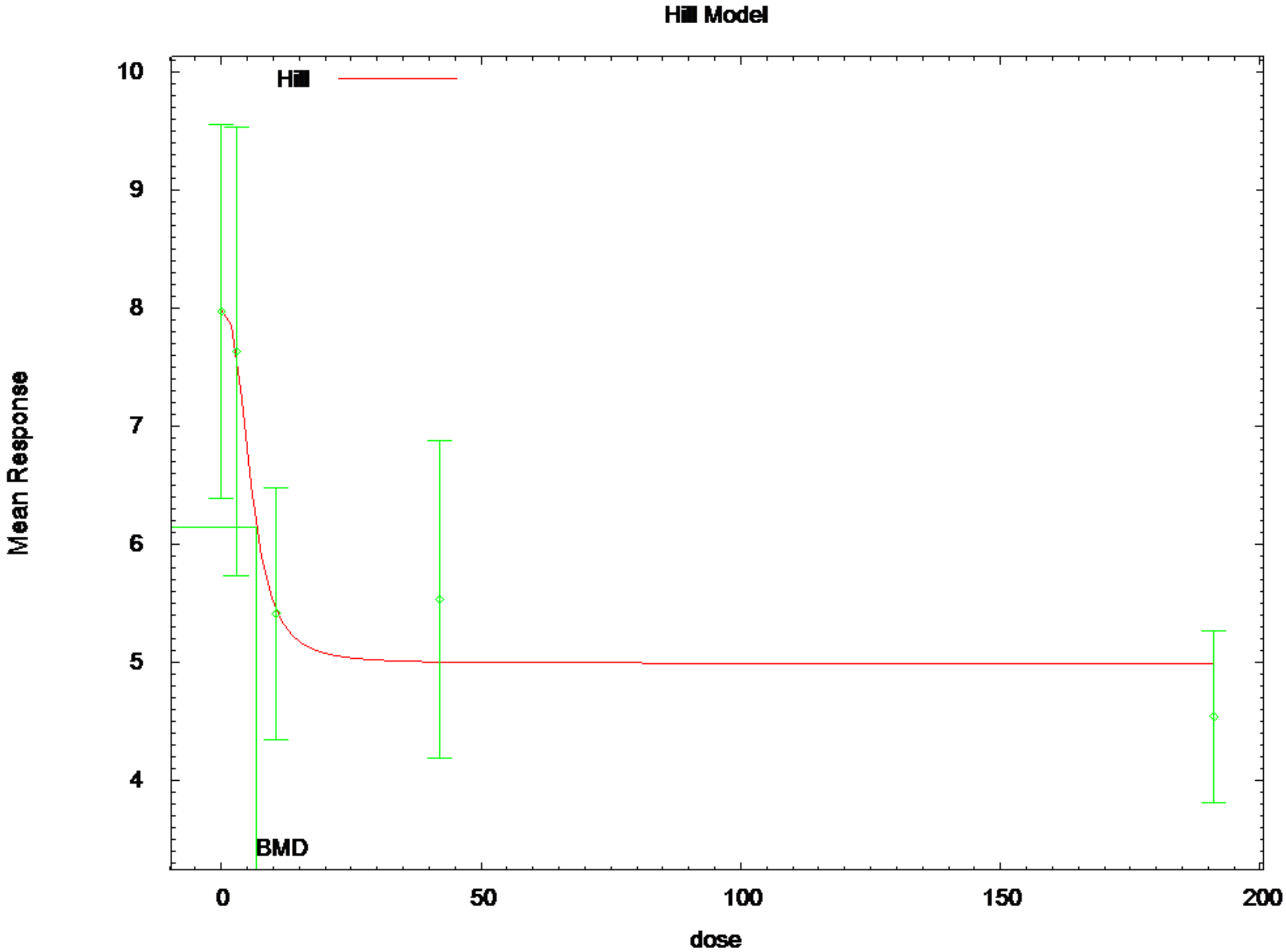
Appendix A

Benchmark Dose Modeling Output

BMDS Model Results for White Blood Cell Count (Untransformed Doses, Concurrent Controls)



12:14 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.plt
                                       Sat Jun 21 12:14:46 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                      intercept =         7.97
                              v =        -3.43
                              n =      2.04485
                              k =      7.66914


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-1.1e-006	-5.8e-007	-5e-008	1.5e-006
intercept	-1.1e-006	1	-0.81	-0.48	-0.5
v	-5.8e-007	-0.81	1	0.59	0.17
n	-5e-008	-0.48	0.59	1	0.094
k	1.5e-006	-0.5	0.17	0.094	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.36457	0.686789	2.01848	4.71065
intercept	7.98132	0.579373	6.84577	9.11687
v	-2.98857	0.748734	-4.45606	-1.52107
n	2.86103	2.49408	-2.02726	7.74933
k	5.76726	3.11705	-0.342045	11.8766

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.98	2.21	1.83	-0.0195

```
  2.9    10       7.63         7.61         2.65         1.83
0.0266
 10.6     9       5.41         5.44         1.39         1.83
-0.0465
   42     9       5.53            5         1.76         1.83
0.862
191.1    10       4.54         4.99         1.02         1.83
-0.781
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-53.119185	5	116.238371
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	1.37553	1	0.2409

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

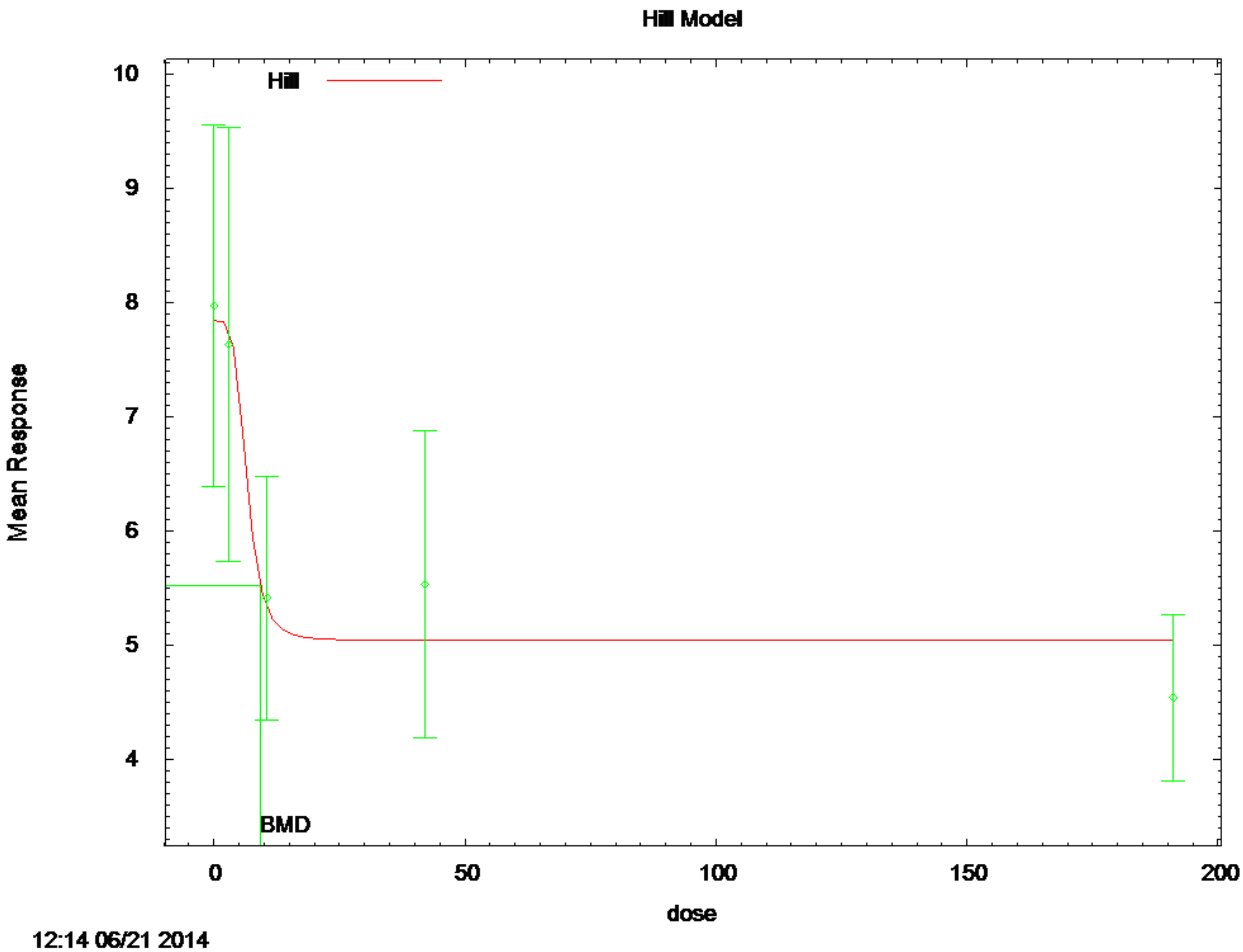
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 6.78072

BMDL computation failed.



Hill Model
Hill
10
9
8
7
6
5
4
Mean Response
BMD
0
50
100
150
200
dose
12:14 06/21 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.plt
                                        Sat Jun 21 12:14:47 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                      intercept =         7.97
                              v =        -3.43
                              n =      2.04485
                              k =      7.66914


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.3	-0.39	-0.13	-0.095
rho	-0.99	1	-0.32	0.4	0.13	0.095
intercept	0.3	-0.32	1	-0.92	-0.67	-0.67
v	-0.39	0.4	-0.92	1	0.66	0.59
n	-0.13	0.13	-0.67	0.66	1	0.93
k	-0.095	0.095	-0.67	0.59	0.93	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.20747	1.98544	-7.09886	0.683917
rho	2.3751	1.09133	0.236133	4.51407
intercept	7.84141	0.710303	6.44924	9.23357
v	-2.7994	0.803986	-4.37518	-1.22362
n	4.58295	11.6557	-18.2617	27.4276
k	6.55959	7.97954	-9.08003	22.1992

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.84	2.21	2.32	0.175

2.9	10	7.63	7.78	2.65	2.3	-0.202
10.6	9	5.41	5.32	1.39	1.46	0.182
42	9	5.53	5.04	1.76	1.37	1.06
191.1	10	4.54	5.04	1.02	1.37	-1.16

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-50.207108	6	112.414215
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	4.89668	1	0.02691

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

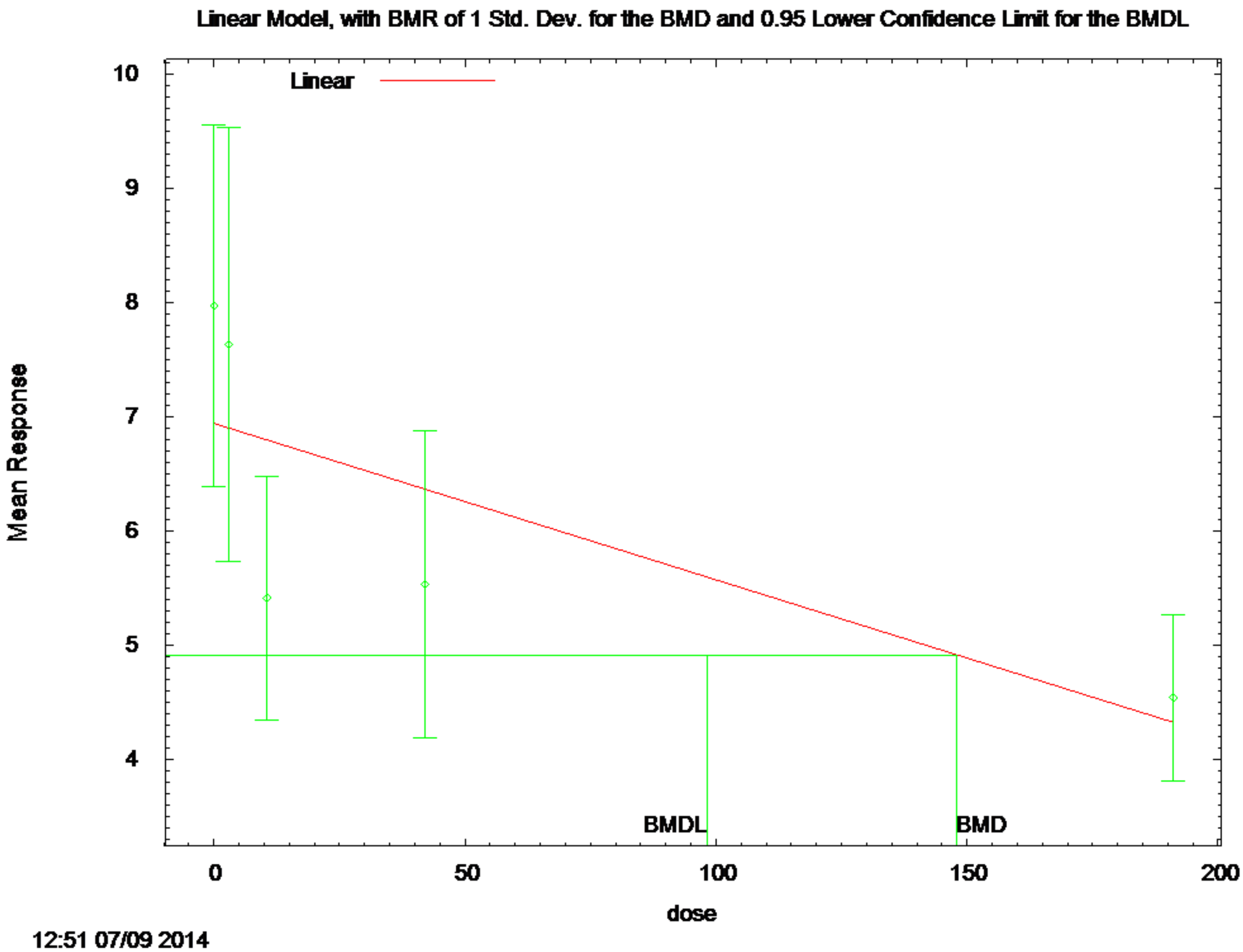
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 9.25758

BMDL computation failed.


Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:51 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-LinearCV-1SD-5d.plt
                                       Wed Jul 09 12:51:15 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =      6.88046
                         beta_1 =   -0.0134724


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	6e-008	-3.1e-008
beta_0	6e-008	1	-0.56
beta_1	-3.1e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	4.10153	0.83722	2.4606	5.74245
beta_0	6.93587	0.35384	6.24236	7.62939
beta_1	-0.0136993	0.00396554	-0.0214716	-0.00592698

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.21	2.03	1.61
2.9	10	7.63	6.9	2.65	2.03	1.15
10.6	9	5.41	6.79	1.39	2.03	-2.05
42	9	5.53	6.36	1.76	2.03	-1.23
191.1	10	4.54	4.32	1.02	2.03	0.347

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-57.872613	3	121.745227
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	10.8824	3	0.01238

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

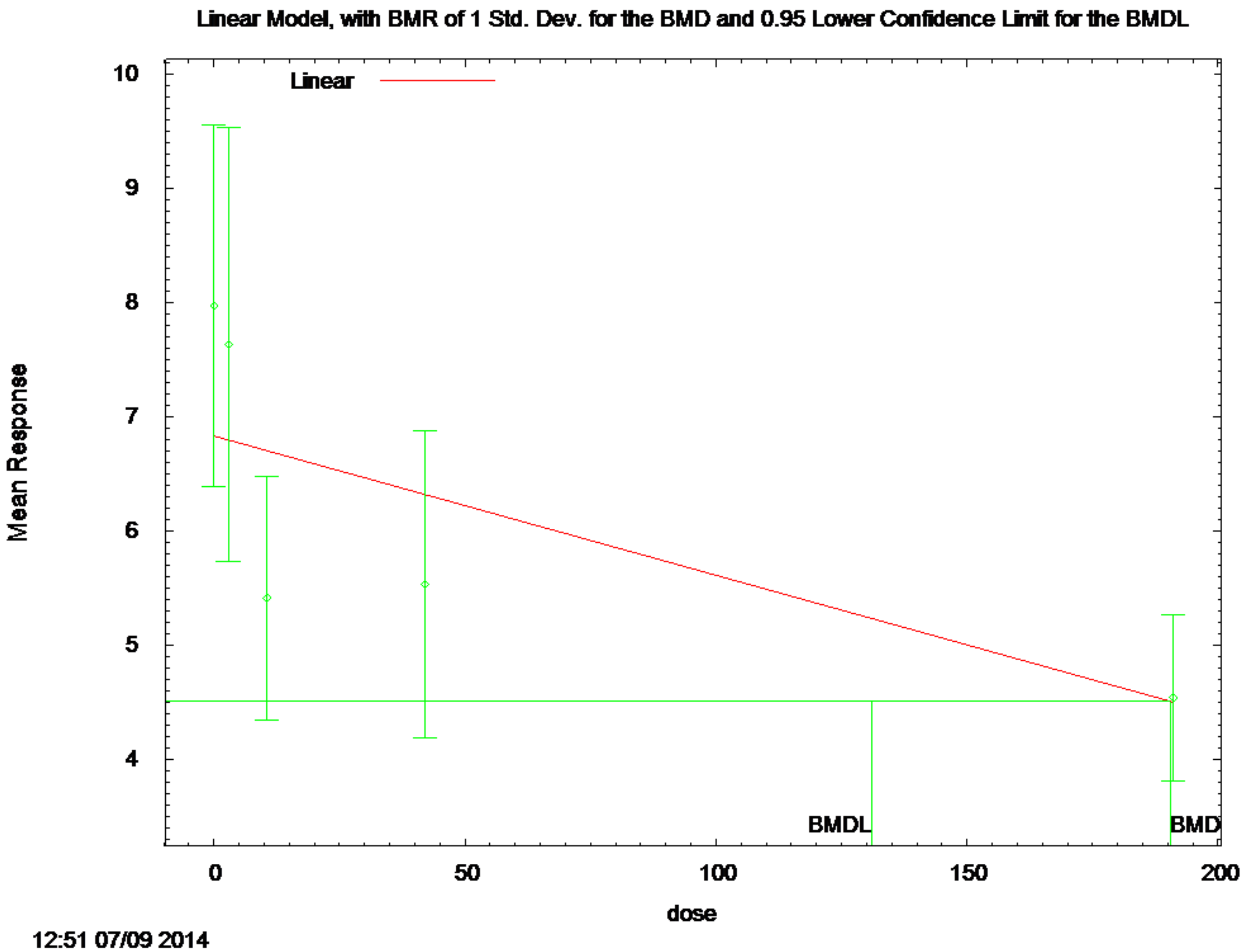
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 147.834

BMDL = 98.2036


Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
50
100
150
200
12:51 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:51:16 2014
====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      6.88046
                         beta_1 =   -0.0134724


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1           -1        0.059       -0.074
```

rho	-1	1	-0.059	0.075
beta_0	0.059	-0.059	1	-0.81
beta_1	-0.074	0.075	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.51621	2.25638	-10.9386	-2.09378
rho	4.27037	1.23797	1.84399	6.69675
beta_0	6.83277	0.388873	6.07059	7.59495
beta_1	-0.0122267	0.00266203	-0.0174442	-0.00700924

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.83	2.21	2.33	1.54
2.9	10	7.63	6.8	2.65	2.3	1.14
10.6	9	5.41	6.7	1.39	2.24	-1.74
42	9	5.53	6.32	1.76	1.97	-1.2
191.1	10	4.54	4.5	1.02	0.953	0.145

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-53.651165	4	115.302330
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	11.7848	3	0.008158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

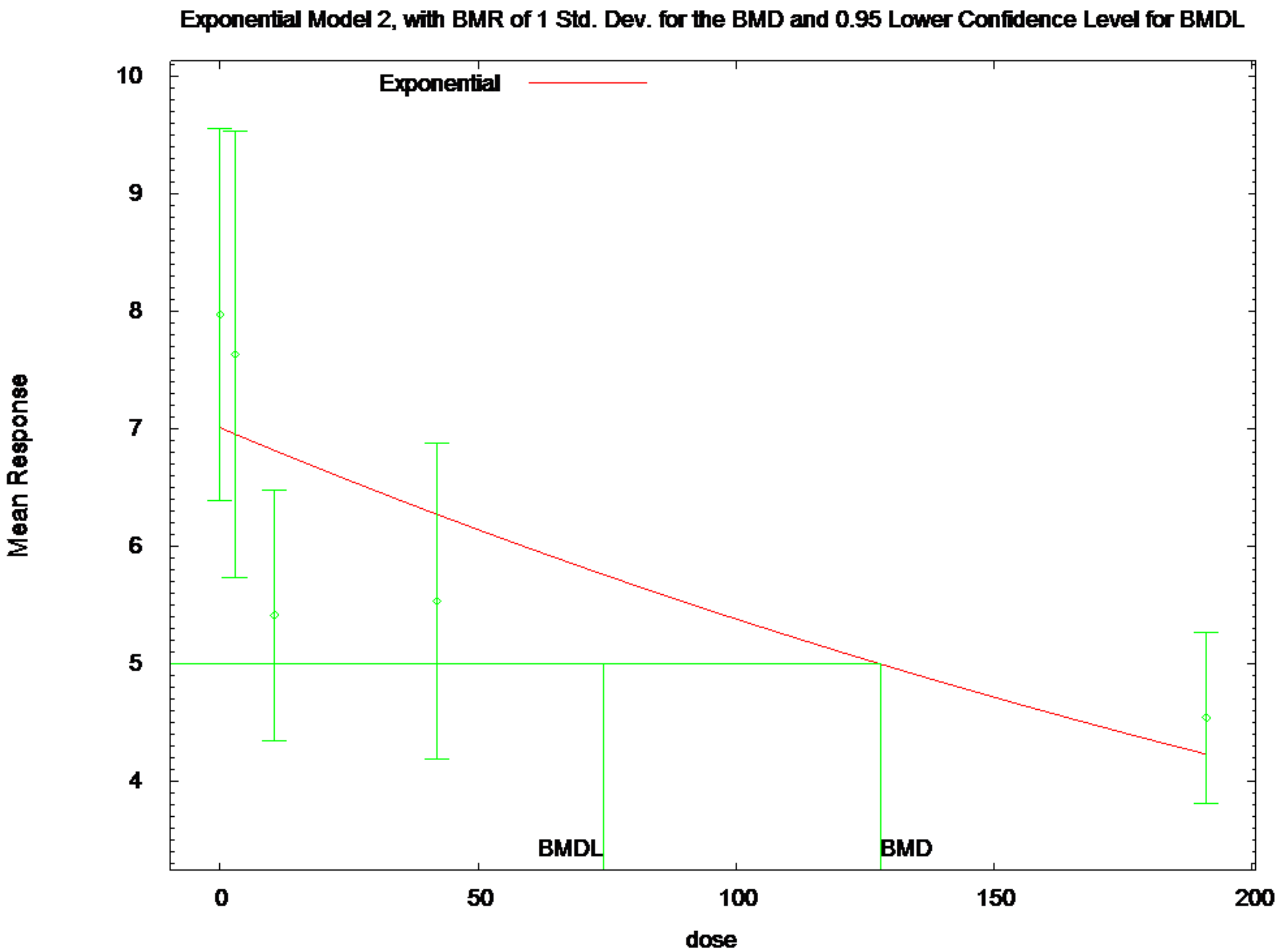
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 190.429

BMDL = 131.056



12:14 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 12:14:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.18464
rho(S)	0
a	5.42664
b	0.00232433
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.39884
rho	0
a	7.00671
b	0.00264475
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.007	2.013	1.514
2.9	6.953	2.013	1.063
10.6	6.813	2.013	-2.091
42	6.27	2.013	-1.103
191.1	4.227	2.013	0.492

