024.4953

WinNonlin 8.0.0.3176
Formulation=R,Subject=4

Date: 9/09/2019
Time: 18:03:33

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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	120.0000
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
Tmax	1.0000
Cmax	208.5420
Cmax_D	1.7379
C0	0.0000
Tlast	72.0000

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Clast                97.6250
Clast_pred           100.7679
AUClast              9317.8358
AUClast_D            77.6486
AUCall               9317.8358
AUCINF_obs           22004.0779
AUCINF_D_obs         183.3673
AUC_%Extrap_obs      57.6541
AUC_%Back_Ext_obs    0.0000
AUCINF_pred          22412.4980
AUCINF_D_pred        186.7708
AUC_%Extrap_pred     58.4257
AUC_%Back_Ext_pred   0.0000
Tmin                 0.0000
Cmin                 0.0000
Ctau                 132.2570
Cavg                 142.5863
Swing                Missing
Swing_Tau            0.5768
Fluctuation%         146.2567
Fluctuation%_Tau     53.5009
CLss                 0.0701
MRTINF_obs           148.3407
MRTINF_pred          151.2051
Vz                   9.1137
Vss_obs              10.4036
Vss_pred             10.6045
Accumulation_Index   11.3368
AUC_TAU              1711.0358
AUC_TAU_D            14.2586
AUC_TAU_%Extrap     0.0000
AUMC_TAU             10299.7208

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WinNonlin 8.0.0.3176
Formulation=R,Subject=7

Date: 9/09/2019
Time: 18:03:34

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

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Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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        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

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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	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
Tmax	2.5000
Cmax	153.2540
Cmax_D	1.2771
C0	0.0000
Tlast	72.0000
Clast	58.0510
Clast_pred	61.1727
AUClast	7029.5735
AUClast_D	58.5798
AUCall	7029.5735
AUCINF_obs	11688.9527
AUCINF_D_obs	97.4079
AUC_%Extrap_obs	39.8614
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	11939.5116
AUCINF_D_pred	99.4959
AUC_%Extrap_pred	41.1234
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	123.3700
Cavg	119.7133
Swing	Missing
Swing_Tau	0.2422
Fluctuation%	128.0175
Fluctuation%_Tau	24.9630
CLss	0.0835
MRTINF_obs	91.9083
MRTINF_pred	94.0013
Vz	6.7046
Vss_obs	7.6774
Vss_pred	7.8522
Accumulation_Index	7.2011
AUC_TAU	1436.5595
AUC_TAU_D	11.9713
AUC_TAU_%Extrap	0.0000
AUMC_TAU	9003.0193

Formulation=R, Subject=8

Date: 9/09/2019
Time: 18:03:33

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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	120.0000
Rsqr	0.9480
Rsqr_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
Tmax	4.0000
Cmax	138.3270
Cmax_D	1.1527
C0	0.0000
Tlast	72.0000
Clast	74.4370
Clast_pred	75.6043
AUClast	7110.6745

AUClast_D	59.2556
AUCall	7110.6745
AUCINF_obs	15446.2103
AUCINF_D_obs	128.7184
AUC_%Extrap_obs	53.9649
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	15576.9232
AUCINF_D_pred	129.8077
AUC_%Extrap_pred	54.3512
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	134.1330
Cavg	92.0892
Swing	Missing
Swing_Tau	0.0313
Fluctuation%	150.2098
Fluctuation%_Tau	4.5543
CLss	0.1086
MRTINF_obs	161.5740
MRTINF_pred	162.9934
Vz	12.1601
Vss_obs	17.5454
Vss_pred	17.6995
Accumulation_Index	9.8407
AUC_TAU	1105.0705
AUC_TAU_D	9.2089
AUC_TAU_%Extrap	0.0000
AUMC_TAU	6457.0058

WinNonlin 8.0.0.3176
 Formulation=R,Subject=10

Date: 9/09/2019
 Time: 18:03:34

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
 8.0.0.3176
 Core Version 22August2017

Settings

 Model: Plasma Data, Bolus IV Administration
 Number of nonmissing observations: 16
 Steady state interval Tau: 12.00
 Dose time: 0.00
 Dose amount: 120.00
 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	125.5	0.01374	125.8	181.9	1.000
2.500 *	116.3	124.4	-8.180	186.2	317.3	1.000
3.000 *	112.7	123.4	-10.74	243.5	474.5	1.000
4.000 *	117.0	121.4	-4.399	358.3	877.5	1.000
5.000 *	119.8	119.4	0.4169	476.7	1411.	1.000
6.000 *	107.6	117.4	-9.877	590.4	2033.	1.000