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
2	-57.57205	3	121.1441

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	

0.0001004
Test 2 10.28 4
0.03599
Test 3 10.28 4
0.03599
Test 4 10.28 3
0.01632

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

Specified Effect = 1.000000

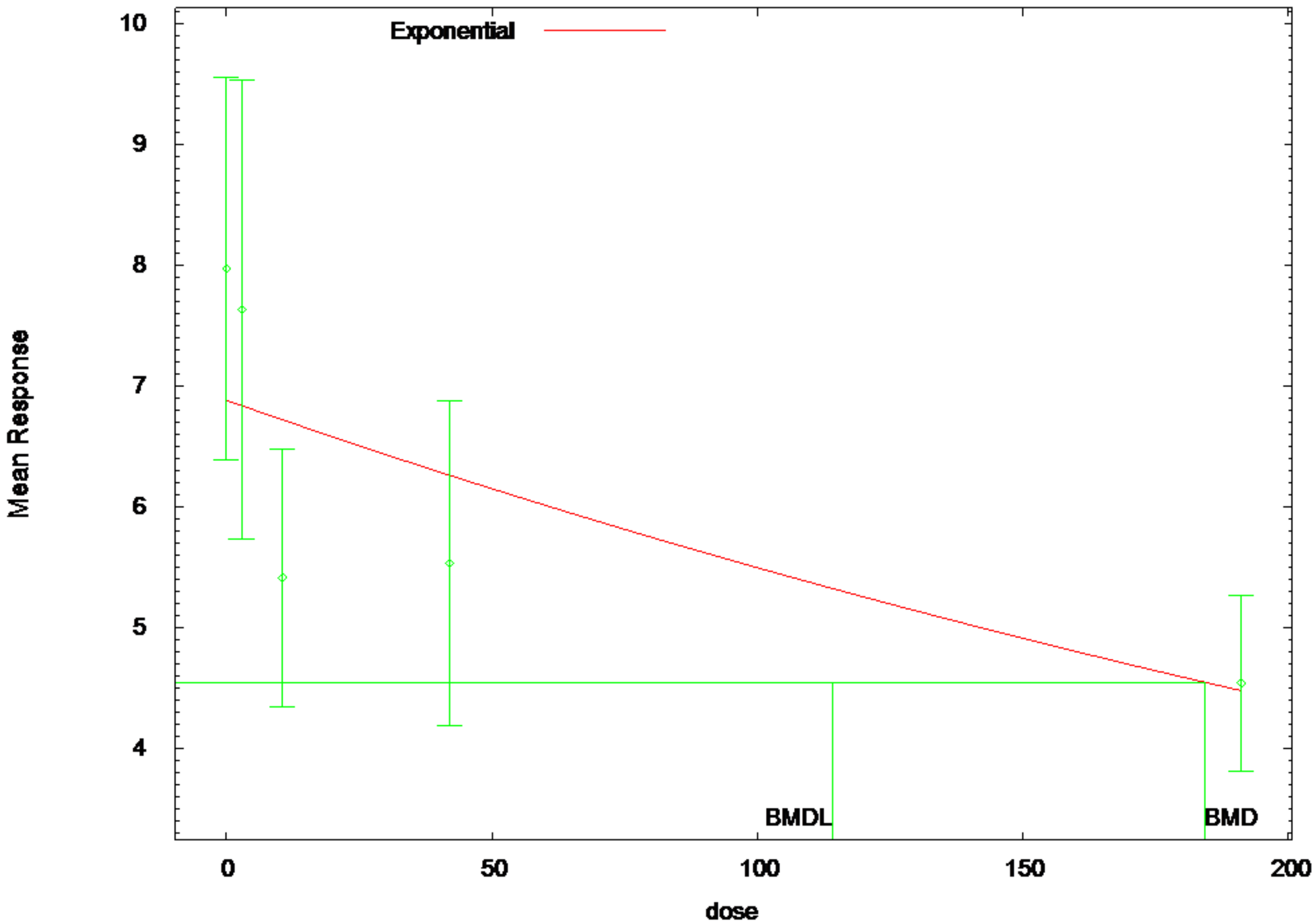
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 128.029

BMDL = 74.2476

Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



12:14 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 12:14:46 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-4.23146
rho	2.9407
a	5.42664
b	0.00232433
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-6.33358
rho	4.16316
a	6.87983
b	0.00225038
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.88	2.334	1.477
2.9	6.835	2.303	1.092
10.6	6.718	2.221	-1.766
42	6.259	1.917	-1.141
191.1	4.475	0.9537	0.2149

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                 Var{e(ij)} = Sigma(i)^2

     Model A3:          Yij = Mu(i) + e(ij)
                 Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:          Yij = Mu + e(i)
                 Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
2	-53.3862	4	114.7724

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

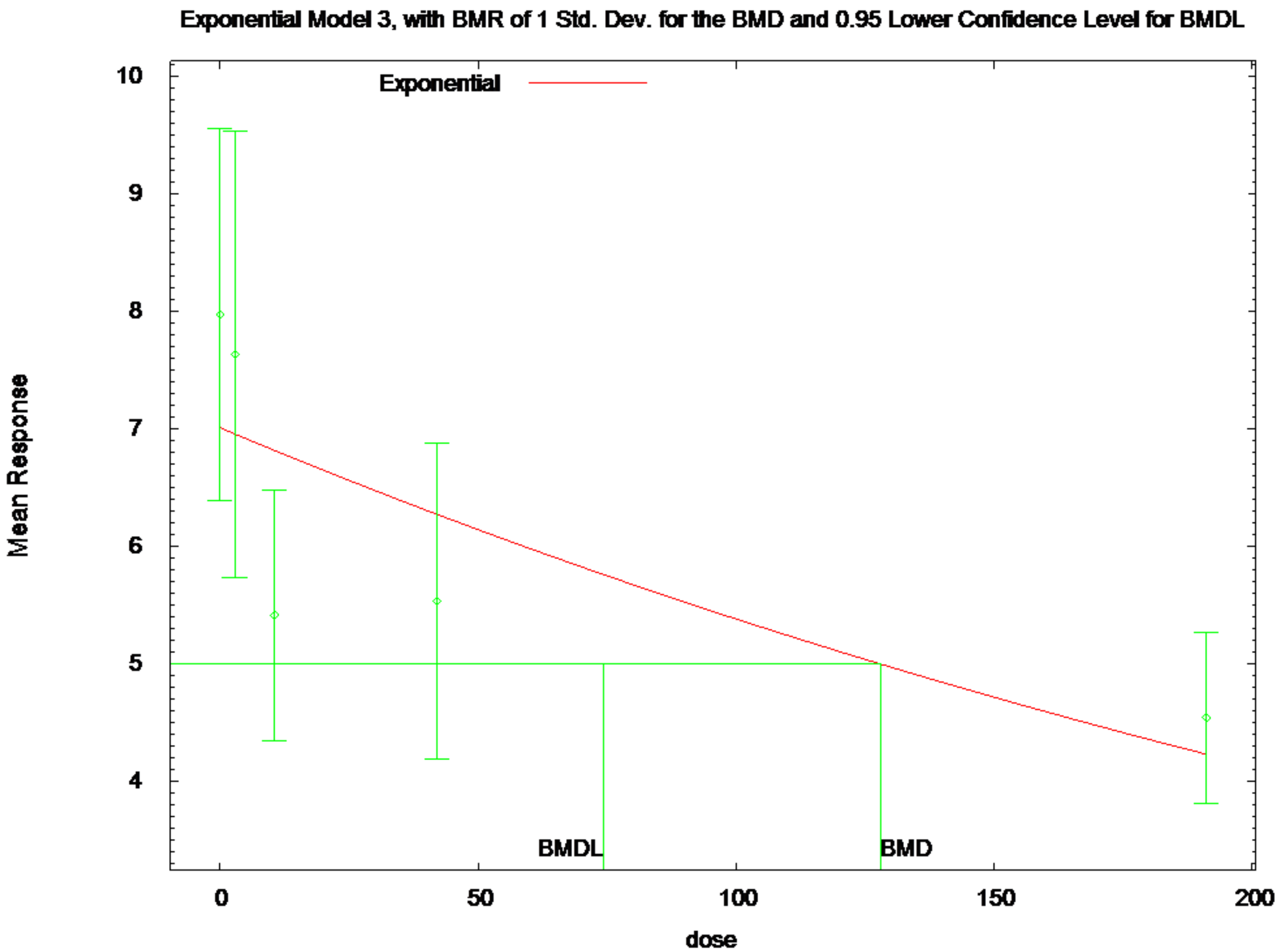
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004
Test 2	10.28	4	

```
0.03599
     Test 3                         0.9332          3
0.8174
     Test 4                          11.25          3
0.01042


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 4 is less than .1.  Model 2 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      184.175

                 BMDL =      114.201
```



12:14 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 12:14:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.18464
rho(S)	0
a	5.42664
b	0.00232433
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.39884
rho	0
a	7.00671
b	0.00264475
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.007	2.013	1.514
2.9	6.953	2.013	1.063
10.6	6.813	2.013	-2.091
42	6.27	2.013	-1.103
191.1	4.227	2.013	0.492

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
3	-57.57205	3	121.1441

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 5a	10.28	3	0.01632

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

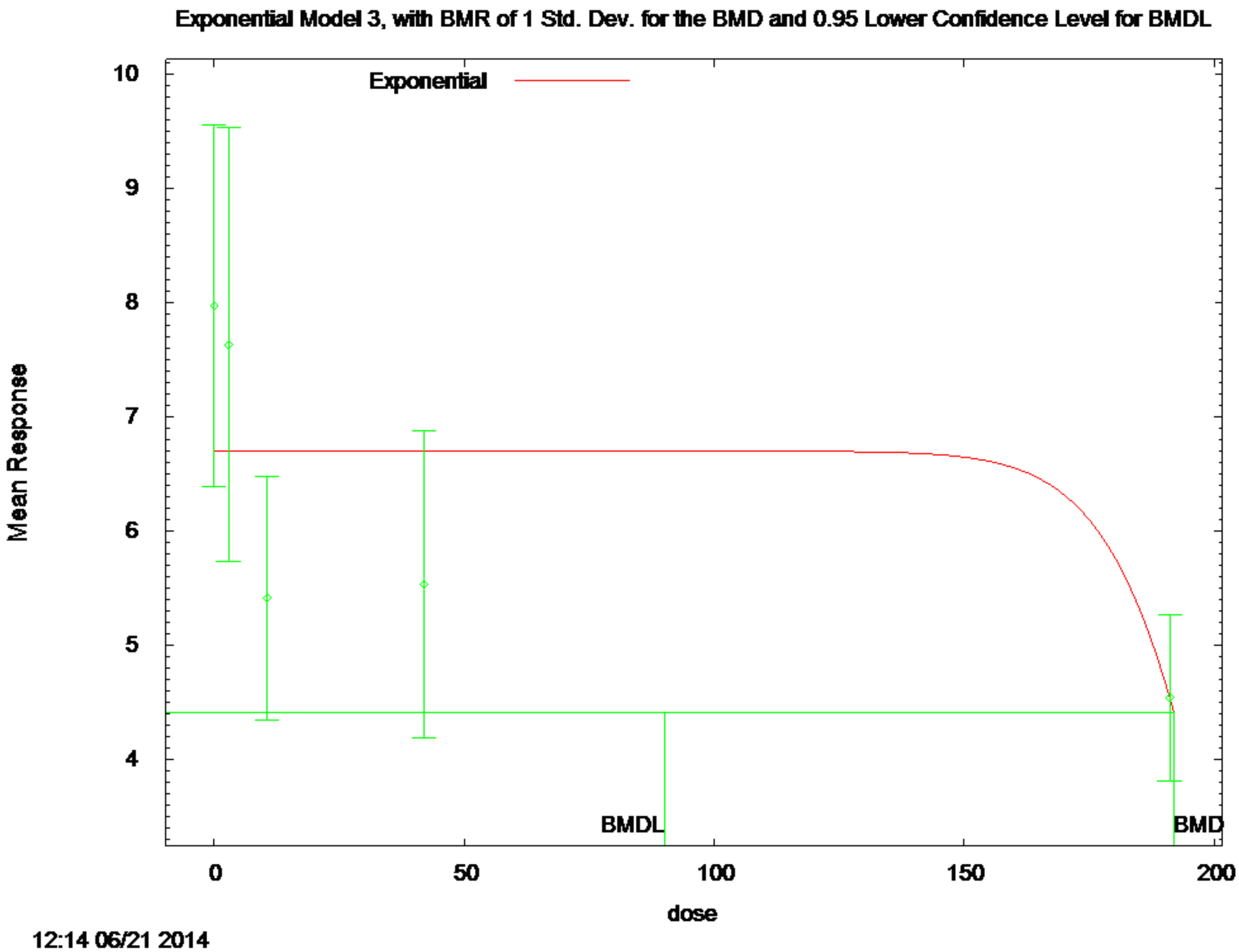
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 128.029

BMDL = 74.2476


Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:14 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 12:14:46 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-4.23146
rho	2.9407
a	5.42664
b	0.00232433
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-6.79001
rho	4.44324
a	6.69632
b	0.00493533
c	0
d	16.145

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.696	2.292	1.757
2.9	6.696	2.292	1.288
10.6	6.696	2.292	-1.683
42	6.696	2.292	-1.526
191.1	4.54	0.9667	-4.057e-007

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                 Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                 Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                 Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
3	-55.18356	5	120.3671

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

Test 2	10.28	4	0.03599
Test 3	0.9332	3	0.8174
Test 5a	14.85	2	0.0005963

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

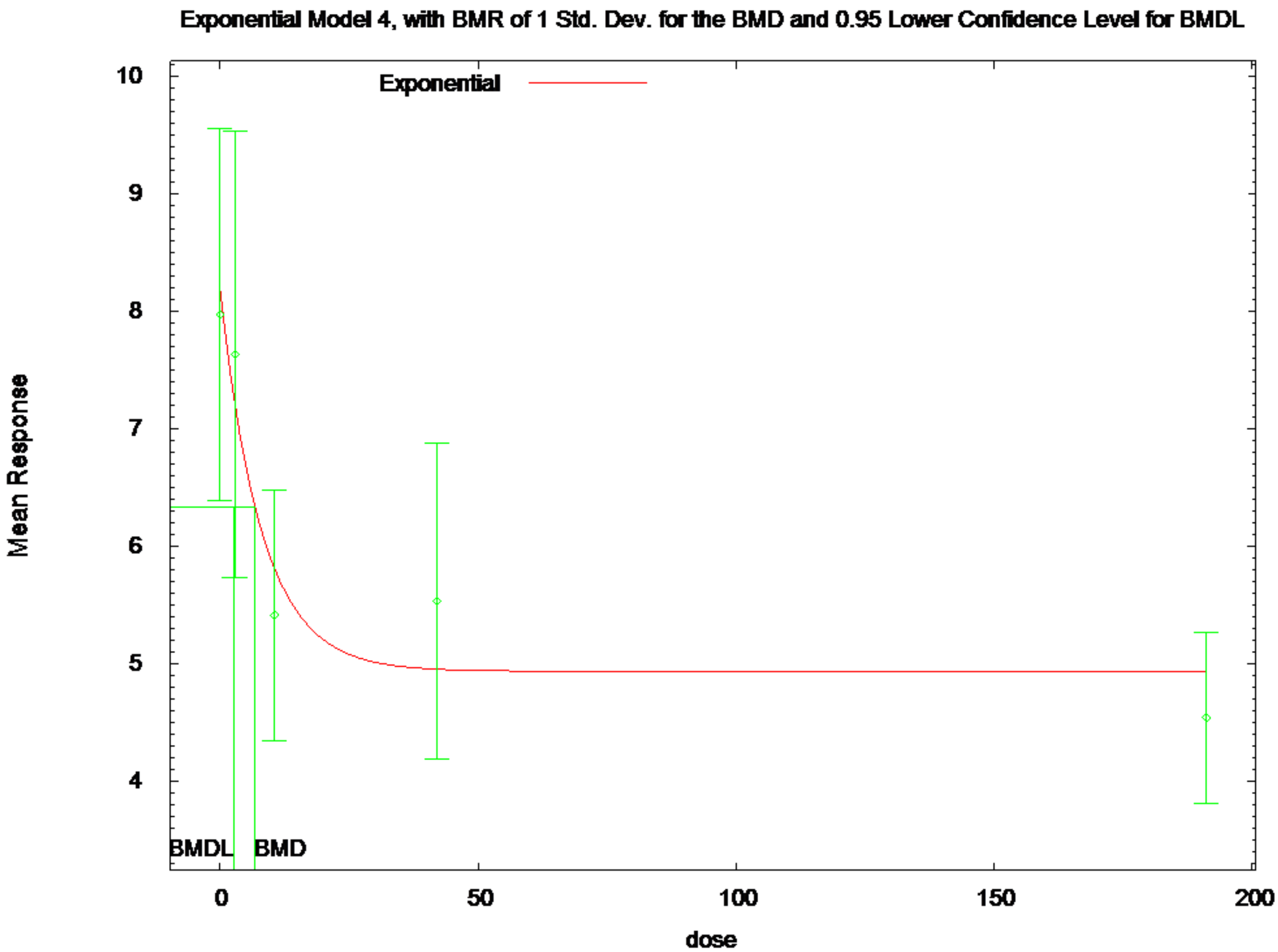
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 191.993

BMDL = 90.1184



12:14 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 12:14:45 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.18464
rho(S)	0
a	8.3685
b	0.0162762
c	0.516677
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.23597
rho	0
a	8.1813
b	0.124602
c	0.602967
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.181	1.855	-0.3602
2.9	7.196	1.855	0.7394
10.6	5.8	1.855	-0.6308
42	4.95	1.855	0.9373
191.1	4.933	1.855	-0.67

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
4	-53.66337	4	115.3267

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 6a	2.464	2	0.2917

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

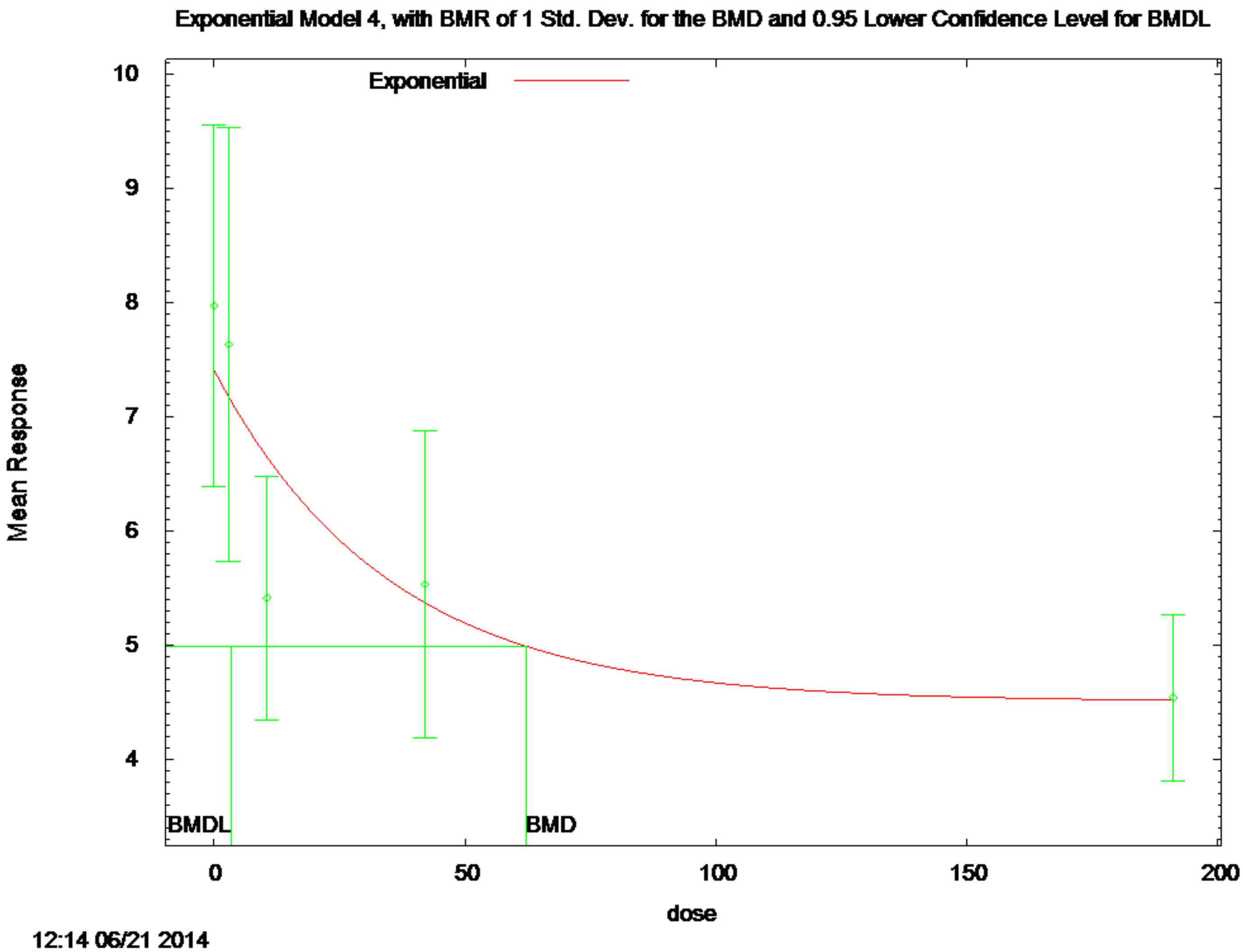
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 6.79455

BMDL = 2.70071


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:14 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 12:14:46 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-4.23146
rho	2.9407
a	8.3685
b	0.0162762
c	0.516677
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-4.82434
rho	3.29183
a	7.40784
b	0.0288406
c	0.608181
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.408	2.42	0.7345
2.9	7.175	2.296	0.6267
10.6	6.643	2.023	-1.829
42	5.37	1.425	0.3374
191.1	4.517	1.072	0.06774

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
4	-51.37641	5	112.7528

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

Test 2	10.28	4	0.03599
Test 3	0.9332	3	0.8174
Test 6a	7.235	2	0.02685

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

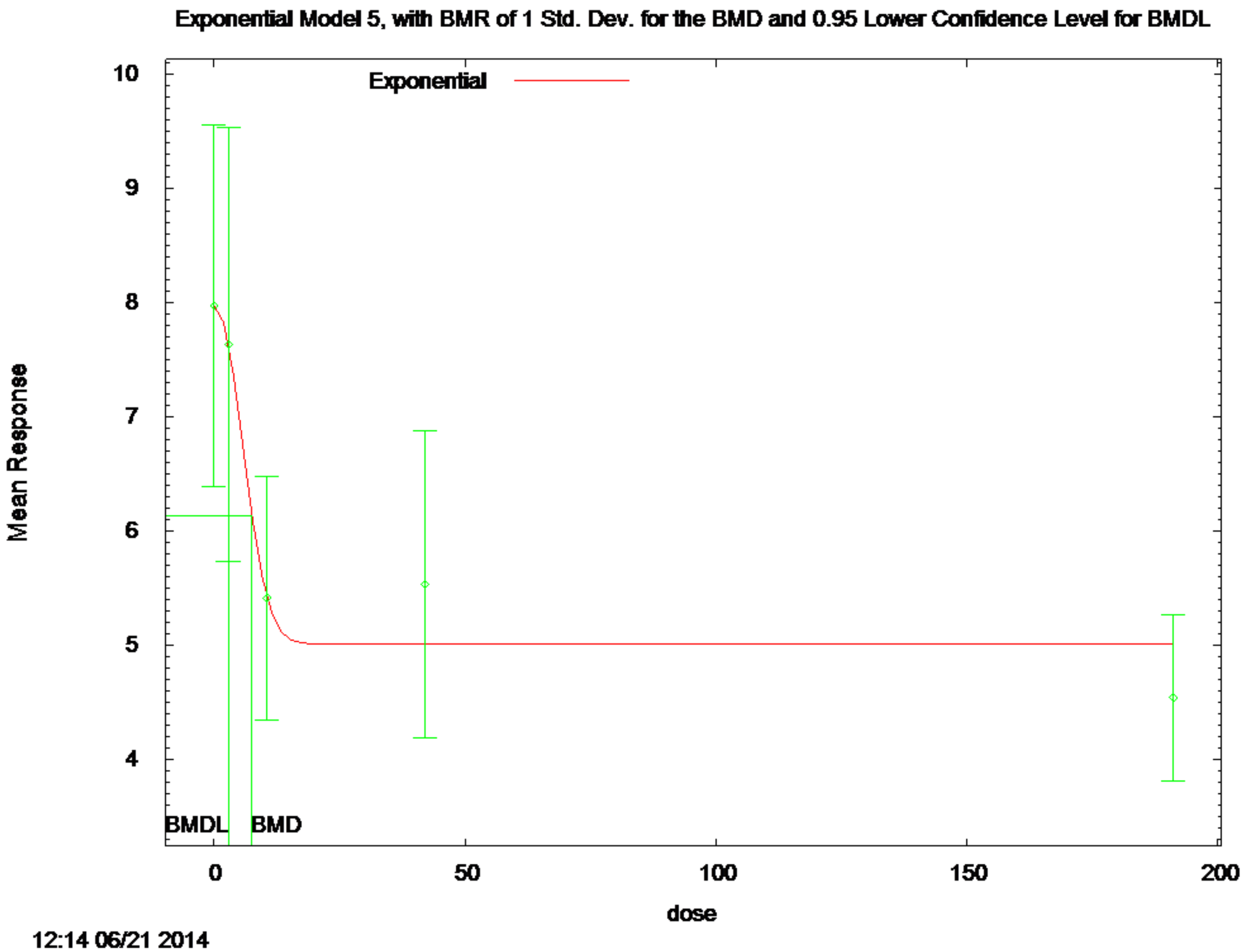
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 62.2262

BMDL = 3.50341


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
50
100
150
200
12:14 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 12:14:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.18464
rho(S)	0
a	8.3685
b	0.0162762
c	0.516677
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.2138
rho	0
a	7.97
b	0.130055
c	0.628475
d	2.15774

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.97	1.835	-1.678e-008
2.9	7.63	1.835	-1.082e-008
10.6	5.41	1.835	-2.061e-008
42	5.009	1.835	0.852
191.1	5.009	1.835	-0.8083

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
5	-53.1311	5	116.2622

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 7a	1.399	1	0.2368

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

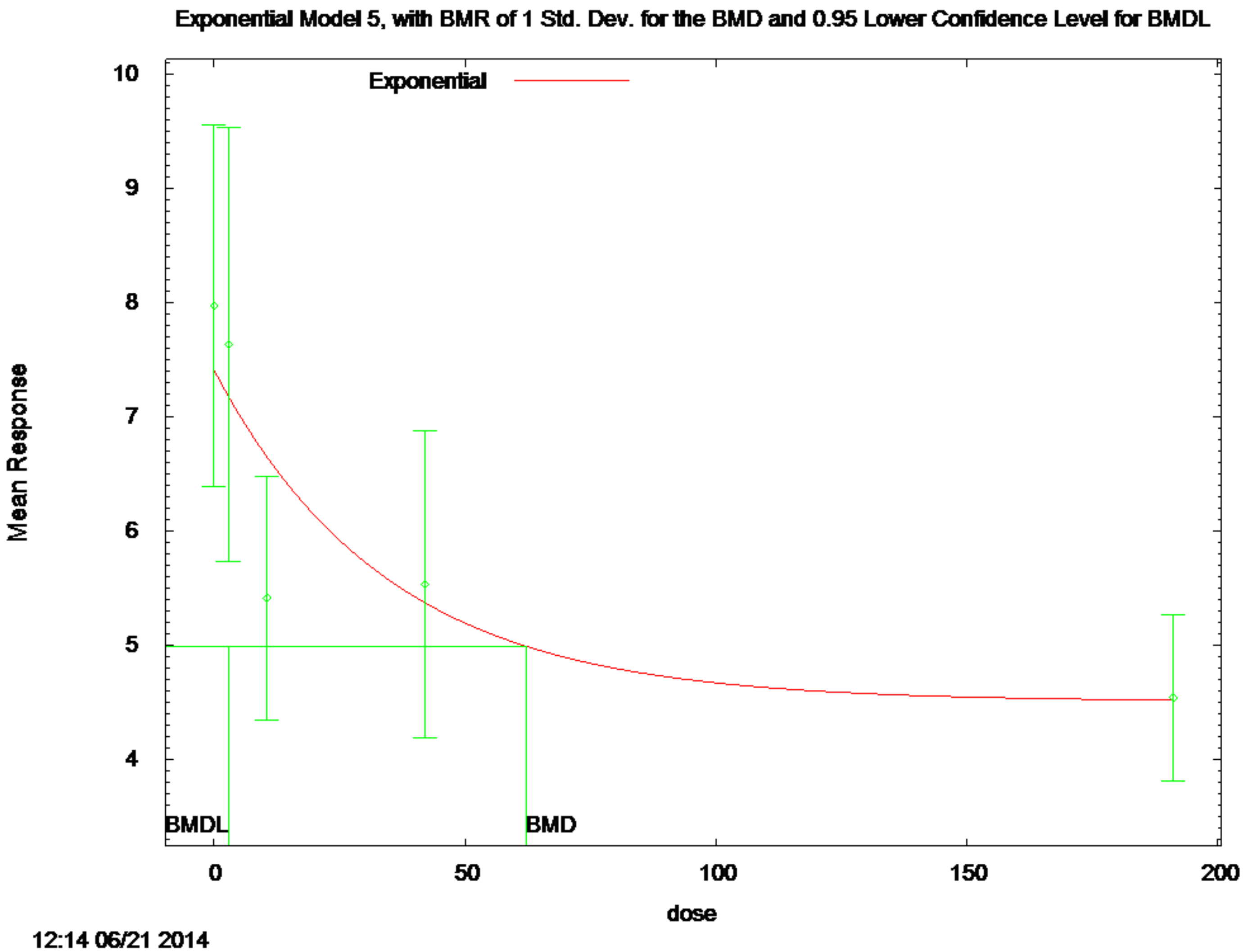
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 7.56892

BMDL = 2.92959


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:14 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 12:14:46 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-4.23146
rho	2.9407
a	8.3685
b	0.0162762
c	0.516677
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-4.82434
rho	3.29183
a	7.40784
b	0.0288406
c	0.608181
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.408	2.42	0.7345
2.9	7.175	2.296	0.6267
10.6	6.643	2.023	-1.829
42	5.37	1.425	0.3374
191.1	4.517	1.072	0.06774

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
5	-51.37641	5	112.7528

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

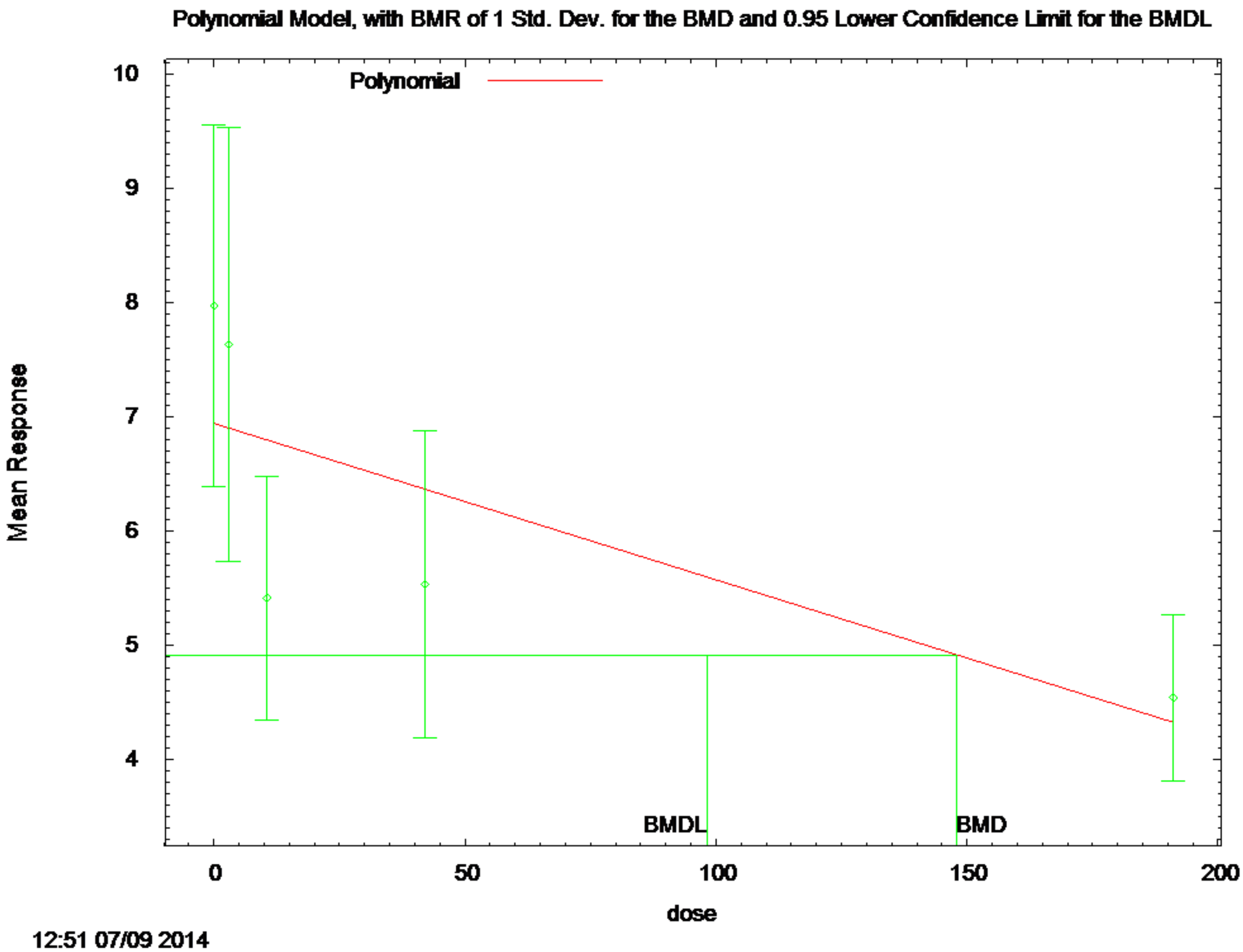
Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

```
     Test 2                              10.28          4
0.03599
     Test 3                             0.9332          3
0.8174
    Test 7a                              7.235          2
0.02685


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 7a is less than .1.  Model 5 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      62.2261

                 BMDL =      2.93936
```



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:51 07/09 2014

```
 ====================================================================
 ===
        Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
        Input Data File:
 C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
 2001-White Blood Cell Count-Poly2CV-1SD-5d.(d)
        Gnuplot Plotting File:
 C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
 2001-White Blood Cell Count-Poly2CV-1SD-5d.plt
                                       Wed Jul 09 12:51:15 2014
 ====================================================================
 ===

  BMDS Model Run
 ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
 ~~~~

    The form of the response function is:

    Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


    Dependent variable = MeanResponse
    Independent variable = Dose
    rho is set to 0
    The polynomial coefficients are restricted to be negative
    A constant variance model is fit

    Total number of dose groups = 5
    Total number of records with missing values = 0
    Maximum number of iterations = 500
    Relative Function Convergence has been set to: 1e-008
    Parameter Convergence has been set to: 1e-008



                   Default Initial Parameter Values
                           alpha =       3.64969
                             rho =             0   Specified
                          beta_0 =       7.40214
                          beta_1 =    -0.0643244
                          beta_2 =             0


            Asymptotic Correlation Matrix of Parameter Estimates

            ( *** The model parameter(s)  -rho    -beta_2
                  have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	2.6e-007	-8.5e-007
beta_0	2.6e-007	1	-0.56
beta_1	-8.5e-007	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	4.10152	0.83722	2.4606	5.74244
beta_0	6.93587	0.35384	6.24236	7.62939
beta_1	-0.0136993	0.00396554	-0.0214716	-0.005927
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.21	2.03	1.61
2.9	10	7.63	6.9	2.65	2.03	1.15
10.6	9	5.41	6.79	1.39	2.03	-2.05
42	9	5.53	6.36	1.76	2.03	-1.23
191.1	10	4.54	4.32	1.02	2.03	0.347

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-57.872613	3	121.745227
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	10.8824	3	0.01238

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

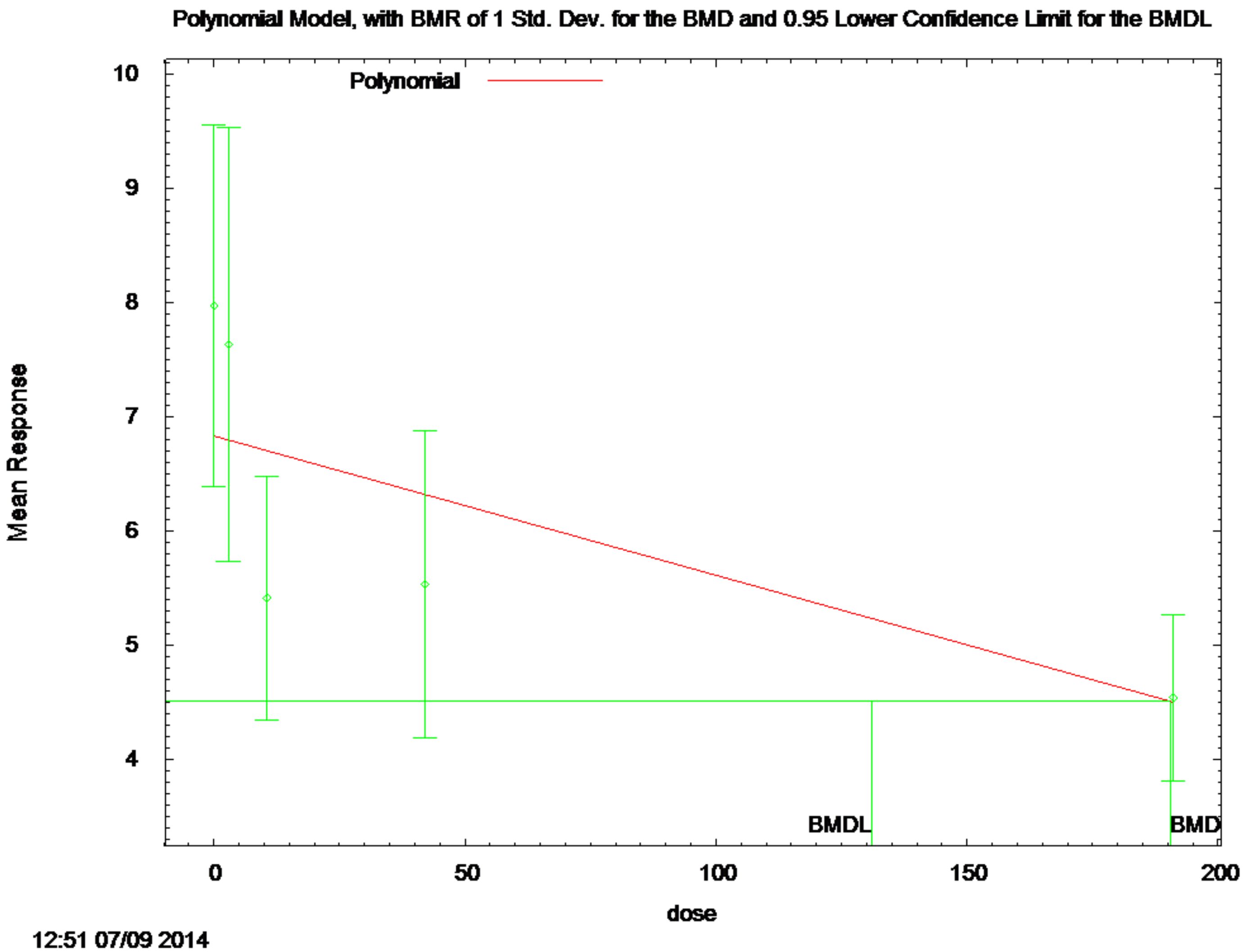
Specified effect =   1

Risk Type   =   Estimated standard deviations from the
control mean

Confidence level =   0.95

BMD =   147.834

BMDL =   98.2036



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
50
100
150
200
12:51 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:51:16 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      7.40214
                         beta_1 =   -0.0643244
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.059	-0.074
rho	-1	1	-0.059	0.075
beta_0	0.059	-0.059	1	-0.81
beta_1	-0.074	0.075	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.5162	2.25638	-10.9386	-2.09377
rho	4.27037	1.23797	1.84399	6.69675
beta_0	6.83277	0.388873	6.07059	7.59495
beta_1	-0.0122267	0.00266203	-0.0174442	-0.00700924
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.83	2.21	2.33	1.54
2.9	10	7.63	6.8	2.65	2.3	1.14
10.6	9	5.41	6.7	1.39	2.24	-1.74
42	9	5.53	6.32	1.76	1.97	-1.2

```
191.1    10       4.54          4.5         1.02        0.953
0.145


 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-53.651165	4	115.302330
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	11.7848	3	0.008158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

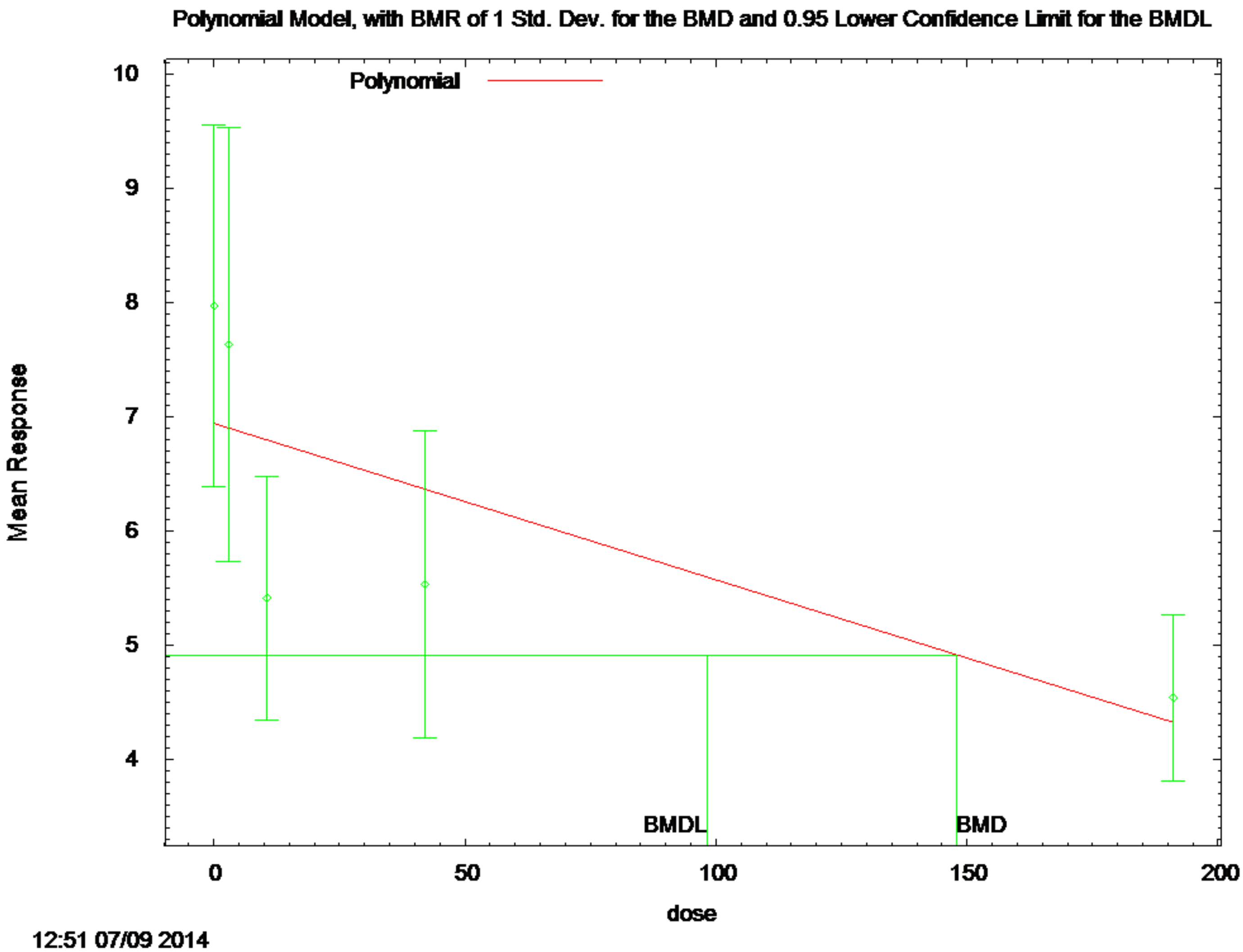
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 190.429

BMDL = 131.056


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
50
100
150
200
12:51 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:51:15 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =      8.18961
                         beta_1 =    -0.328545
                         beta_2 =            0
                         beta_3 = -3.14654e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.3e-008	-7.5e-008
beta_0	1.3e-008	1	-0.56
beta_1	-7.5e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	4.10152	0.83722	2.4606	5.74244
beta_0	6.93587	0.35384	6.24236	7.62939
beta_1	-0.0136993	0.00396554	-0.0214716	-0.00592698
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.21	2.03	1.61
2.9	10	7.63	6.9	2.65	2.03	1.15
10.6	9	5.41	6.79	1.39	2.03	-2.05
42	9	5.53	6.36	1.76	2.03	-1.23
191.1	10	4.54	4.32	1.02	2.03	

0.347

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-57.872613	3	121.745227
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	10.8824	3	0.01238

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

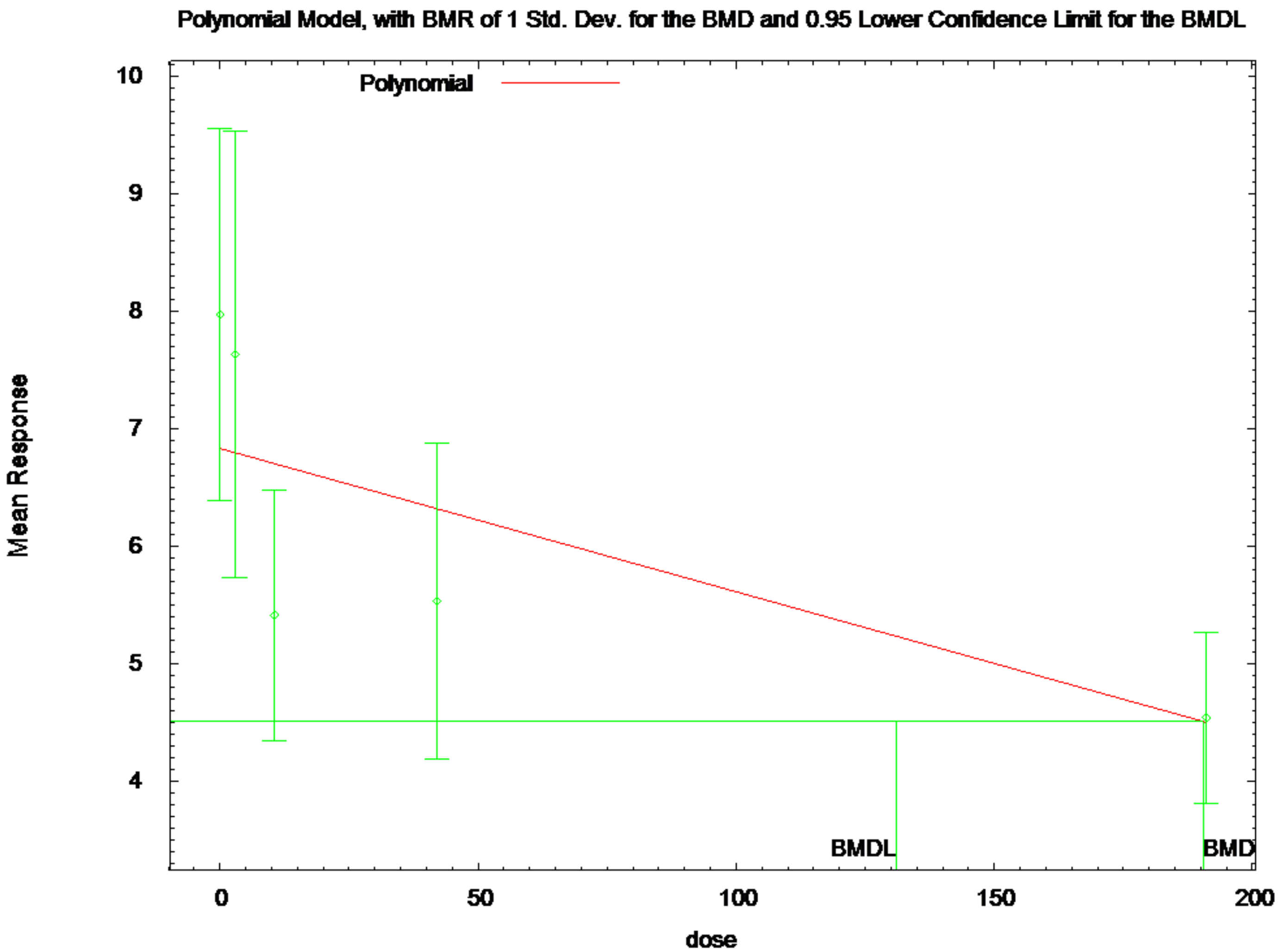
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 147.834

BMDL = 98.2036



12:51 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly3NCV-1SD-5d.plt
                                       Wed Jul 09 12:51:16 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      8.18961
                         beta_1 =    -0.328545
                         beta_2 =            0
                         beta_3 = -3.14654e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.059	-0.074
rho	-1	1	-0.059	0.075
beta_0	0.059	-0.059	1	-0.81
beta_1	-0.074	0.075	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.5162	2.25638	-10.9386	-2.09378
rho	4.27037	1.23797	1.84399	6.69675
beta_0	6.83277	0.388873	6.07059	7.59495
beta_1	-0.0122267	0.00266203	-0.0174442	-0.00700924
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.83	2.21	2.33	1.54
2.9	10	7.63	6.8	2.65	2.3	1.14
10.6	9	5.41	6.7	1.39	2.24	-1.74

42	9	5.53	6.32	1.76	1.97	-1.2
191.1	10	4.54	4.5	1.02	0.953	0.145

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-53.651165	4	115.302330
R	-63.201706	2	130.403412

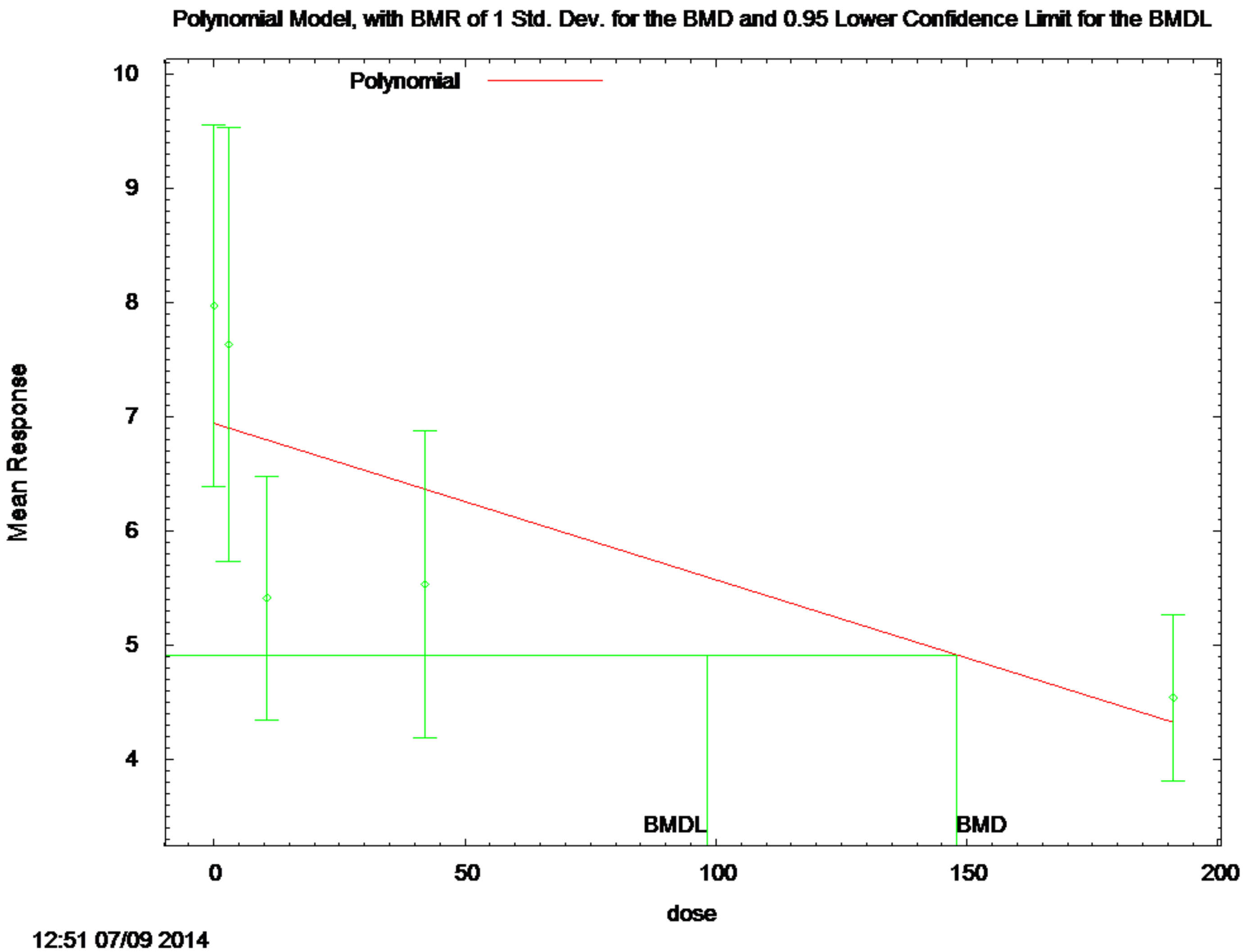
Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174