8.000 *	120.5	113.6	6.867	818.4	3642.	1.000
10.00 *	124.2	109.9	14.26	1063.	5848.	1.000
12.00 *	106.5	106.3	0.1388	1294.	8367.	1.000
24.00 *	116.5	87.19	29.32	2632.	3.281e+04	1.000
48.00 *	45.20	58.62	-13.41	4572.	9.240e+04	1.000
72.00 *	42.19	39.41	2.782	5621.	1.549e+05	1.000

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

Final Parameters

N_Samples	16
Dose	120.0000
Rsq	0.8797
Rsq_adjusted	0.8677
Corr_XY	-0.9379
No_points_lambda_z	12
Lambda_z	0.0165
Lambda_z_intercept	4.8651
Lambda_z_lower	2.0000
Lambda_z_upper	72.0000
HL_Lambda_z	41.8978
Span	1.6707
Tmax	2.0000
Cmax	125.4820
Cmax_D	1.0457
C0	0.0000
Tlast	72.0000
Clast	42.1910
Clast_pred	39.4088
AUClast	5620.8945
AUClast_D	46.8408
AUCall	5620.8945
AUCINF_obs	8171.1624
AUCINF_D_obs	68.0930
AUC_%Extrap_obs	31.2106
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	8002.9926
AUCINF_D_pred	66.6916
AUC_%Extrap_pred	29.7651
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	106.4760
Cavg	107.8089
Swing	Missing
Swing_Tau	0.1785
Fluctuation%	116.3930
Fluctuation%_Tau	17.6293
CLss	0.0928
MRTINF_obs	70.2607
MRTINF_pred	68.7008
Vz	5.6068
Vss_obs	6.5172
Vss_pred	6.3725
Accumulation_Index	5.5537
AUC_TAU	1293.7065
AUC_TAU_D	10.7809
AUC_TAU_%Extrap	0.0000
AUMC_TAU	8367.3005

WinNonlin 8.0.0.3176
Formulation=T,Subject=1

Date: 9/09/2019

Time: 18:03:34

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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	120.0000
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
Tmax	1.0000
Cmax	190.8690
Cmax_D	1.5906
C0	0.0000
Tlast	72.0000
Clast	112.8460
Clast_pred	117.3058
AUClast	9585.4218
AUClast_D	79.8785
AUCall	9585.4218
AUCINF_obs	42925.0191

```

AUCINF_D_obs          357.7085
AUC_%Extrap_obs      77.6694
AUC_%Back_Ext_obs    0.0000
AUCINF_pred          44242.6313
AUCINF_D_pred        368.6886
AUC_%Extrap_pred     78.3344
AUC_%Back_Ext_pred   0.0000
Tmin                  0.0000
Cmin                  0.0000
Ctau                  144.9640
Cavg                  139.1751
Swing                 Missing
Swing_Tau             0.3167
Fluctuation%         137.1430
Fluctuation%_Tau     32.9836
CLss                  0.0719
MRTINF_obs           302.4030
MRTINF_pred          311.8703
Vz                    21.2282
Vss_obs               21.7282
Vss_pred              22.4085
Accumulation_Index   25.1237
AUC_TAU              1670.1018
AUC_TAU_D            13.9175
AUC_TAU_%Extrap     0.0000
AUMC_TAU             9984.8168

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WinNonlin 8.0.0.3176
Formulation=T,Subject=5

Date: 9/09/2019
Time: 18:03:35

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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

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-----
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      167.7      1.635      439.3      1164.      1.000
5.000 *   162.9      166.6     -3.646      605.4      1909.      1.000
6.000 *   166.7      165.4      1.236      770.2      2817.      1.000
8.000 *   168.7      163.2      5.507      1106.      5166.      1.000
10.00 *   155.1      160.9     -5.836      1429.      8066.      1.000
12.00 *   154.1      158.7     -4.680      1738.      1.147e+04  1.000

```

24.00 *	163.0	146.2	16.77	3641.	4.603e+04	1.000
48.00 *	109.8	124.0	-14.20	6914.	1.562e+05	1.000
72.00 *	110.8	105.2	5.582	9561.	3.152e+05	1.000