```
   Test 4              11.7848          3        0.008158

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance
appears
 to be appropriate here

The p-value for Test 4 is less than .1.  You may want to try a
different
model


             Benchmark Dose Computation

Specified effect =            1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =         0.95

             BMD =        190.429


            BMDL =        131.056
```



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:51 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly4CV-1SD-5d.plt
                                        Wed Jul 09 12:51:15 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =         7.97
                         beta_1 =   -0.0490906
                         beta_2 =   -0.0256112
                         beta_3 =            0
                         beta_4 = -3.15099e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.2e-008	1.8e-008
beta_0	-1.2e-008	1	-0.56
beta_1	1.8e-008	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	4.10153	0.83722	2.4606	5.74245
beta_0	6.93587	0.35384	6.24236	7.62939
beta_1	-0.0136993	0.00396554	-0.0214716	-0.00592698
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.21	2.03	1.61
2.9	10	7.63	6.9	2.65	2.03	1.15
10.6	9	5.41	6.79	1.39	2.03	-2.05
42	9	5.53	6.36	1.76	2.03	

-1.23
191.1 10 4.54 4.32 1.02 2.03
0.347

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-57.872613	3	121.745227
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	10.8824	3	0.01238

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

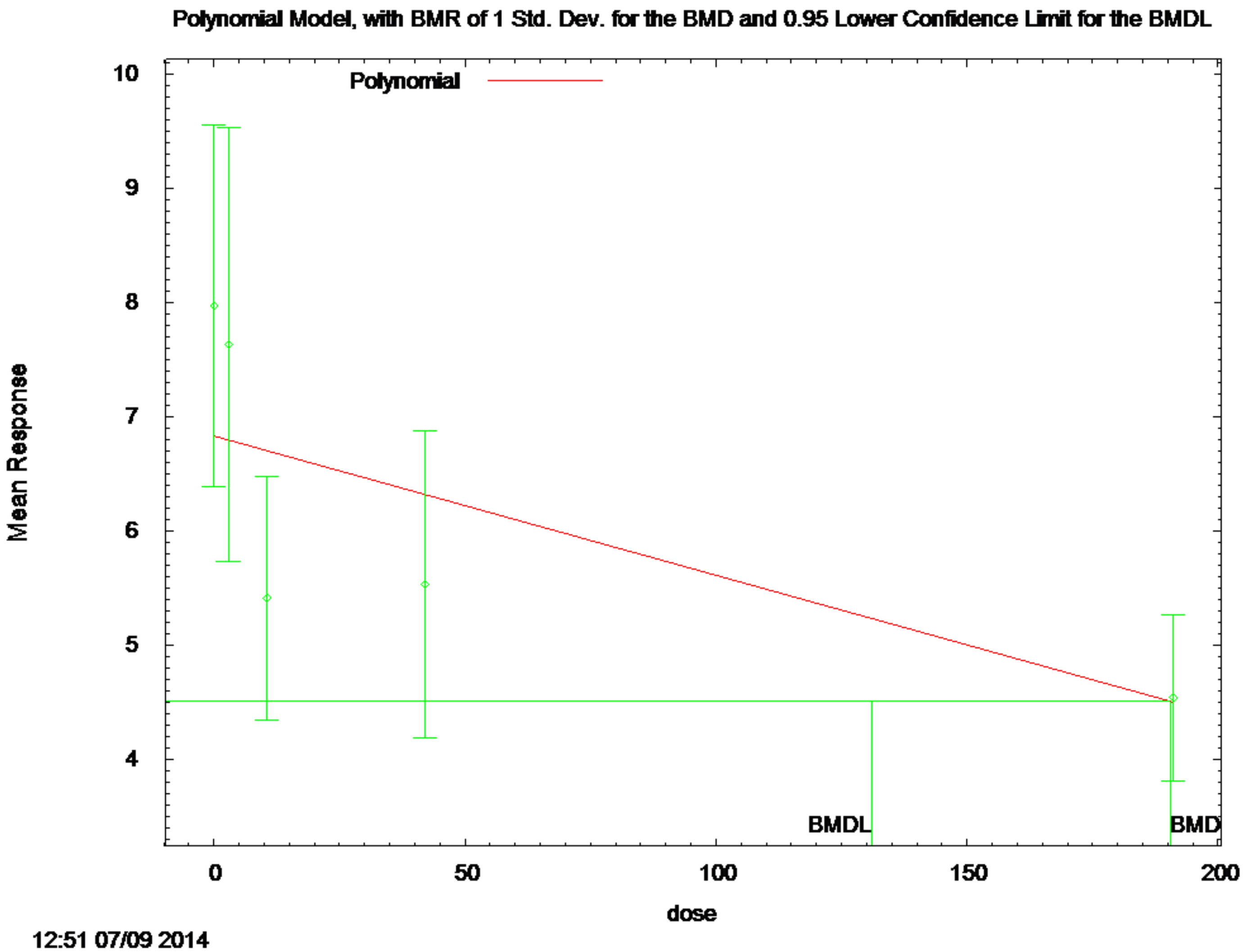
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 147.834

BMDL = 98.2036


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:51 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent/WBC_Concurrent-HLS
2001-White Blood Cell Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:51:16 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =         7.97
                         beta_1 =   -0.0490906
                         beta_2 =   -0.0256112
                         beta_3 =            0
                         beta_4 = -3.15099e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.059	-0.074
rho	-1	1	-0.059	0.075
beta_0	0.059	-0.059	1	-0.81
beta_1	-0.074	0.075	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.5162	2.25638	-10.9386	-2.09377
rho	4.27037	1.23797	1.84399	6.69675
beta_0	6.83277	0.388873	6.07059	7.59495
beta_1	-0.0122267	0.00266204	-0.0174442	-0.00700925
beta_2	0	NA		
beta_3	-2.01002e-197	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.83	2.21	2.33	1.54
2.9	10	7.63	6.8	2.65	2.3	

```
1.14
 10.6     9       5.41           6.7          1.39          2.24
-1.74
   42     9       5.53          6.32          1.76          1.97
-1.2
191.1    10       4.54           4.5          1.02         0.953
0.145



 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -52.431420           6     116.862840
             A2          -47.292184          10     114.584369
             A3          -47.758770           7     109.517540
         fitted          -53.651165           4     115.302330
              R          -63.201706           2     130.403412


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	11.7848	3	0.008158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

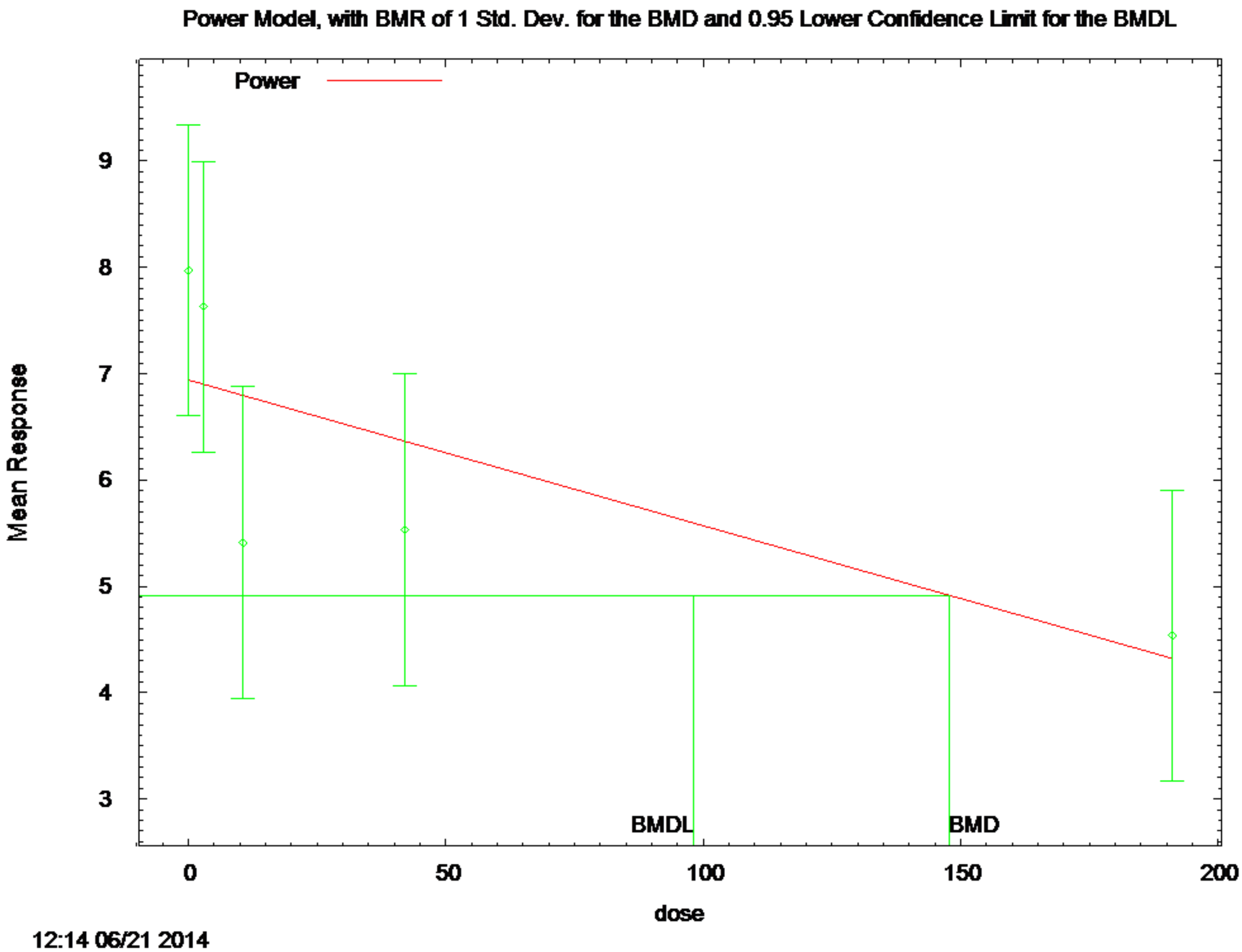
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 190.429

BMDL = 131.056


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:14 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.plt
                                      Sat Jun 21 12:14:46 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                        control =         4.54
                          slope =       3.7818
                          power =    -0.420444


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-2.7e-009	-1.7e-010
control	-2.7e-009	1	-0.56
slope	-1.7e-010	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	4.10153	0.83722	2.4606	5.74245
control	6.93587	0.35384	6.24236	7.62939
slope	-0.0136993	0.00396554	-0.0214716	-0.00592698
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.21	2.03	1.61
2.9	10	7.63	6.9	2.65	2.03	1.15
10.6	9	5.41	6.79	1.39	2.03	-2.05
42	9	5.53	6.36	1.76	2.03	-1.23
191.1	10	4.54	4.32	1.02	2.03	0.347

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-57.872613	3	121.745227
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	10.8824	3	0.01238

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

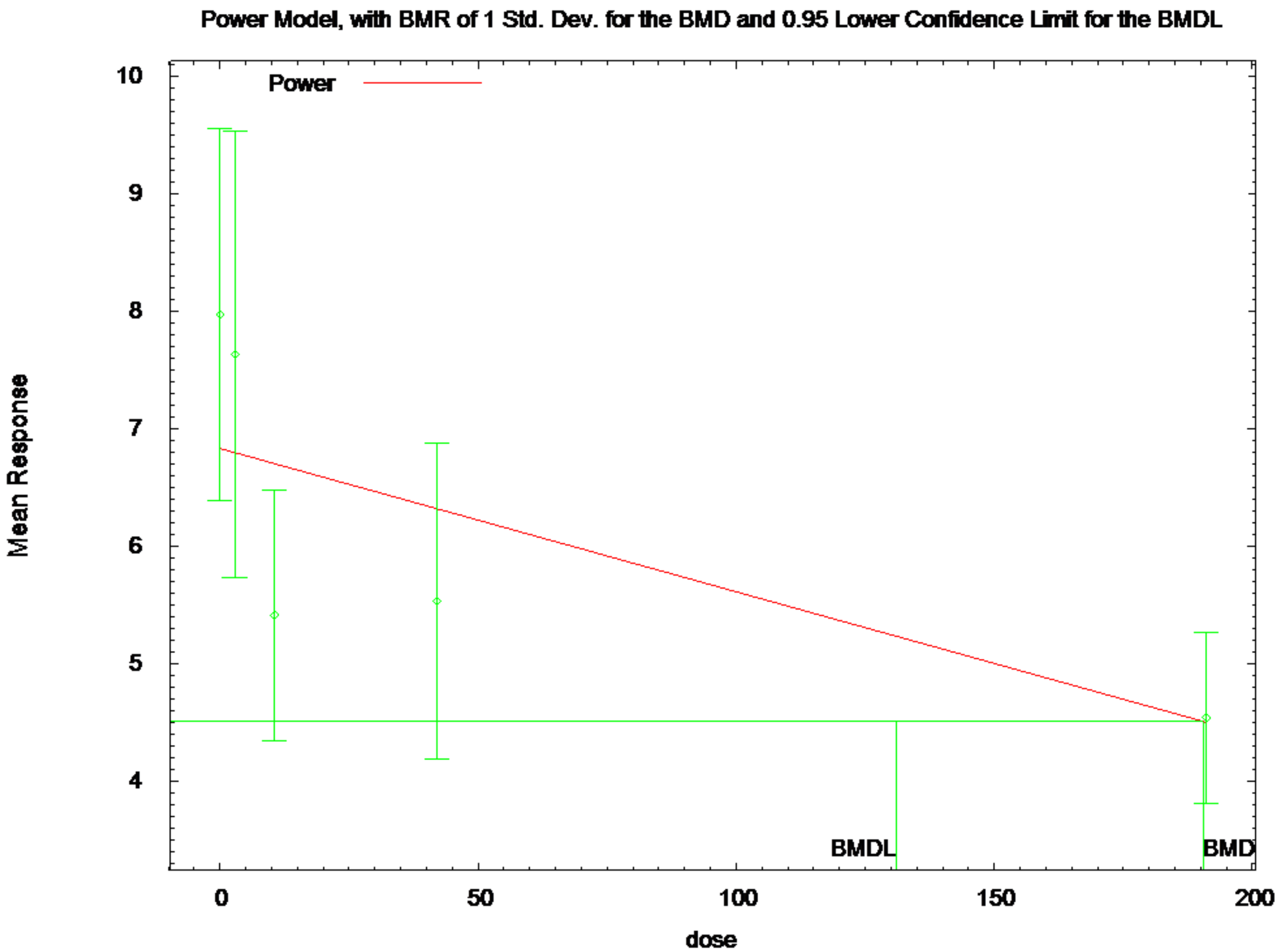
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 147.834

BMDL = 98.2036



12:14 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Concurrent-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.plt
                                      Sat Jun 21 12:14:47 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                        control =         4.54
                          slope =       3.7818
                          power =    -0.420444


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-1	0.39	-0.61
rho	-1	1	-0.45	0.64
control	0.39	-0.45	1	-0.81
slope	-0.61	0.64	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.5162	2.91702	-12.2334	-0.798956
rho	4.27037	1.62588	1.0837	7.45704
control	6.83277	0.390856	6.06671	7.59883
slope	-0.0122267	0.00266832	-0.0174565	-0.00699694
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.83	2.21	2.33	1.54
2.9	10	7.63	6.8	2.65	2.3	1.14
10.6	9	5.41	6.7	1.39	2.24	-1.74
42	9	5.53	6.32	1.76	1.97	-1.2

191.1   10   4.54   4.5   1.02   0.953
0.145

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-53.651165	4	115.302330
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	11.7848	3	0.008158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

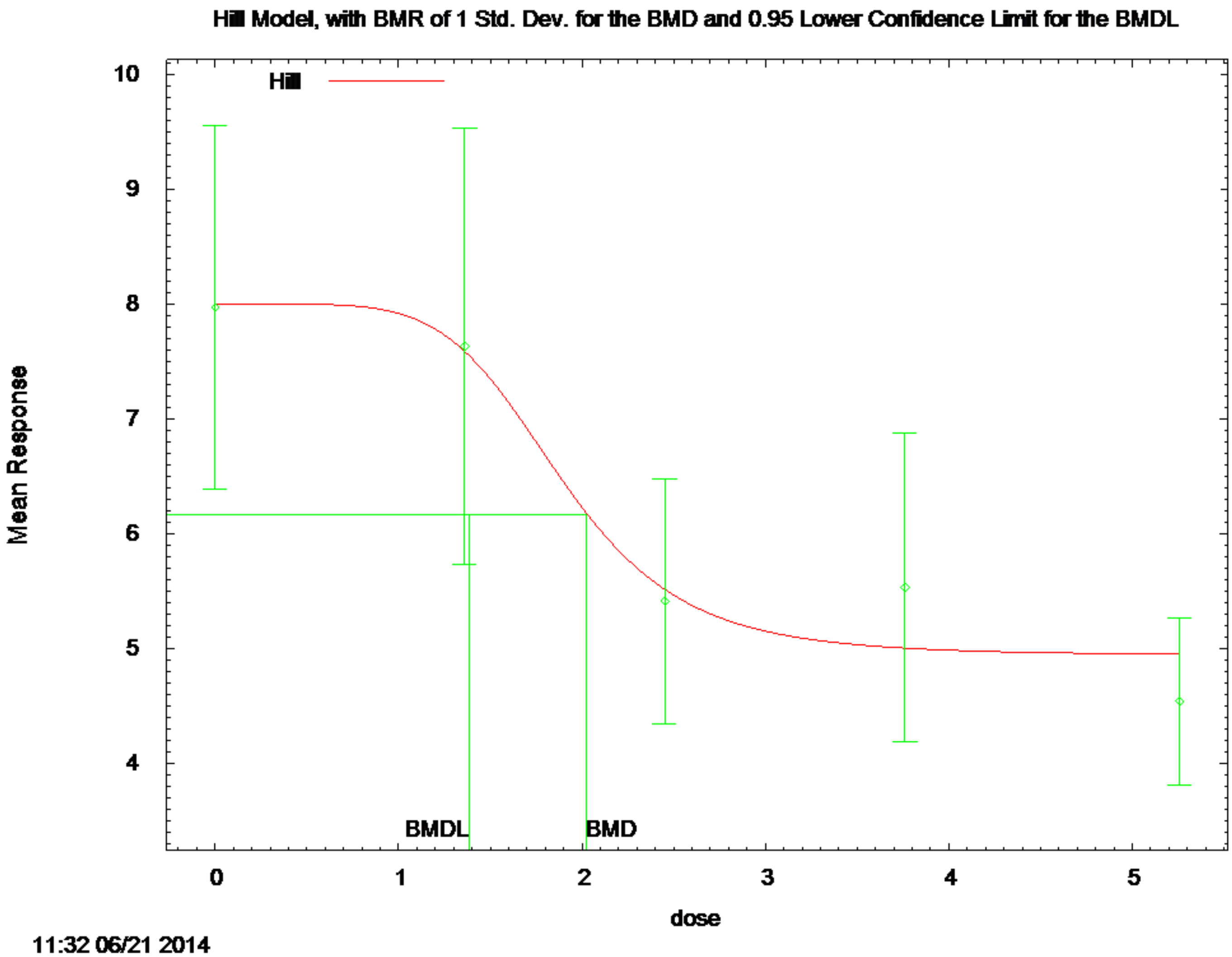
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 190.429

BMDL = 131.056

BMDS Model Results for White Blood Cell Count (Log-transformed Doses, Concurrent Controls)



Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Hill
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
11:32 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.plt
                                       Sat Jun 21 11:32:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                      intercept =         7.97
                              v =        -3.43
                              n =      4.25613
                              k =      2.03611


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-1.2e-009	-7.3e-009	2.5e-009	2.9e-009
intercept	-1.2e-009	1	-0.78	-0.46	-0.4
v	-7.3e-009	-0.78	1	0.68	-0.02
n	2.5e-009	-0.46	0.68	1	-0.1
k	2.9e-009	-0.4	-0.02	-0.1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.35938	0.68573	2.01537	4.70338
intercept	8.0005	0.570983	6.88139	9.1196
v	-3.06445	0.838523	-4.70792	-1.42097
n	5.65284	5.36582	-4.86398	16.1697
k	1.88908	0.444332	1.0182	2.75995

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	8	2.21	1.83	-0.0526

1.361	10	7.63	7.59	2.65	1.83	0.0771
2.451	9	5.41	5.51	1.39	1.83	-0.16
3.761	9	5.53	5	1.76	1.83	0.872
5.258	10	4.54	4.95	1.02	1.83	-0.699

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-53.082138	5	116.164276
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	1.30144	1	0.254

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

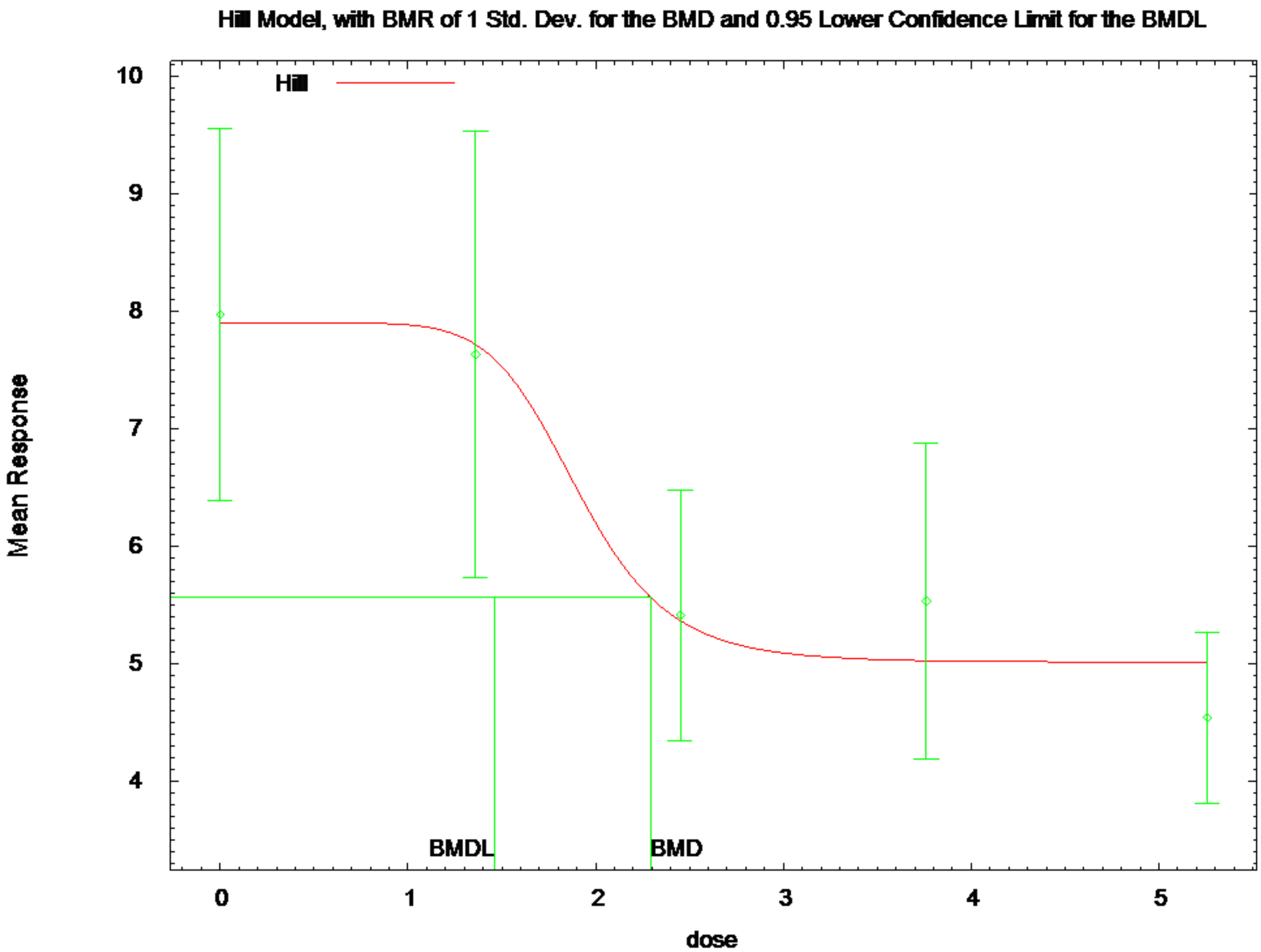
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.02672

BMDL = 1.38253



11:32 06/21 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.plt
                                        Sat Jun 21 11:32:13 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                      intercept =         7.97
                              v =        -3.43
                              n =      4.25613
                              k =      2.03611


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.29	-0.36	-0.12	-0.041
rho	-0.99	1	-0.32	0.37	0.12	0.041
intercept	0.29	-0.32	1	-0.92	-0.61	-0.57
v	-0.36	0.37	-0.92	1	0.71	0.47
n	-0.12	0.12	-0.61	0.71	1	0.61
k	-0.041	0.041	-0.57	0.47	0.61	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.17799	1.97663	-7.05212	0.696131
rho	2.35847	1.08644	0.229084	4.48786
intercept	7.90015	0.704723	6.51891	9.28138
v	-2.88616	0.877394	-4.60582	-1.1665
n	7.90728	11.0414	-13.7334	29.548
k	1.91117	0.488665	0.953404	2.86894

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.9	2.21	2.34	0.0946

```
1.361    10       7.63         7.72         2.65         2.27
-0.119
2.451     9       5.41         5.37         1.39         1.48
0.0849
3.761     9       5.53         5.03         1.76         1.37
1.1
5.258    10       4.54         5.01         1.02         1.37
-1.1
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-50.185289	6	112.370578
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	4.85304	1	0.0276

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

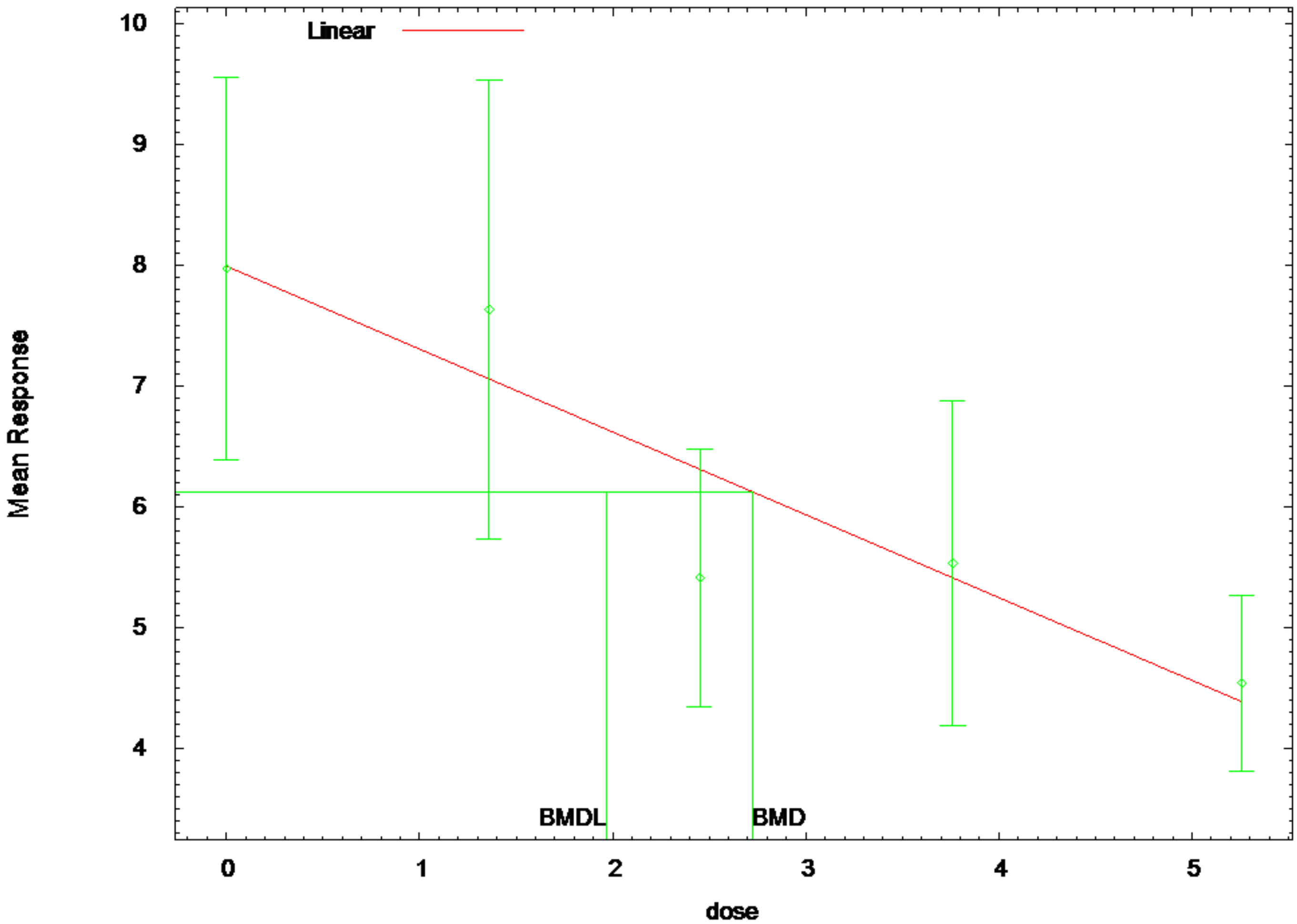
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.29451

BMDL = 1.4635

Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:43:41 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =      7.97189
                         beta_1 =    -0.684236


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.6e-007	-9.6e-008
beta_0	-1.6e-007	1	-0.81
beta_1	-9.6e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.49739	0.713902	2.09817	4.89662
beta_0	7.9913	0.457566	7.09448	8.88811
beta_1	-0.685697	0.145247	-0.970375	-0.401018

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.21	1.87	-0.036
1.361	10	7.63	7.06	2.65	1.87	0.967
2.451	9	5.41	6.31	1.39	1.87	-1.44
3.761	9	5.53	5.41	1.76	1.87	0.189
5.258	10	4.54	4.39	1.02	1.87	0.261

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-54.048454	3	114.096907
R	-63.201706	2	130.403412

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	3.23407	3	0.3569

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a

different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

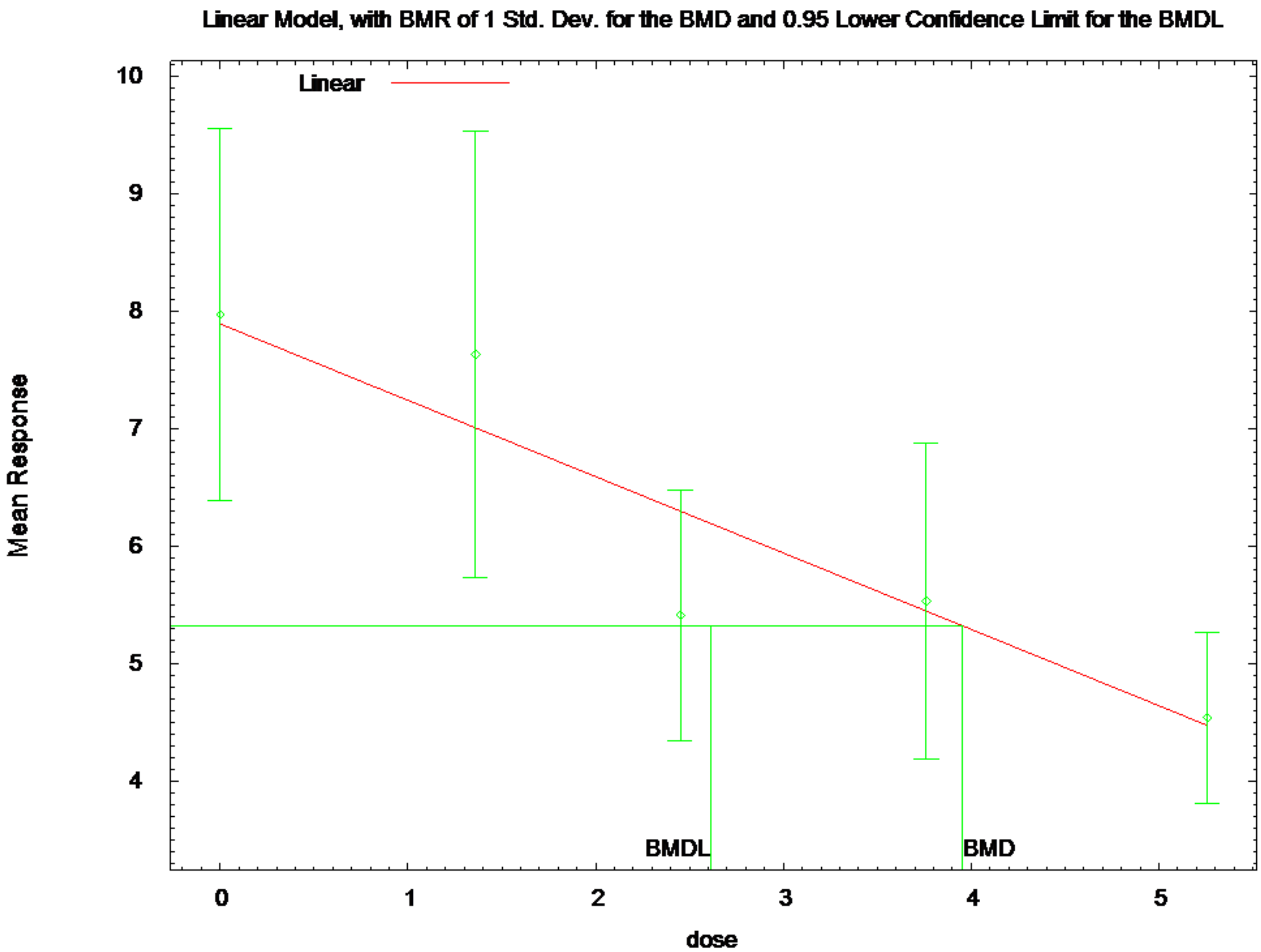
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.72735

BMDL = 1.96547



12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:43:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      7.97189
                         beta_1 =    -0.684236


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99         0.15        -0.18
```

rho	-0.99	1	-0.15	0.18
beta_0	0.15	-0.15	1	-0.91
beta_1	-0.18	0.18	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.45485	2.03072	-8.43498	-0.474715
rho	3.07104	1.1156	0.884506	5.25758
beta_0	7.88794	0.536104	6.83719	8.93868
beta_1	-0.649741	0.131724	-0.907915	-0.391568

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.89	2.21	2.57	0.101
1.361	10	7.63	7	2.65	2.14	0.925
2.451	9	5.41	6.3	1.39	1.82	-1.46
3.761	9	5.53	5.44	1.76	1.45	0.177
5.258	10	4.54	4.47	1.02	1.08	0.201

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-50.527570	4	109.055140
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	5.5376	3	0.1364

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears

to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

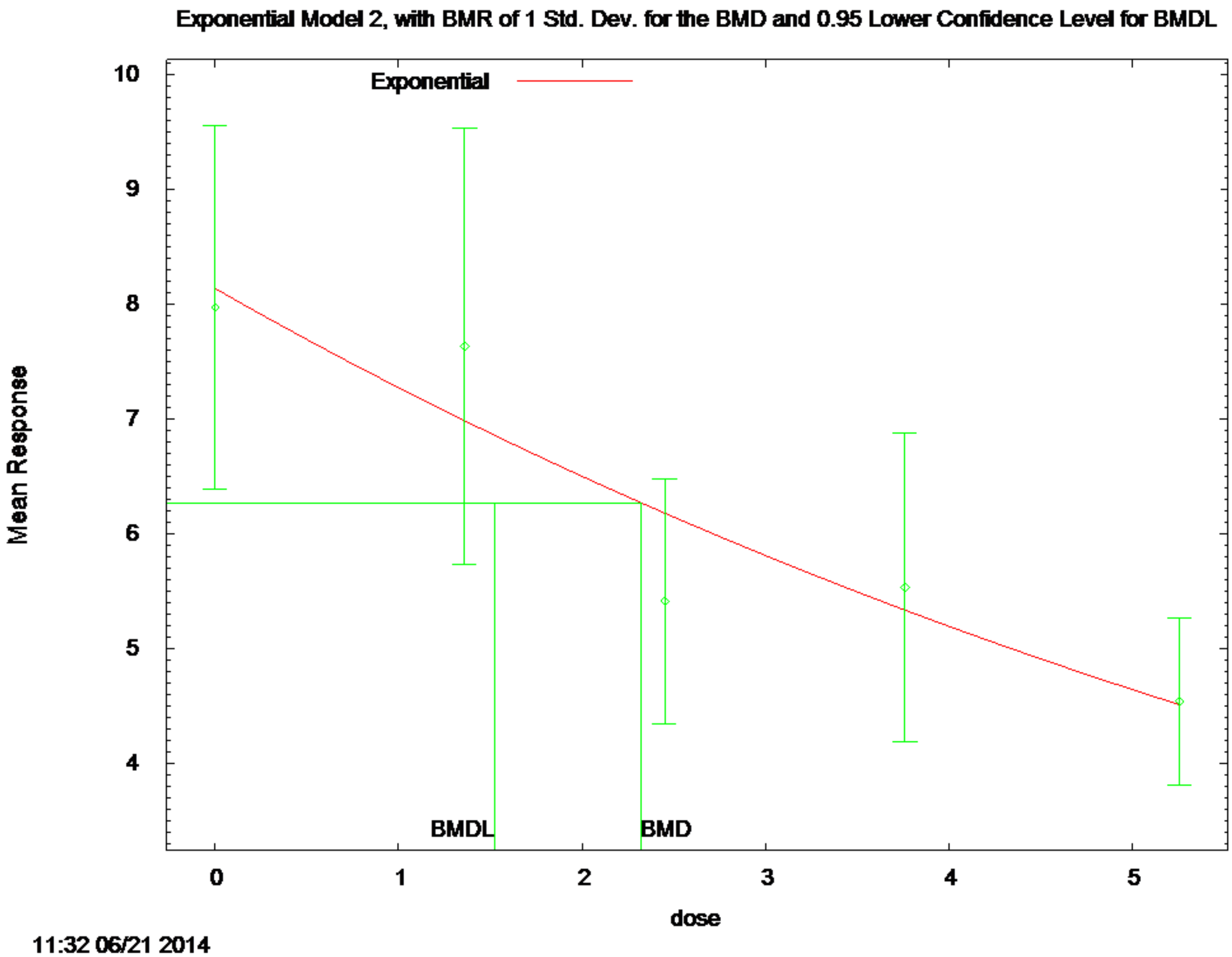
Specified effect =   1

Risk Type   =   Estimated standard deviations from the control mean

Confidence level =   0.95

BMD =   3.95557

BMDL =   2.61437


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
11:32 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 11:32:11 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.18464
rho(S)	0
a	4.59625
b	0.111233
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.24723
rho	0
a	8.1349
b	0.112266
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.135	1.866	-0.2795
1.361	6.982	1.866	1.098
2.451	6.178	1.866	-1.235
3.761	5.333	1.866	0.3166
5.258	4.508	1.866	0.05411

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
2	-53.93348	3	113.867

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	

0.0001004
Test 2 10.28 4
0.03599
Test 3 10.28 4
0.03599
Test 4 3.004 3
0.391

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

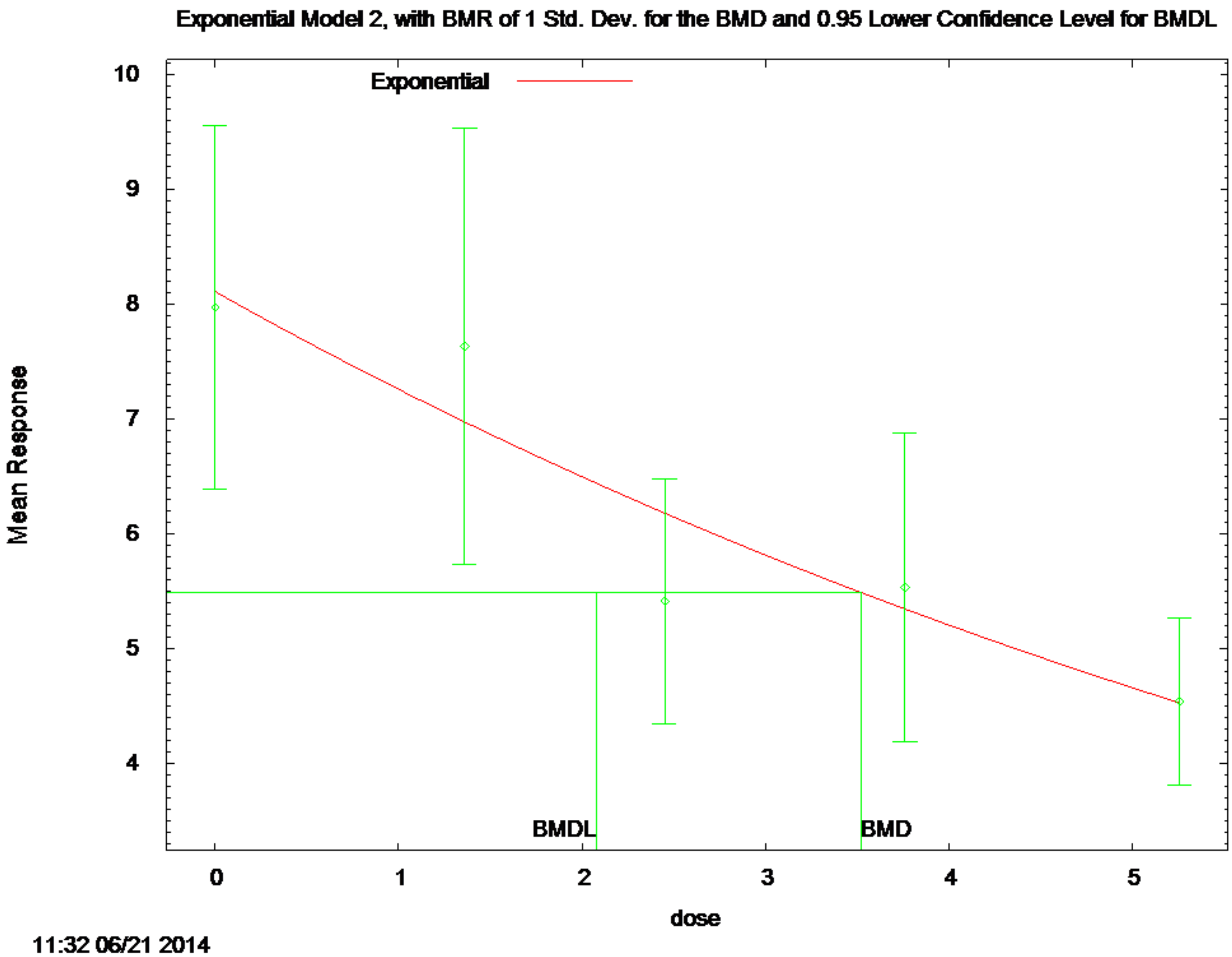
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.32046

BMDL = 1.52174


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
11:32 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 11:32:13 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-4.23146
rho	2.9407
a	4.59625
b	0.111233
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-4.1642
rho	2.91163
a	8.10768
b	0.110918
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.108	2.624	-0.1659
1.361	6.972	2.106	0.9884
2.451	6.178	1.766	-1.304
3.761	5.342	1.43	0.394
5.258	4.525	1.123	0.0424

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
2	-50.58738	4	109.1748

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

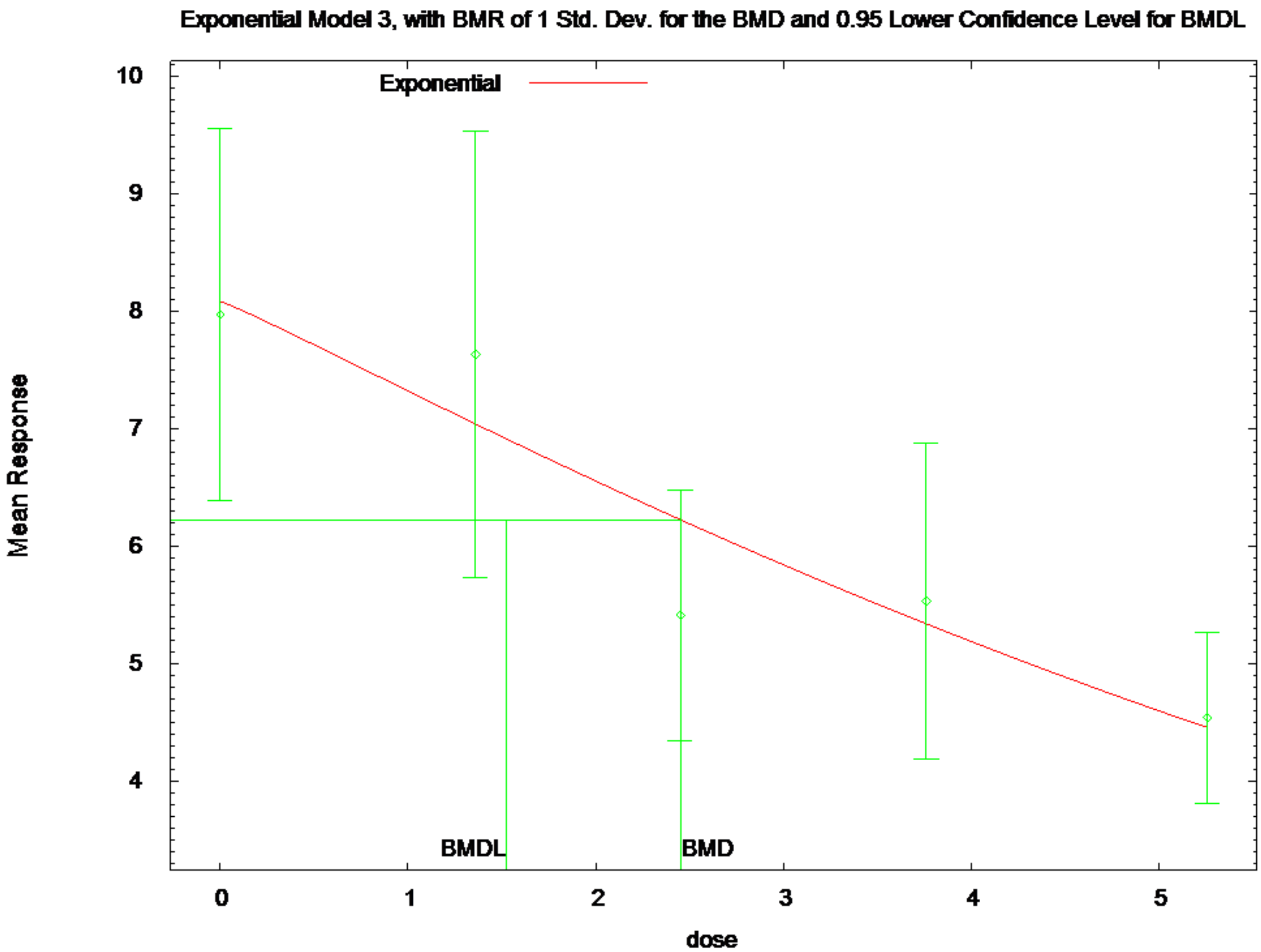
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004
Test 2	10.28	4	

```
0.03599
     Test 3                         0.9332           3
0.8174
     Test 4                          5.657           3
0.1295


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 4 is greater than .1.  Model 2 seems
     to adequately describe the data.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      3.52524

                 BMDL =      2.07864
```



11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 11:32:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.18464
rho(S)	0
a	4.59625
b	0.111233
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.24644
rho	0
a	8.0841
b	0.117784
c	0
d	1.07945

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.084	1.865	-0.1935
1.361	7.038	1.865	1.004
2.451	6.224	1.865	-1.309
3.761	5.337	1.865	0.3105
5.258	4.454	1.865	0.1464