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

Final Parameters

```

-----
N_Samples                16
Dose                    120.0000
Rsq                     0.8637
Rsq_adjusted            0.8442
Corr_XY                 -0.9293
No_points_lambda_z      9
Lambda_z                0.0069
Lambda_z_intercept      5.1496
Lambda_z_lower          4.0000
Lambda_z_upper          72.0000
HL_Lambda_z            101.0715
Span                    0.6728
Tmax                    4.0000
Cmax                    169.3340
Cmax_D                  1.4111
C0                      0.0000
Tlast                   72.0000
Clast                   110.7780
Clast_pred              105.1962
AUClast                 9561.2600
AUClast_D              79.6772
AUCall                  9561.2600
AUCINF_obs             25714.3934
AUCINF_D_obs           214.2866
AUC_%Extrap_obs        62.8175
AUC_%Back_Ext_obs      0.0000
AUCINF_pred            24900.4861
AUCINF_D_pred          207.5041
AUC_%Extrap_pred       61.6021
AUC_%Back_Ext_pred     0.0000
Tmin                    0.0000
Cmin                    0.0000
Ctau                    154.0660
Cavg                    144.8717
Swing                   Missing
Swing_Tau               0.0991
Fluctuation%           116.8855
Fluctuation%_Tau       10.5390
CLss                    0.0690
MRTINF_obs             172.0933
MRTINF_pred            166.4752
Vz                      10.0651
Vss_obs                11.8790
Vss_pred                11.4912
Accumulation_Index     12.6581
AUC_TAU                1738.4600
AUC_TAU_D              14.4872
AUC_TAU_%Extrap        0.0000
AUMC_TAU               11466.1225

```

WinNonlin 8.0.0.3176
Formulation=T,Subject=6

Date: 9/09/2019
Time: 18:03:35

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
8.0.0.3176
Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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                     120.0000
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
Tmax                     2.5000
Cmax                     154.6480
Cmax_D                   1.2887
C0                       0.0000
Tlast                    72.0000
Clast                    69.5010
Clast_pred               71.9399
AUClast                  6966.5980
AUClast_D                58.0550
AUCall                   6966.5980
AUCINF_obs               16001.7597
AUCINF_D_obs             133.3480
AUC_%Extrap_obs         56.4636
AUC_%Back_Ext_obs       0.0000
  
```

```

AUCINF_pred          16318.8233
AUCINF_D_pred        135.9902
AUC_%Extrap_pred     57.3094
AUC_%Back_Ext_pred   0.0000
Tmin                 0.0000
Cmin                 0.0000
Ctau                 113.7510
Cavg                 117.4998
Swing                Missing
Swing_Tau            0.3595
Fluctuation%         131.6155
Fluctuation%_Tau     34.8060
CLss                 0.0851
MRTINF_obs           130.1906
MRTINF_pred          132.8890
Vz                   11.0639
Vss_obs              11.0801
Vss_pred             11.3097
Accumulation_Index   11.3411
AUC_TAU              1409.9980
AUC_TAU_D            11.7500
AUC_TAU_%Extrap     0.0000
AUMC_TAU             8467.3568

```

WinNonlin 8.0.0.3176
 Formulation=T,Subject=9

Date: 9/09/2019
 Time: 18:03:35

WINNONLIN NONCOMPARTMENTAL ANALYSIS PROGRAM
 8.0.0.3176
 Core Version 22August2017

Settings

```

-----
Model: Plasma Data, Bolus IV Administration
Number of nonmissing observations: 16
Steady state interval Tau: 12.00
Dose time: 0.00
Dose amount: 120.00
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    113.4
1.000     128.3
1.500     125.4
2.000     146.9
2.500     140.6
3.000     167.3
4.000     157.5
5.000     141.4
6.000     140.3
8.000     105.4
10.00     164.8
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	120.0000
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
Tmax	3.0000
Cmax	167.3470
Cmax_D	1.3946
C0	0.0000
Tlast	72.0000
Clast	93.4400
Clast_pred	93.7618
AUClast	8315.0803
AUClast_D	69.2923
AUCall	8315.0803
AUCINF_obs	24865.2460
AUCINF_D_obs	207.2104
AUC_%Extrap_obs	66.5594
AUC_%Back_Ext_obs	0.0000
AUCINF_pred	24922.2366
AUCINF_D_pred	207.6853
AUC_%Extrap_pred	66.6359
AUC_%Back_Ext_pred	0.0000
Tmin	0.0000
Cmin	0.0000
Ctau	135.5800
Cavg	136.5159
Swing	Missing
Swing_Tau	0.2343
Fluctuation%	122.5843
Fluctuation%_Tau	23.2698
CLss	0.0733
MRTINF_obs	176.3046
MRTINF_pred	176.7221
Vz	12.9744
Vss_obs	12.9146
Vss_pred	12.9452
Accumulation_Index	15.2657
AUC_TAU	1638.1903
AUC_TAU_D	13.6516
AUC_TAU_%Extrap	0.0000
AUMC_TAU	10095.8178