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
3	-53.91457	4	115.8291

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 5a	2.966	2	0.2269

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

Specified Effect = 1.000000

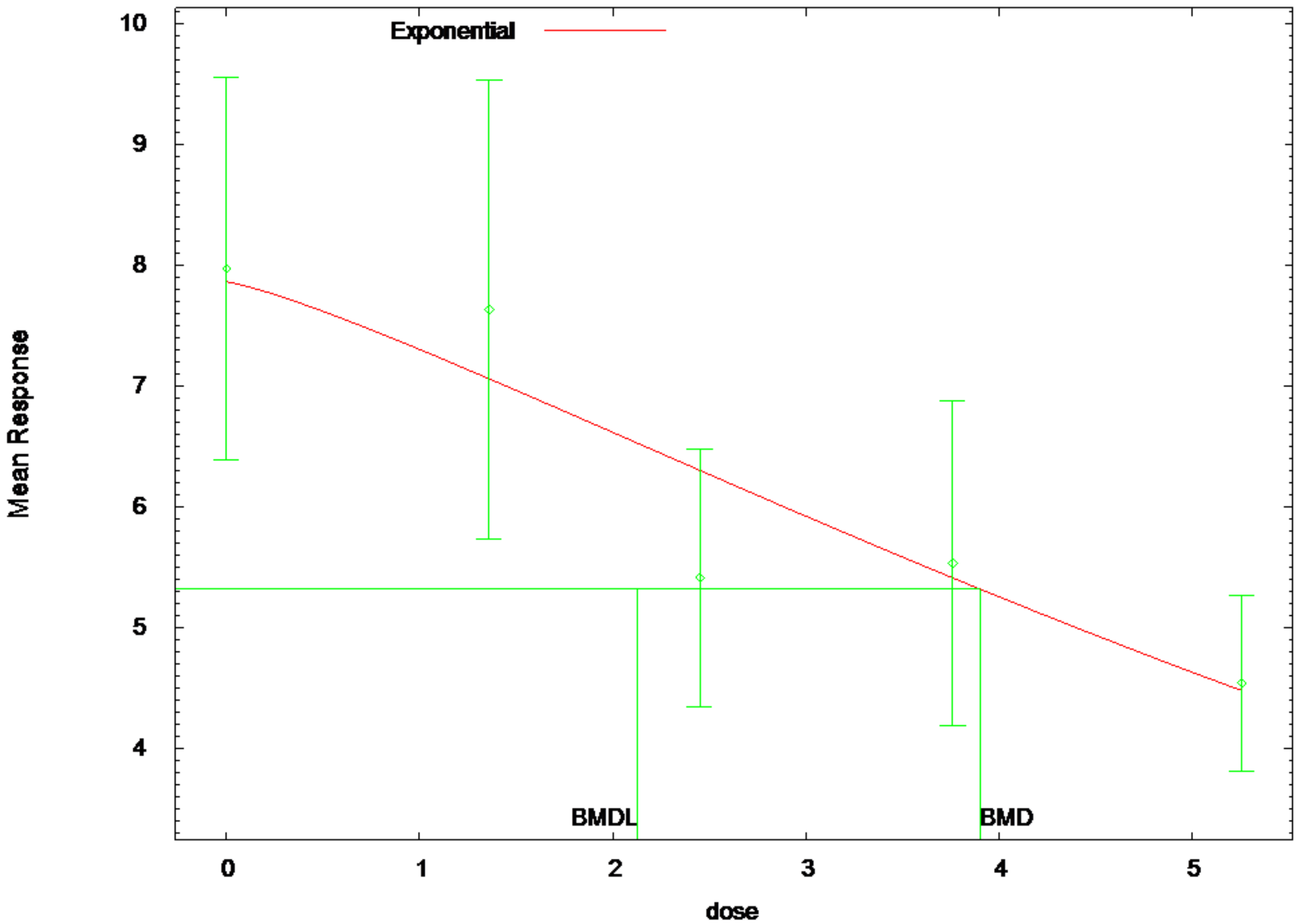
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.45714

BMDL = 1.52567

Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 11:32:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-4.23146
rho	2.9407
a	4.59625
b	0.111233
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-4.4078
rho	3.04324
a	7.86137
b	0.118958
c	0
d	1.22317

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.861	2.544	0.135
1.361	7.058	2.159	0.8383
2.451	6.3	1.816	-1.47
3.761	5.409	1.44	0.252
5.258	4.476	1.079	0.1883

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
3	-50.44861	5	110.8972

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

Test 2	10.28	4	0.03599
Test 3	0.9332	3	0.8174
Test 5a	5.38	2	0.06789

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

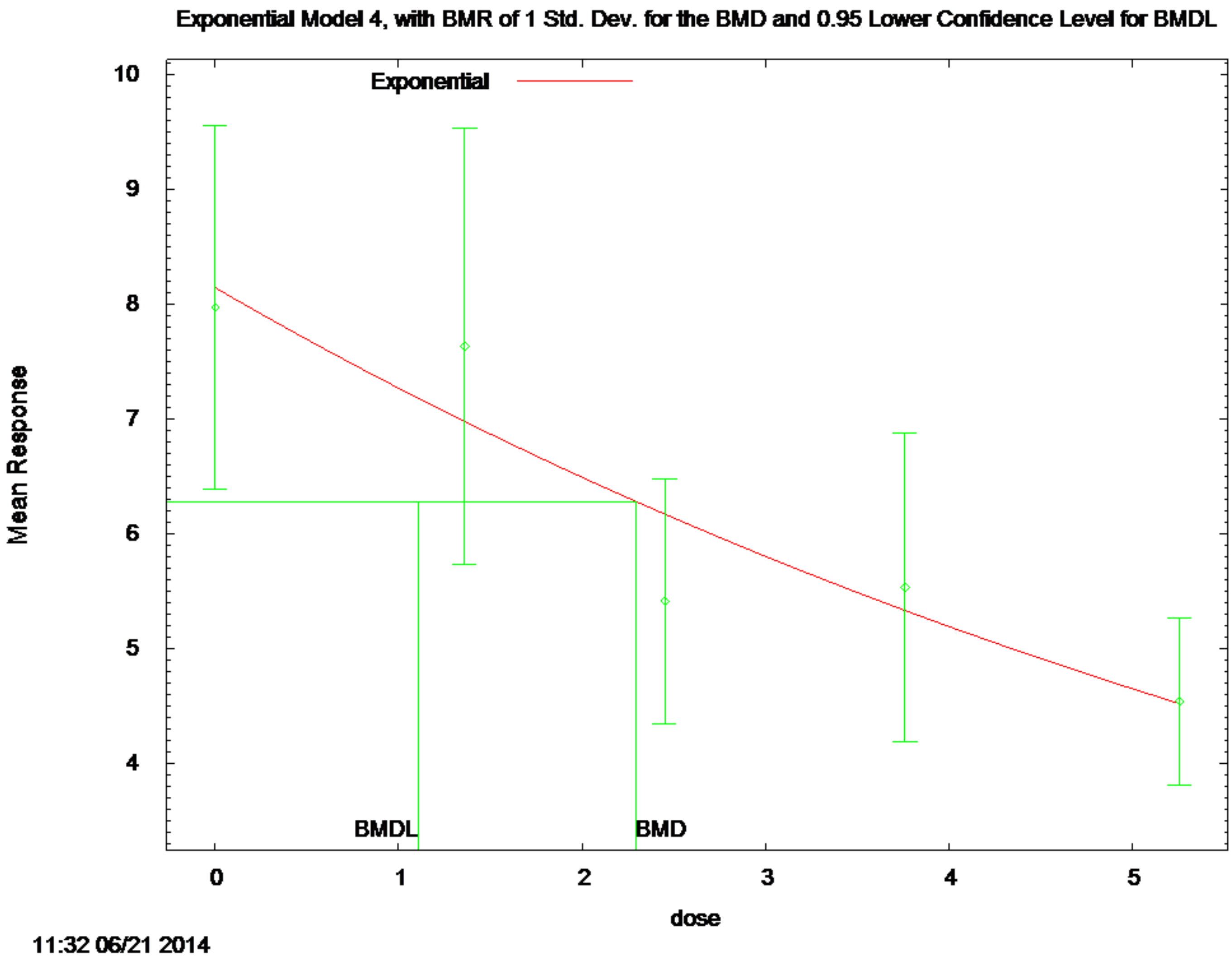
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.90052

BMDL = 2.1309


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                    Sat Jun 21 11:32:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.18464
rho(S)	0
a	8.3685
b	0.188405
c	0.271255
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.24721
rho	0
a	8.14254
b	0.119801
c	0.0476533
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.143	1.866	-0.2925
1.361	6.976	1.866	1.109
2.451	6.169	1.866	-1.221
3.761	5.33	1.866	0.3221
5.258	4.518	1.866	0.03665

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
4	-53.93301	4	115.866

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 6a	3.003	2	0.2228

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

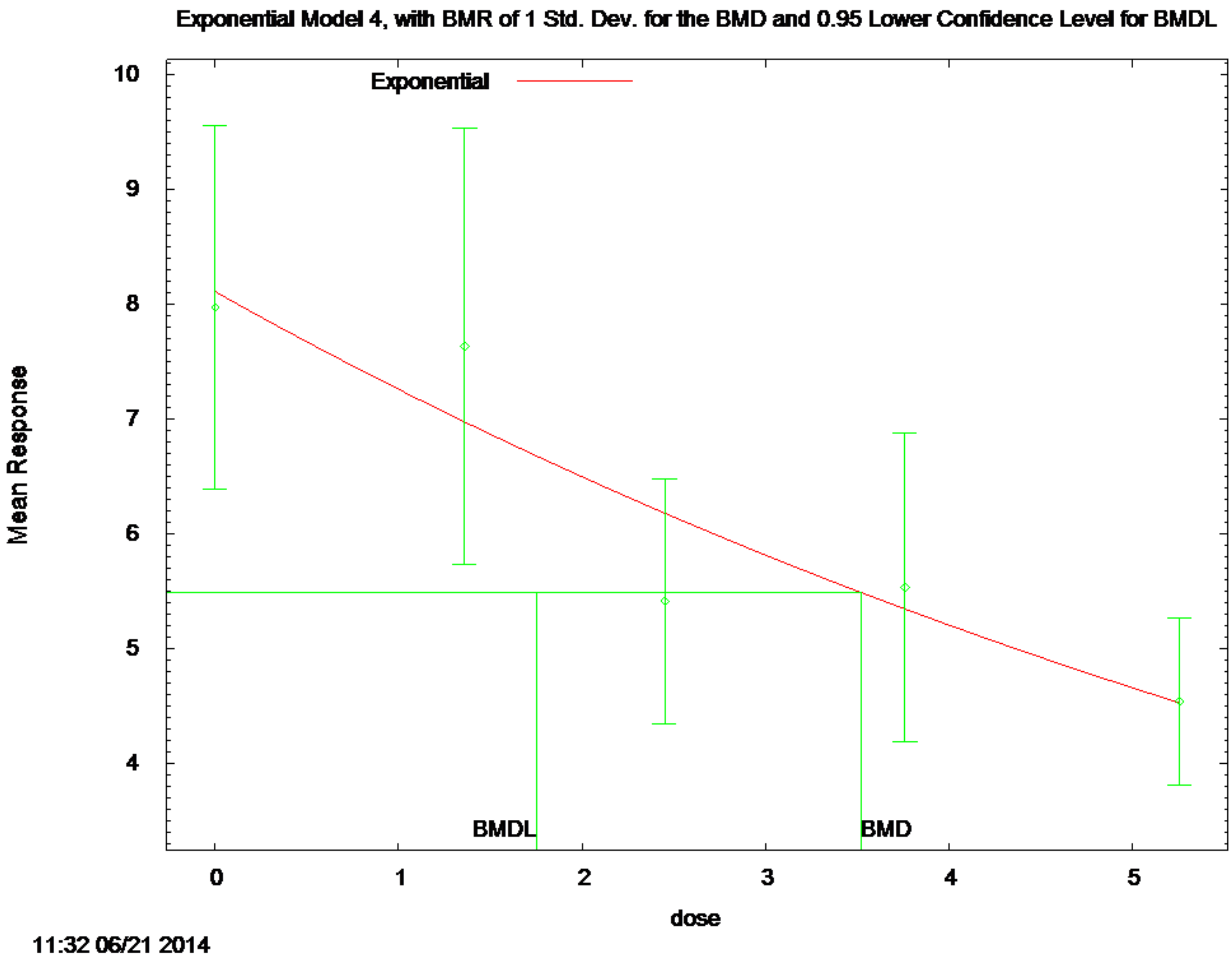
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.29723

BMDL = 1.10573


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
0
1
2
3
4
5
4
5
6
7
8
9
10
11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 11:32:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-4.23146
rho	2.9407
a	8.3685
b	0.12945
c	0.0542511
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-4.1642
rho	2.91163
a	8.10768
b	0.110918
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.108	2.624	-0.1659
1.361	6.972	2.106	0.9884
2.451	6.178	1.766	-1.304
3.761	5.342	1.43	0.394
5.258	4.525	1.123	0.04241

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
4	-50.58738	4	109.1748

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

Test 2	10.28	4	0.03599
Test 3	0.9332	3	0.8174
Test 6a	5.657	3	0.1295

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

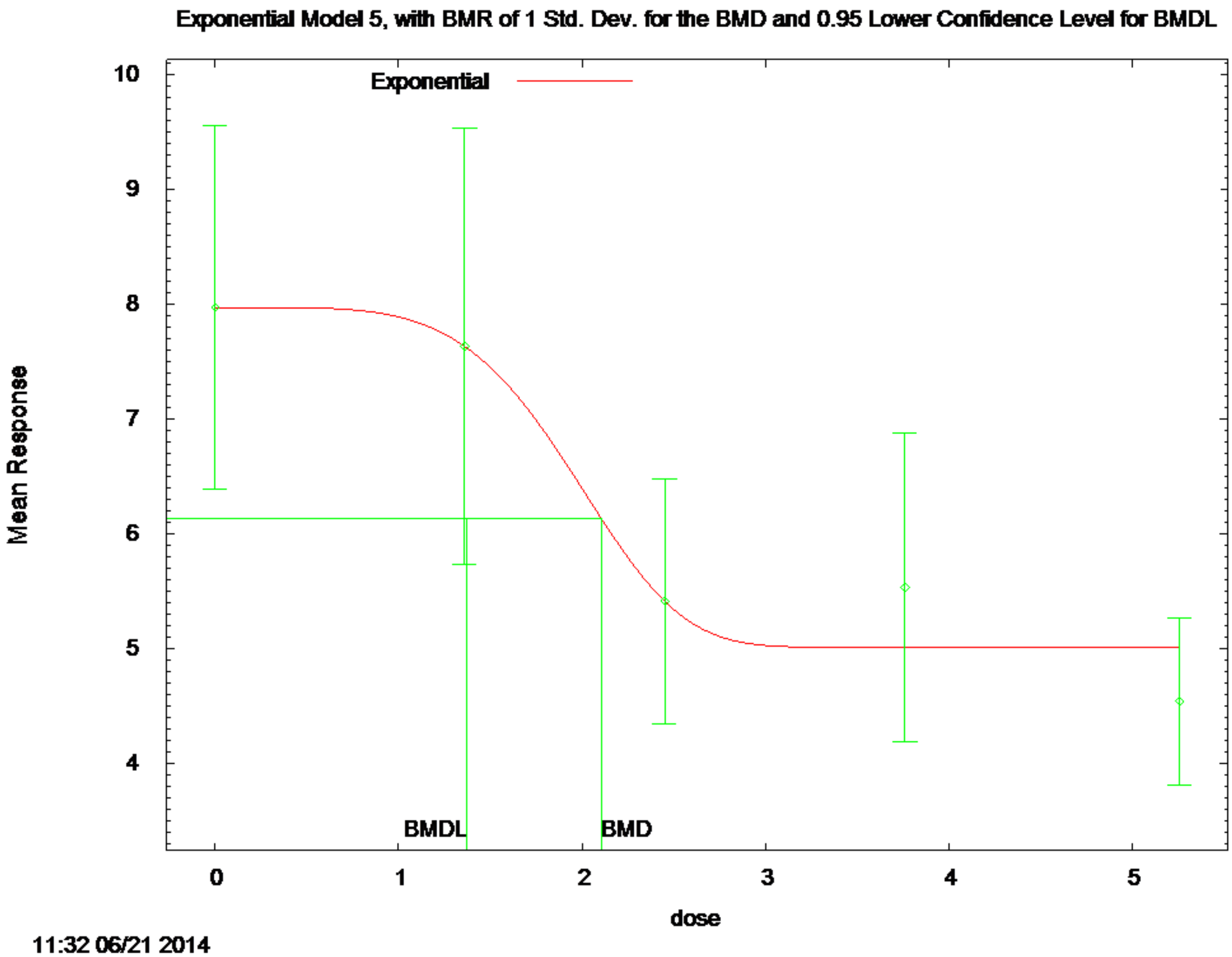
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.52524

BMDL = 1.74989



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 11:32:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.18464
rho(S)	0
a	8.3685
b	0.188405
c	0.271255
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.2138
rho	0
a	7.97001
b	0.471998
c	0.628474
d	4.754

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.97	1.835	-1.442e-005
1.361	7.63	1.835	1.875e-005
2.451	5.41	1.835	-1.872e-005
3.761	5.009	1.835	0.852
5.258	5.009	1.835	-0.8083

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-52.43142	6	116.8628
R	-63.20171	2	130.4034
5	-53.1311	5	116.2622

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.82	8	0.0001004
Test 2	10.28	4	0.03599
Test 3	10.28	4	0.03599
Test 7a	1.399	1	0.2368

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

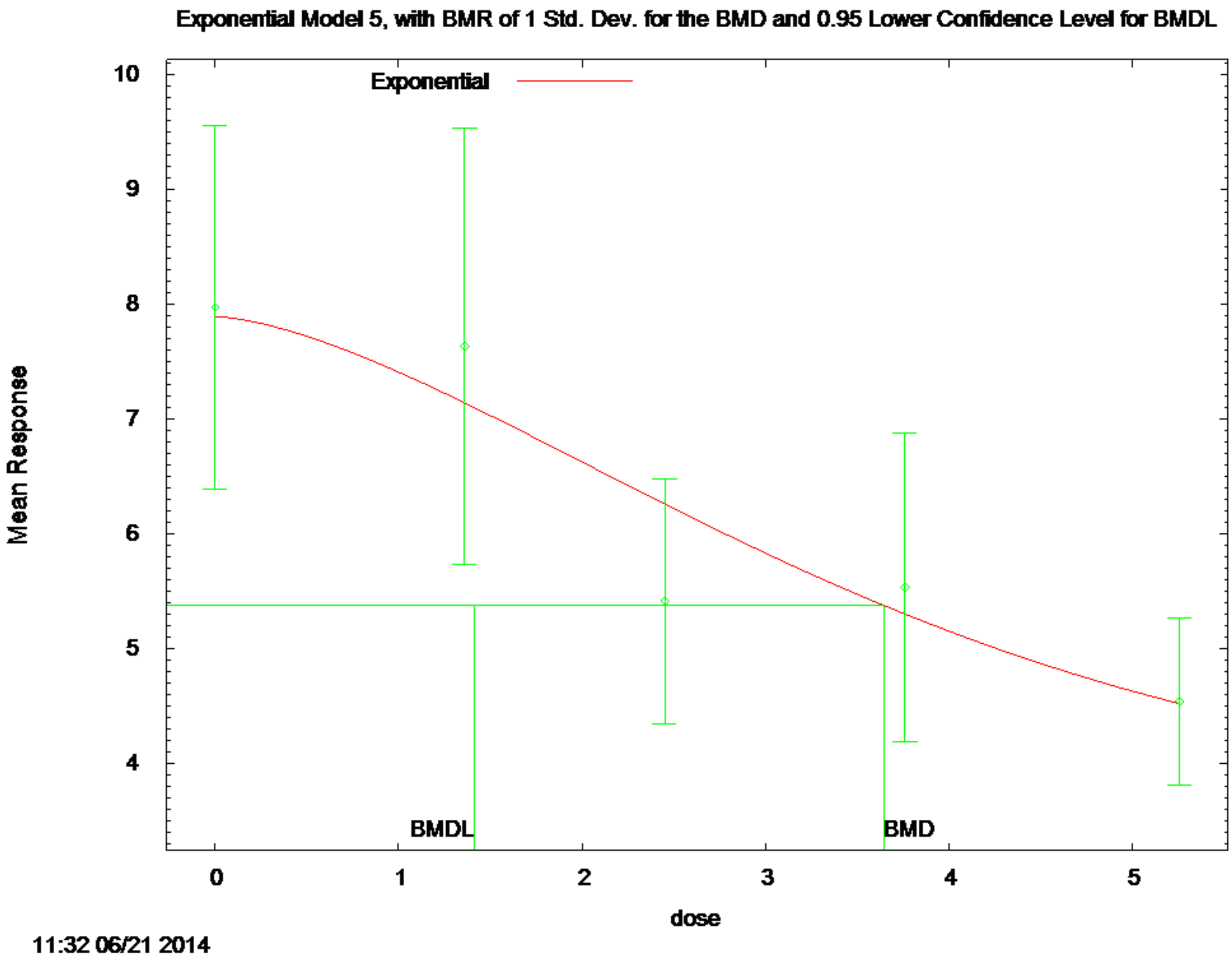
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.10356

BMDL = 1.37489



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
11:32 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 11:32:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-4.23146
rho	2.9407
a	8.3685
b	0.12945
c	0.0542511
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-4.19069
rho	2.92196
a	7.88959
b	0.256919
c	0.46383
d	1.55237

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.213
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.89	2.515	0.1011
1.361	7.138	2.173	0.7164
2.451	6.257	1.792	-1.417
3.761	5.298	1.406	0.4941
5.258	4.518	1.114	0.06318

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-52.43142	6	116.8628
A2	-47.29218	10	114.5844
A3	-47.75877	7	109.5175
R	-63.20171	2	130.4034
5	-50.38152	6	112.763

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.82	8	0.0001004

Test 2	10.28	4	0.03599
Test 3	0.9332	3	0.8174
Test 7a	5.245	1	0.022

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

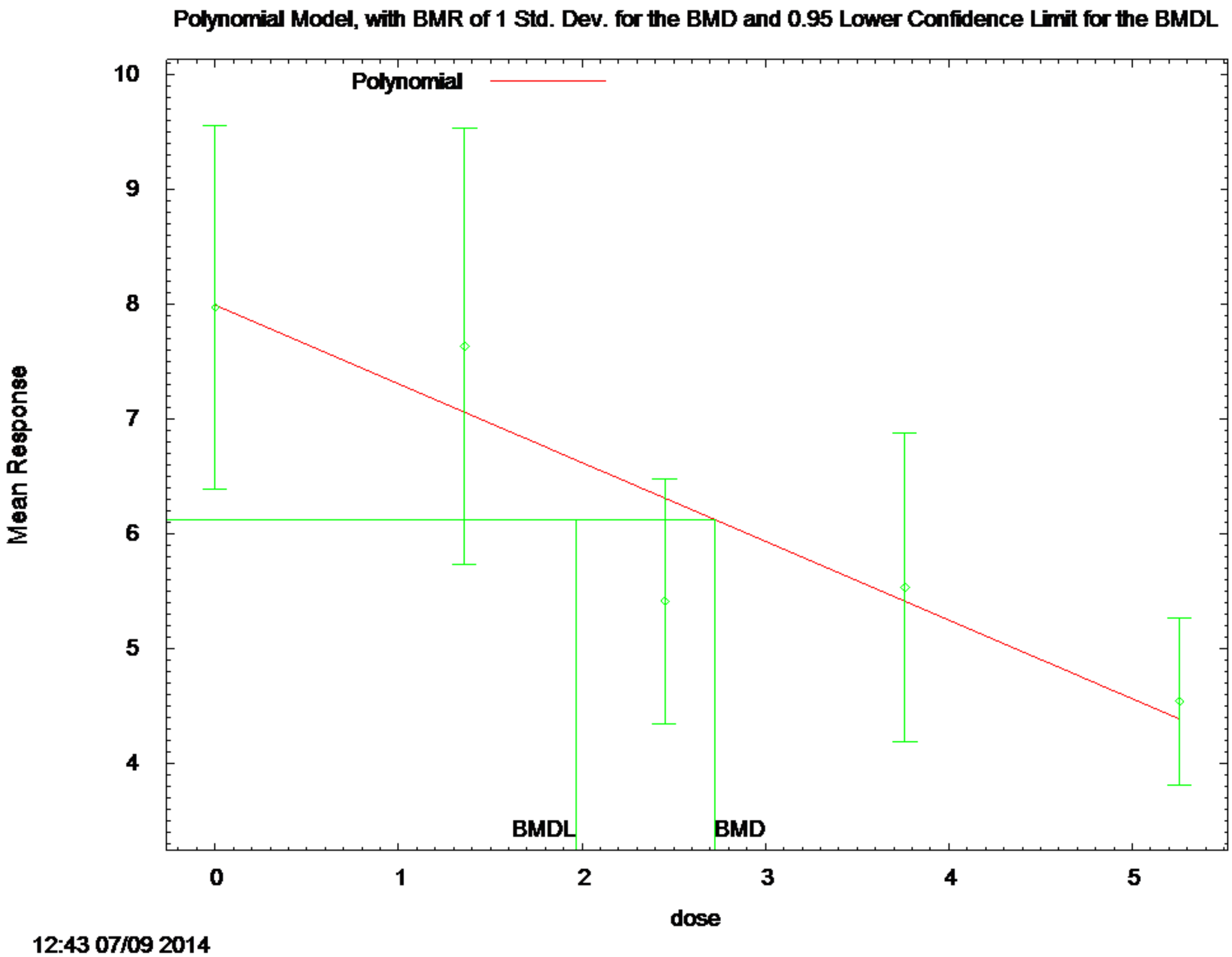
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.64435

BMDL = 1.41031


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:43:41 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =      8.15662
                         beta_1 =    -0.952983
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.8e-008	6.2e-009
beta_0	-1.8e-008	1	-0.81
beta_1	6.2e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.4974	0.713903	2.09817	4.89662
beta_0	7.9913	0.457567	7.09448	8.88811
beta_1	-0.685697	0.145247	-0.970375	-0.401018
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.21	1.87	-0.036
1.361	10	7.63	7.06	2.65	1.87	0.967
2.451	9	5.41	6.31	1.39	1.87	-1.44
3.761	9	5.53	5.41	1.76	1.87	0.189
5.258	10	4.54	4.39	1.02	1.87	0.261

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-54.048454	3	114.096907
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	3.23407	3	0.3569

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

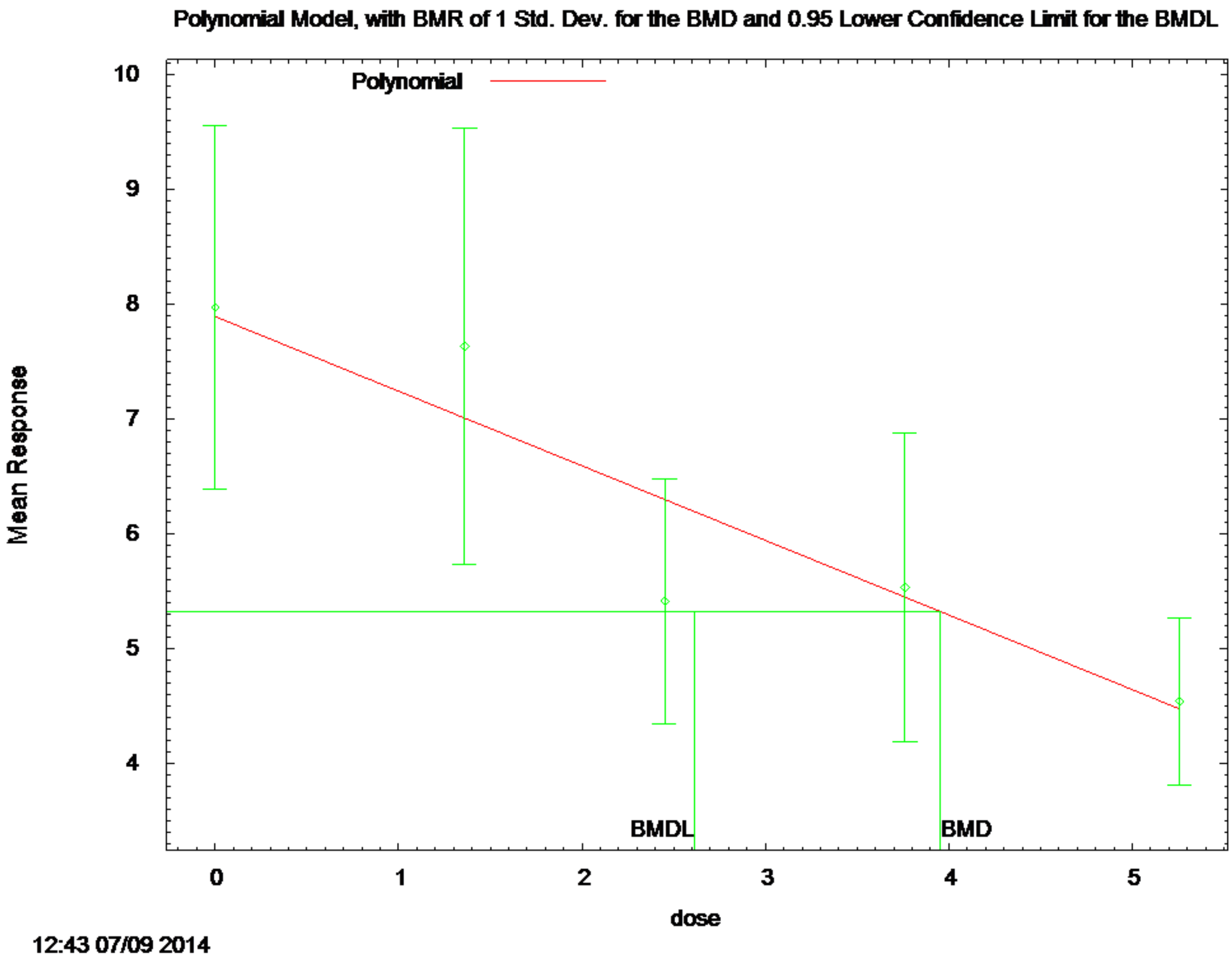
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.72735

BMDL = 1.96547



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:43:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      8.15662
                         beta_1 =    -0.952983
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.15	-0.18
rho	-0.99	1	-0.15	0.18
beta_0	0.15	-0.15	1	-0.91
beta_1	-0.18	0.18	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.45485	2.03072	-8.43498	-0.474714
rho	3.07104	1.1156	0.884506	5.25758
beta_0	7.88794	0.536104	6.83719	8.93868
beta_1	-0.649741	0.131724	-0.907915	-0.391568
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.89	2.21	2.57	0.101
1.361	10	7.63	7	2.65	2.14	0.925
2.451	9	5.41	6.3	1.39	1.82	-1.46
3.761	9	5.53	5.44	1.76	1.45	0.177

5.258   10   4.54   4.47   1.02   1.08
0.201

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-50.527570	4	109.055140
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	5.5376	3	0.1364

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

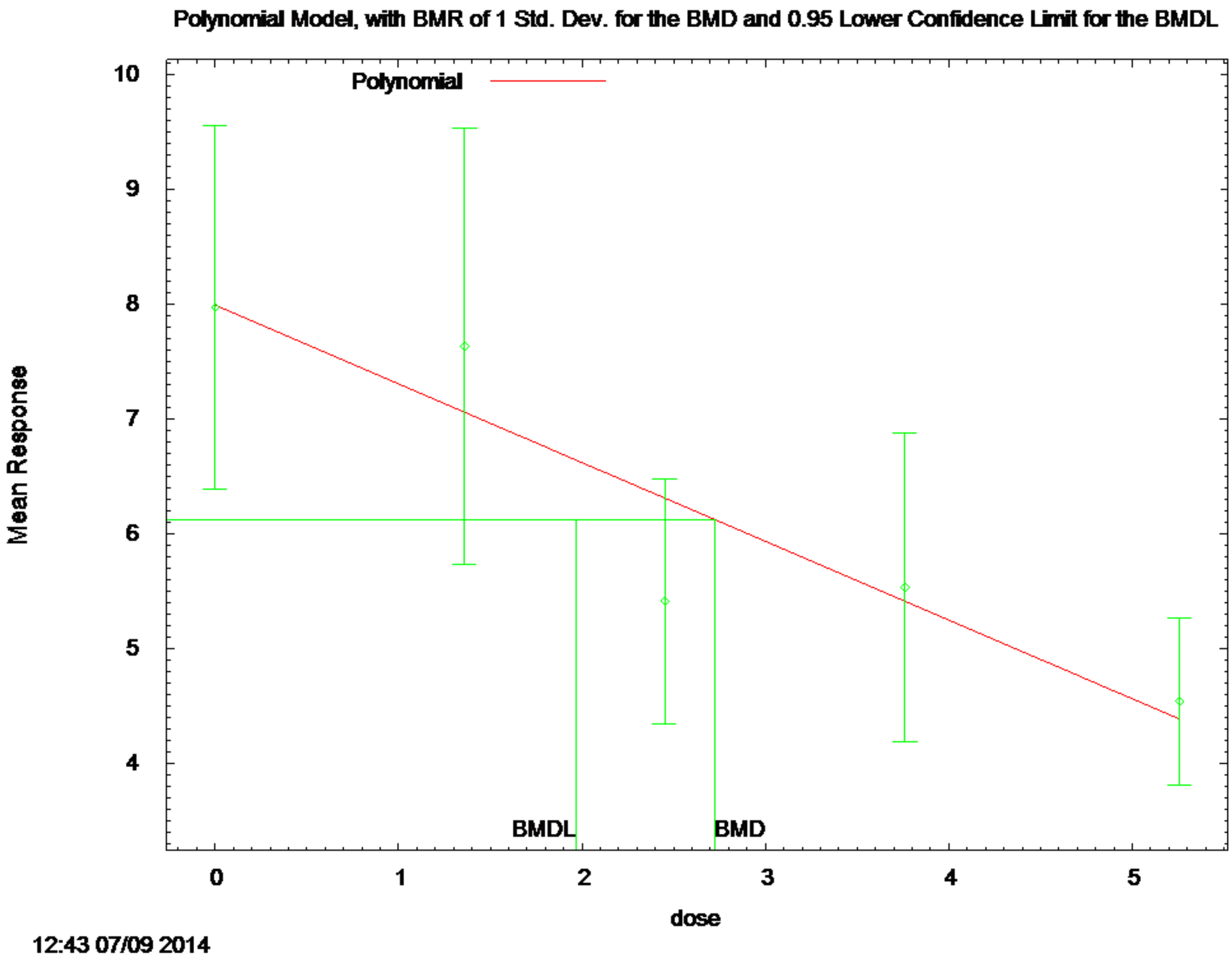
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.95557

BMDL = 2.61437


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:43 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly3CV-1SD-5d.plt
                                       Wed Jul 09 12:43:40 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =      8.07952
                         beta_1 =    -0.517572
                         beta_2 =    -0.184335
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-6.3e-008	4.1e-009
beta_0	-6.3e-008	1	-0.81
beta_1	4.1e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.4974	0.713903	2.09817	4.89662
beta_0	7.9913	0.457567	7.09448	8.88811
beta_1	-0.685697	0.145247	-0.970375	-0.401018
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.21	1.87	-0.036
1.361	10	7.63	7.06	2.65	1.87	0.967
2.451	9	5.41	6.31	1.39	1.87	-1.44
3.761	9	5.53	5.41	1.76	1.87	0.189
5.258	10	4.54	4.39	1.02	1.87	

0.261

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-54.048454	3	114.096907
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	3.23407	3	0.3569

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

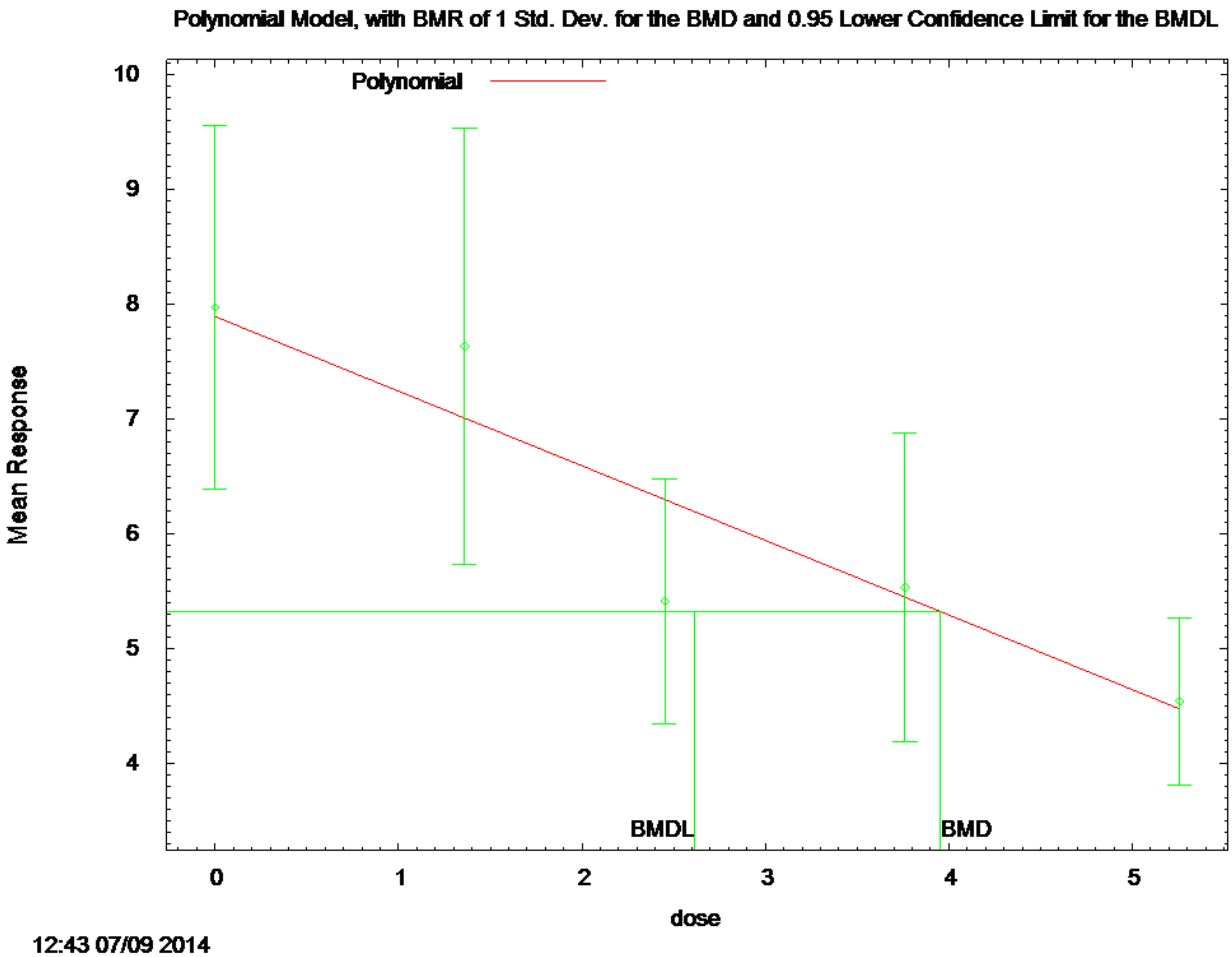
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.72735

BMDL = 1.96547


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:43 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:43:42 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =      8.07952
                         beta_1 =    -0.517572
                         beta_2 =    -0.184335
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.15	-0.18
rho	-0.99	1	-0.15	0.18
beta_0	0.15	-0.15	1	-0.91
beta_1	-0.18	0.18	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.45485	2.03072	-8.43498	-0.474719
rho	3.07105	1.1156	0.884508	5.25759
beta_0	7.88794	0.536104	6.83719	8.93868
beta_1	-0.649741	0.131724	-0.907914	-0.391567
beta_2	0	NA		
beta_3	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.89	2.21	2.57	0.101
1.361	10	7.63	7	2.65	2.14	0.925
2.451	9	5.41	6.3	1.39	1.82	-1.46

```
3.761     9       5.53         5.44         1.76         1.45
0.177
5.258    10       4.54         4.47         1.02         1.08
0.201
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -52.431420            6     116.862840
             A2          -47.292184           10     114.584369
             A3          -47.758770            7     109.517540
         fitted          -50.527570            4     109.055140
              R          -63.201706            2     130.403412


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              31.819          8       0.0001004
   Test 2             10.2785          4         0.03599
   Test 3            0.933171          3          0.8174
```

Test 4	5.5376	3	0.1364

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

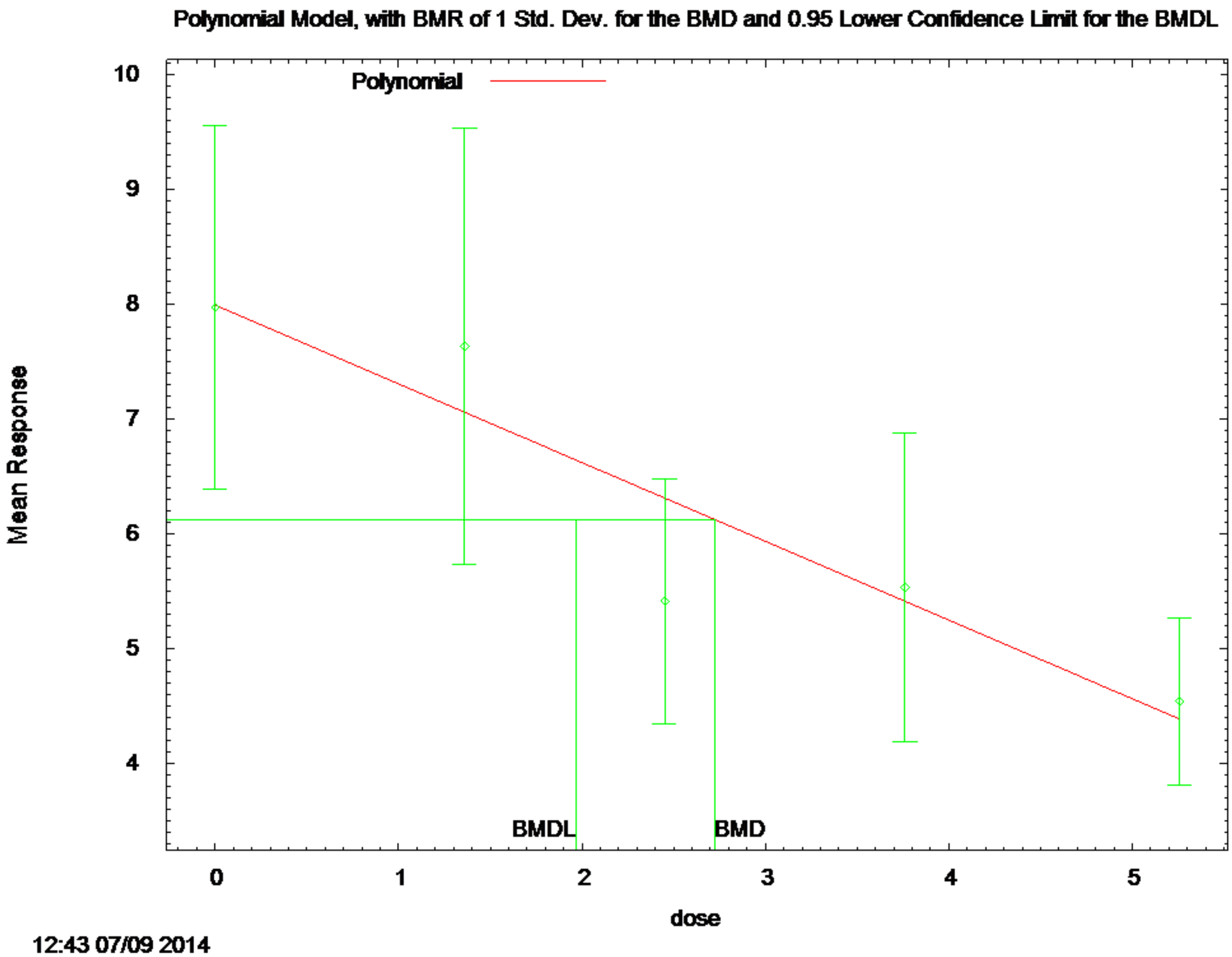
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.95557

BMDL = 2.61437


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly4CV-1SD-5d.plt
                                        Wed Jul 09 12:43:40 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                         beta_0 =         7.97
                         beta_1 =            0
                         beta_2 =     -4.80701
                         beta_3 =            0
                         beta_4 =    -0.138078


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	4.7e-007	-1.9e-007
beta_0	4.7e-007	1	-0.81
beta_1	-1.9e-007	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.49739	0.713902	2.09817	4.89662
beta_0	7.9913	0.457566	7.09448	8.88811
beta_1	-0.685697	0.145247	-0.970375	-0.401019
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.21	1.87	-0.036
1.361	10	7.63	7.06	2.65	1.87	0.967
2.451	9	5.41	6.31	1.39	1.87	-1.44
3.761	9	5.53	5.41	1.76	1.87	

```
0.189
5.258    10       4.54         4.39         1.02         1.87
0.261


 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -52.431420           6     116.862840
             A2          -47.292184          10     114.584369
             A3          -52.431420           6     116.862840
         fitted          -54.048454           3     114.096907
              R          -63.201706           2     130.403412


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              31.819          8       0.0001004
   Test 2             10.2785          4         0.03599
   Test 3             10.2785          4         0.03599
   Test 4             3.23407          3          0.3569
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

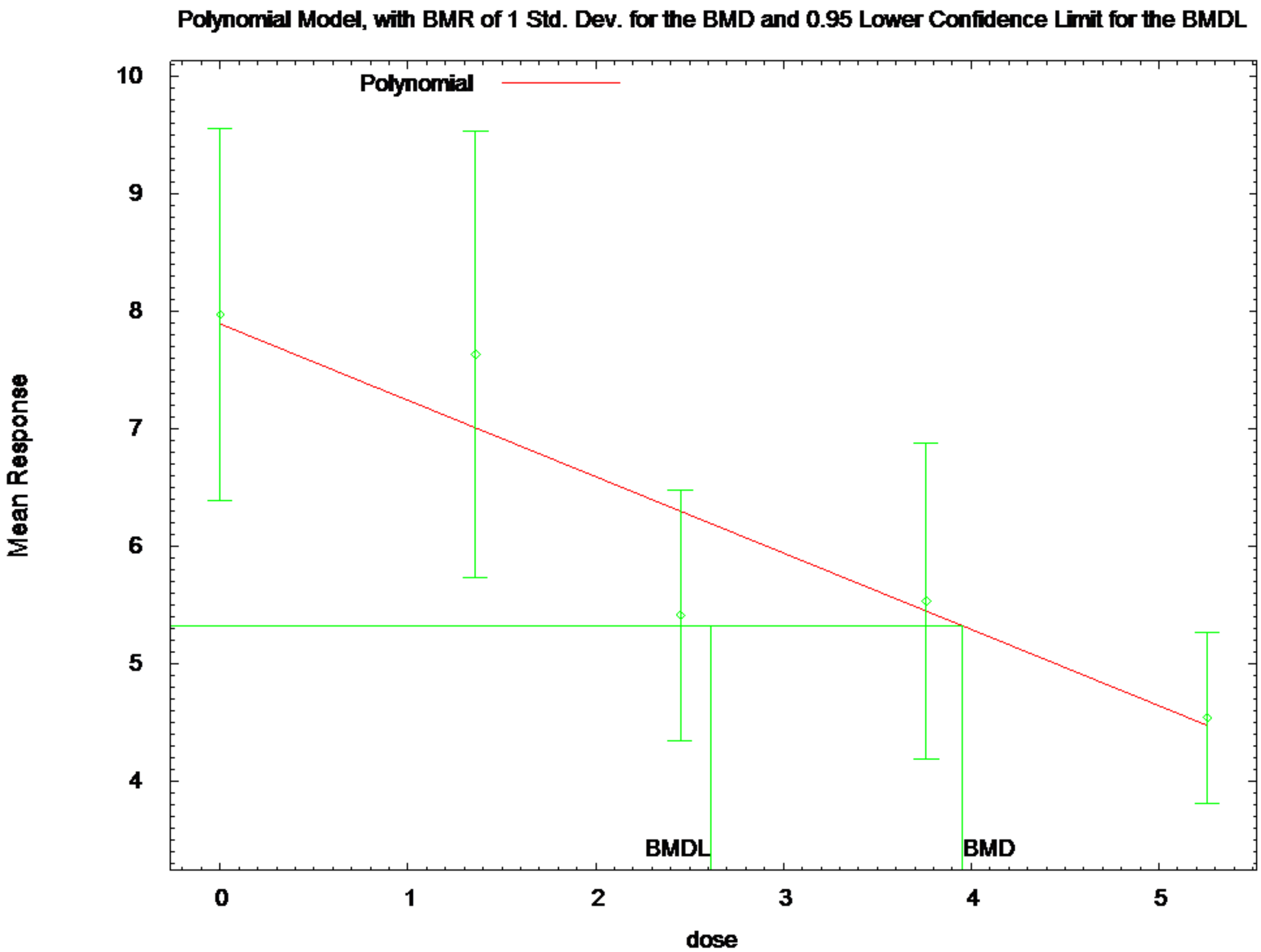
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.72734

BMDL = 1.96547



12:43 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Concurrent_Ln/WBC_Concurrent_L
n-HLS 2001-White Blood Cell Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:43:41 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                         beta_0 =         7.97
                         beta_1 =            0
                         beta_2 =     -4.80701
                         beta_3 =            0
                         beta_4 =    -0.138078


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.15	-0.18
rho	-0.99	1	-0.15	0.18
beta_0	0.15	-0.15	1	-0.91
beta_1	-0.18	0.18	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.45484	2.03072	-8.43497	-0.474713
rho	3.07104	1.1156	0.884505	5.25758
beta_0	7.88794	0.536104	6.83719	8.93868
beta_1	-0.649741	0.131724	-0.907915	-0.391568
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.89	2.21	2.57	0.101
1.361	10	7.63	7	2.65	2.14	

```
0.925
2.451     9       5.41          6.3          1.39          1.82
-1.46
3.761     9       5.53         5.44          1.76          1.45
0.177
5.258    10       4.54         4.47          1.02          1.08
0.201
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -52.431420            6     116.862840
             A2          -47.292184           10     114.584369
             A3          -47.758770            7     109.517540
         fitted          -50.527570            4     109.055140
              R          -63.201706            2     130.403412


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	5.5376	3	0.1364

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

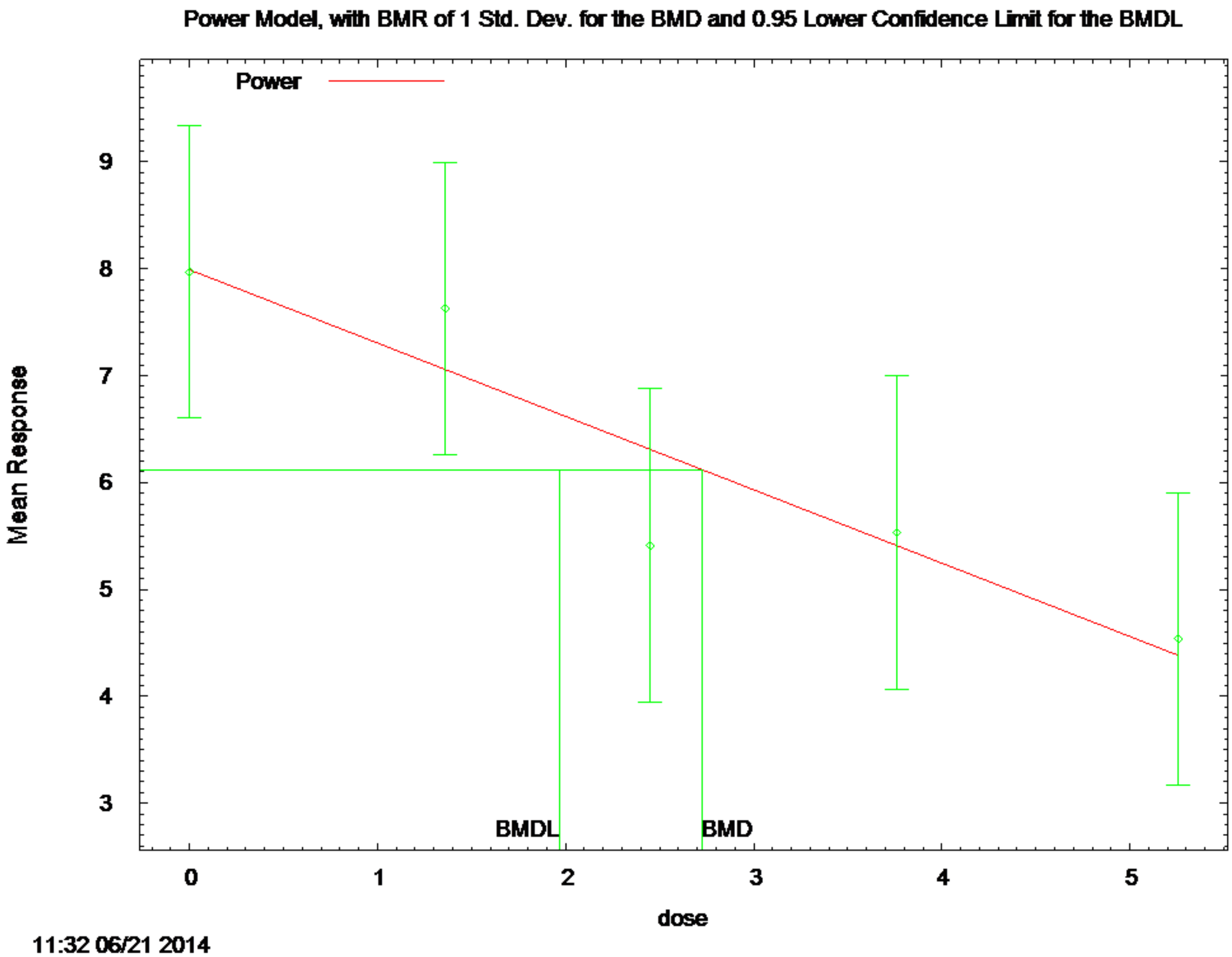
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.95557

BMDL = 2.61437



Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
11:32 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.plt
                                      Sat Jun 21 11:32:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.64969
                            rho =            0   Specified
                        control =         4.54
                          slope =      3.75463
                          power =     -1.18214


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-4.1e-009	7.4e-009
control	-4.1e-009	1	-0.81
slope	7.4e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.4974	0.713903	2.09817	4.89662
control	7.9913	0.457567	7.09448	8.88811
slope	-0.685697	0.145247	-0.970375	-0.401018
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.21	1.87	-0.036
1.361	10	7.63	7.06	2.65	1.87	0.967
2.451	9	5.41	6.31	1.39	1.87	-1.44
3.761	9	5.53	5.41	1.76	1.87	0.189
5.258	10	4.54	4.39	1.02	1.87	0.261

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-52.431420	6	116.862840
fitted	-54.048454	3	114.096907
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	10.2785	4	0.03599
Test 4	3.23407	3	0.3569

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

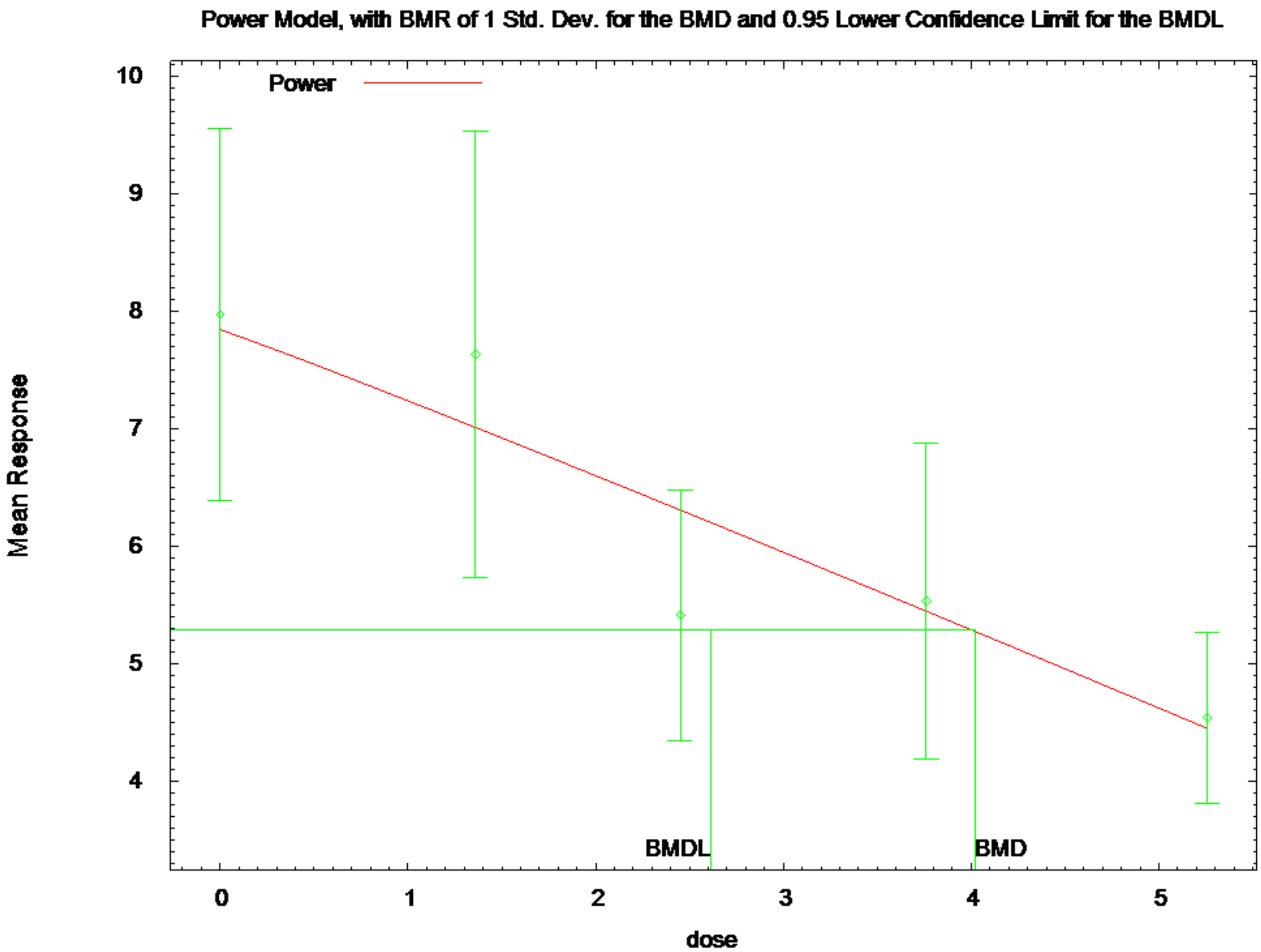
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.72735

BMDL = 1.96547



11:32 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Concurrent_Ln-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.plt
                                      Sat Jun 21 11:32:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.29464
                            rho =            0
                        control =         4.54
                          slope =      3.75463
                          power =     -1.18214


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho      control        slope
power
```

lalpha	1	-1	0.47	-0.37	-0.27
rho	-1	1	-0.49	0.38	0.27
control	0.47	-0.49	1	-0.82	-0.7
slope	-0.37	0.38	-0.82	1	0.97
power	-0.27	0.27	-0.7	0.97	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.51069	2.46794	-9.34776	0.326384
rho	3.10193	1.36559	0.425425	5.77844
control	7.84366	0.738466	6.3963	9.29103
slope	-0.603526	0.542692	-1.66718	0.460131
power	1.03741	0.445048	0.165135	1.90969

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.84	2.21	2.56	0.156
1.361	10	7.63	7.01	2.65	2.15	0.908
2.451	9	5.41	6.31	1.39	1.83	-1.48
3.761	9	5.53	5.46	1.76	1.46	0.147

5.258 10 4.54 4.47 1.02 1.07
0.216

Model Descriptions for likelihoods calculated

```
 Model A1:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-52.431420	6	116.862840
A2	-47.292184	10	114.584369
A3	-47.758770	7	109.517540
fitted	-50.523874	5	111.047748
R	-63.201706	2	130.403412

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.819	8	0.0001004
Test 2	10.2785	4	0.03599
Test 3	0.933171	3	0.8174
Test 4	5.53021	2	0.06297

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

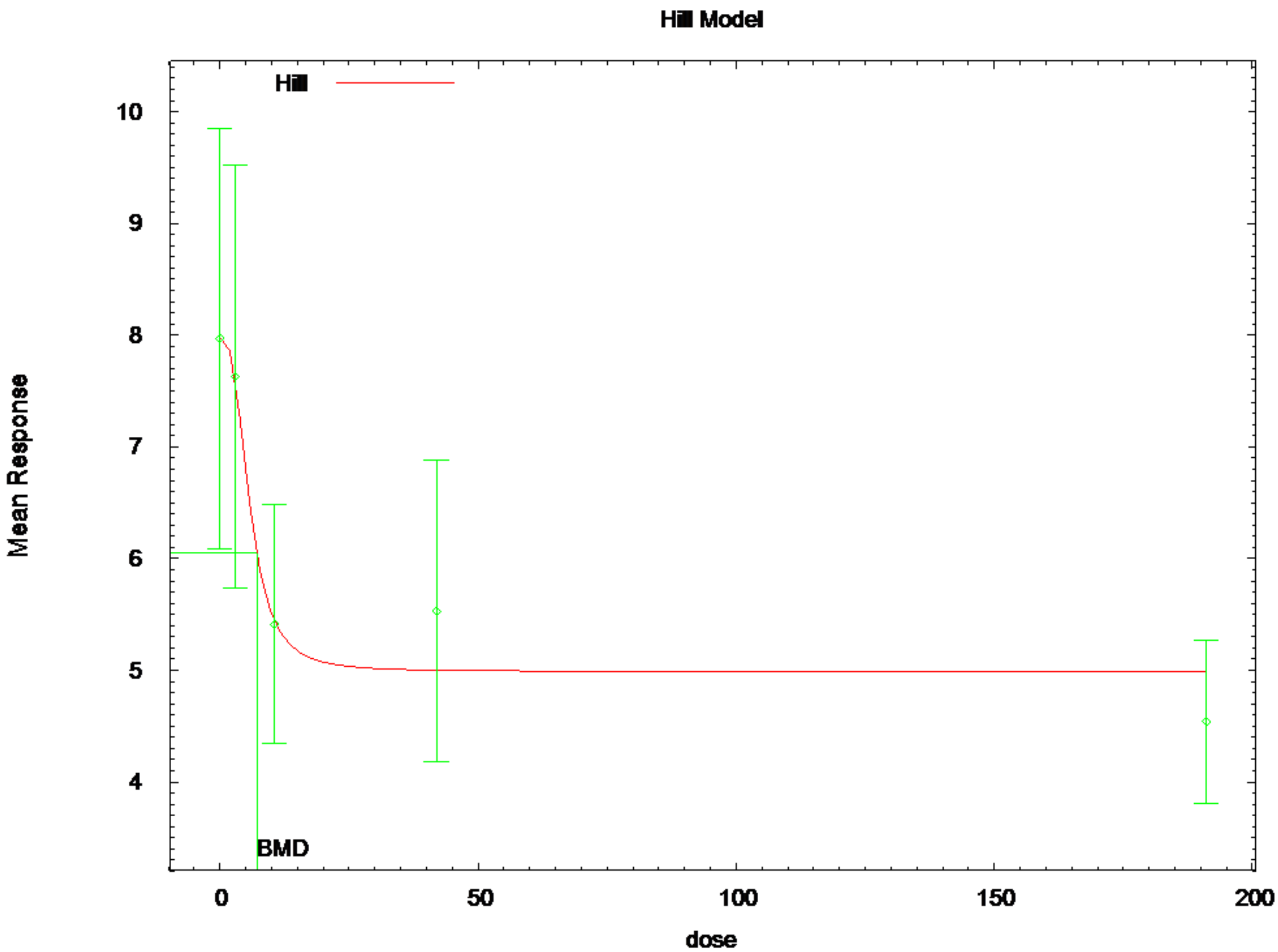
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.02318

BMDL = 2.61571

BMDS Model Results for White Blood Cell Count (Untransformed Doses, Historical Controls)



09:34 06/22 2014

```
==================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.plt
                                        Sun Jun 22 09:34:41 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                      intercept =         7.97
                              v =        -3.43
                              n =      2.04485
                              k =      7.66914


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-6.8e-008	1.6e-007	3e-007	-2.4e-007
intercept	-6.8e-008	1	-0.81	-0.48	-0.5
v	1.6e-007	-0.81	1	0.59	0.17
n	3e-007	-0.48	0.59	1	0.094
k	-2.4e-007	-0.5	0.17	0.094	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.73939	0.763299	2.24335	5.23543
intercept	7.98132	0.610793	6.78419	9.17845
v	-2.98856	0.789337	-4.53564	-1.44149
n	2.86104	2.62932	-2.29234	8.01442
k	5.76723	3.28608	-0.673363	12.2078

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.98	2.63	1.93	-0.0185

```
  2.9    10       7.63         7.61         2.65         1.93
0.0253
 10.6     9       5.41         5.44         1.39         1.93
-0.0441
   42     9       5.53            5         1.76         1.93
0.818
191.1    10       4.54         4.99         1.02         1.93
-0.741
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-55.654114	5	121.308228
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	1.23586	1	0.2663

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

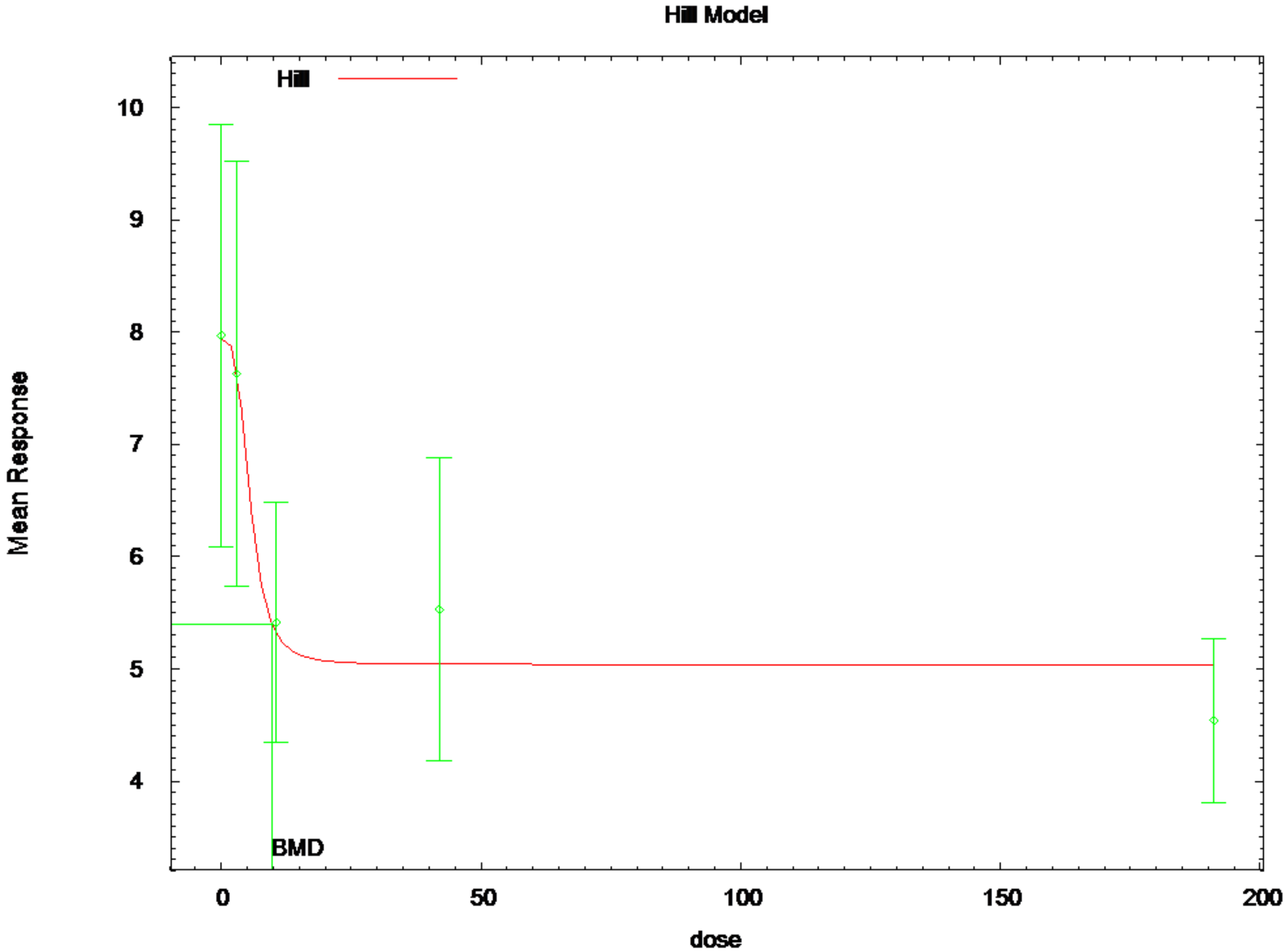
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 7.12804

BMDL computation failed.



09:34 06/22 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.plt
                                      Sun Jun 22 09:34:42 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                      intercept =         7.97
                              v =        -3.43
                              n =      2.04485
                              k =      7.66914


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.31	-0.41	-0.076	0.0005
rho	-0.99	1	-0.34	0.42	0.076	-0.00025
intercept	0.31	-0.34	1	-0.93	-0.55	-0.57
v	-0.41	0.42	-0.93	1	0.61	0.43
n	-0.076	0.076	-0.55	0.61	1	0.51
k	0.0005	-0.00025	-0.57	0.43	0.51	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.78741	2.04747	-7.80039	0.225565
rho	2.73058	1.12838	0.518992	4.94217
intercept	7.94128	0.756311	6.45893	9.42362
v	-2.89843	0.846166	-4.55688	-1.23997
n	3.53412	3.51116	-3.34763	10.4159
k	5.58094	3.3883	-1.06001	12.2219

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.94	2.63	2.55	0.0357

```
  2.9    10       7.63         7.68         2.65         2.43
-0.0655
 10.6     9       5.41         5.31         1.39         1.47
0.194
   42     9       5.53         5.05         1.76         1.37
1.06
191.1    10       4.54         5.04         1.02         1.37
-1.16
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.729259	6	115.458518
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	5.02942	1	0.02492

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

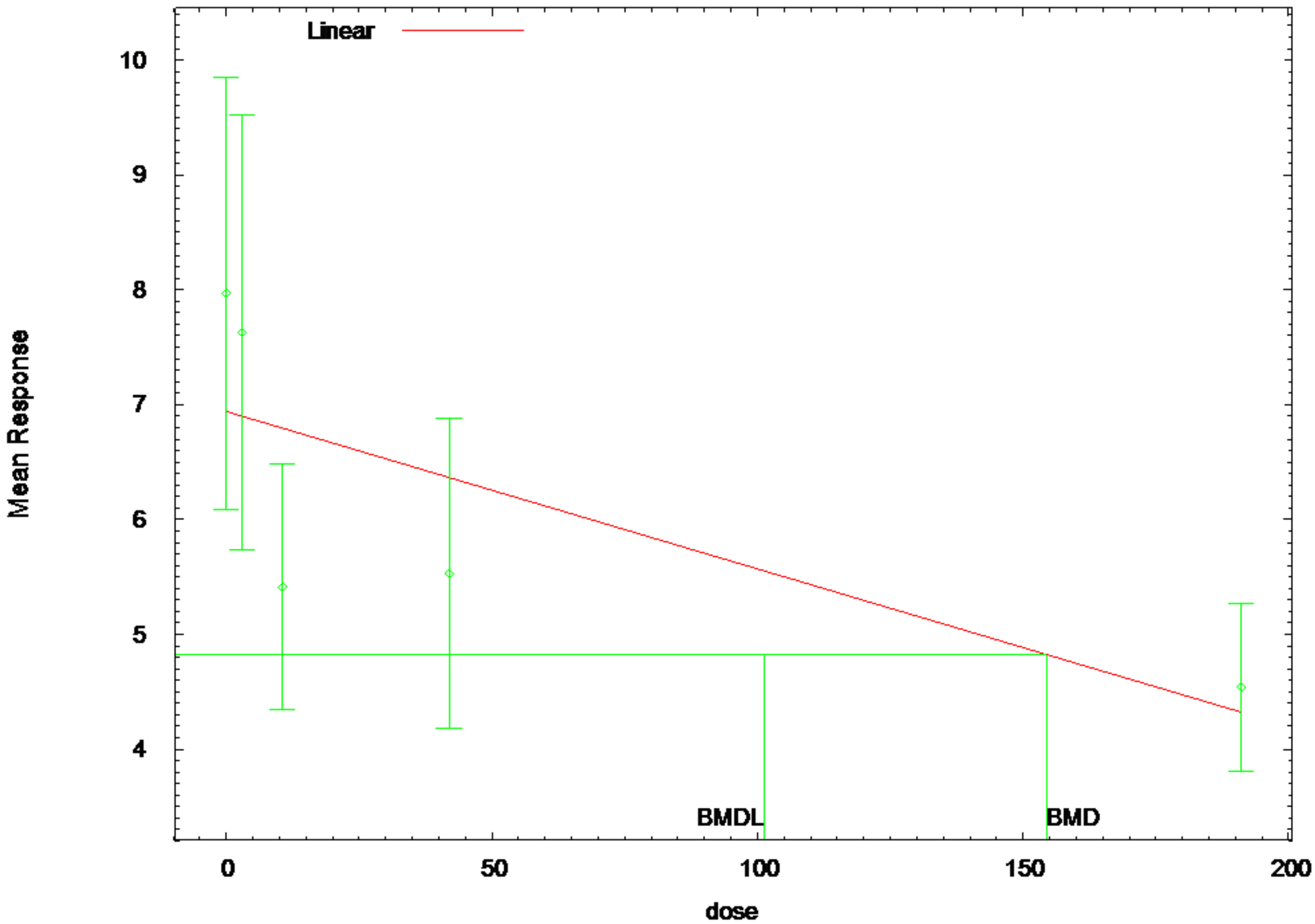
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 9.78299

BMDL computation failed.

Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:44:57 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      6.88046
                         beta_1 =   -0.0134724


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	3.5e-007	-6.3e-008
beta_0	3.5e-007	1	-0.56
beta_1	-6.3e-008	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	4.47635	0.913731	2.68547	6.26723
beta_0	6.93587	0.369654	6.21136	7.66038
beta_1	-0.0136993	0.00414278	-0.021819	-0.0055796

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.63	2.12	1.55
2.9	10	7.63	6.9	2.65	2.12	1.1
10.6	9	5.41	6.79	1.39	2.12	-1.96
42	9	5.53	6.36	1.76	2.12	-1.18
191.1	10	4.54	4.32	1.02	2.12	0.332

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-59.971358	3	125.942715
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	9.87035	3	0.0197

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

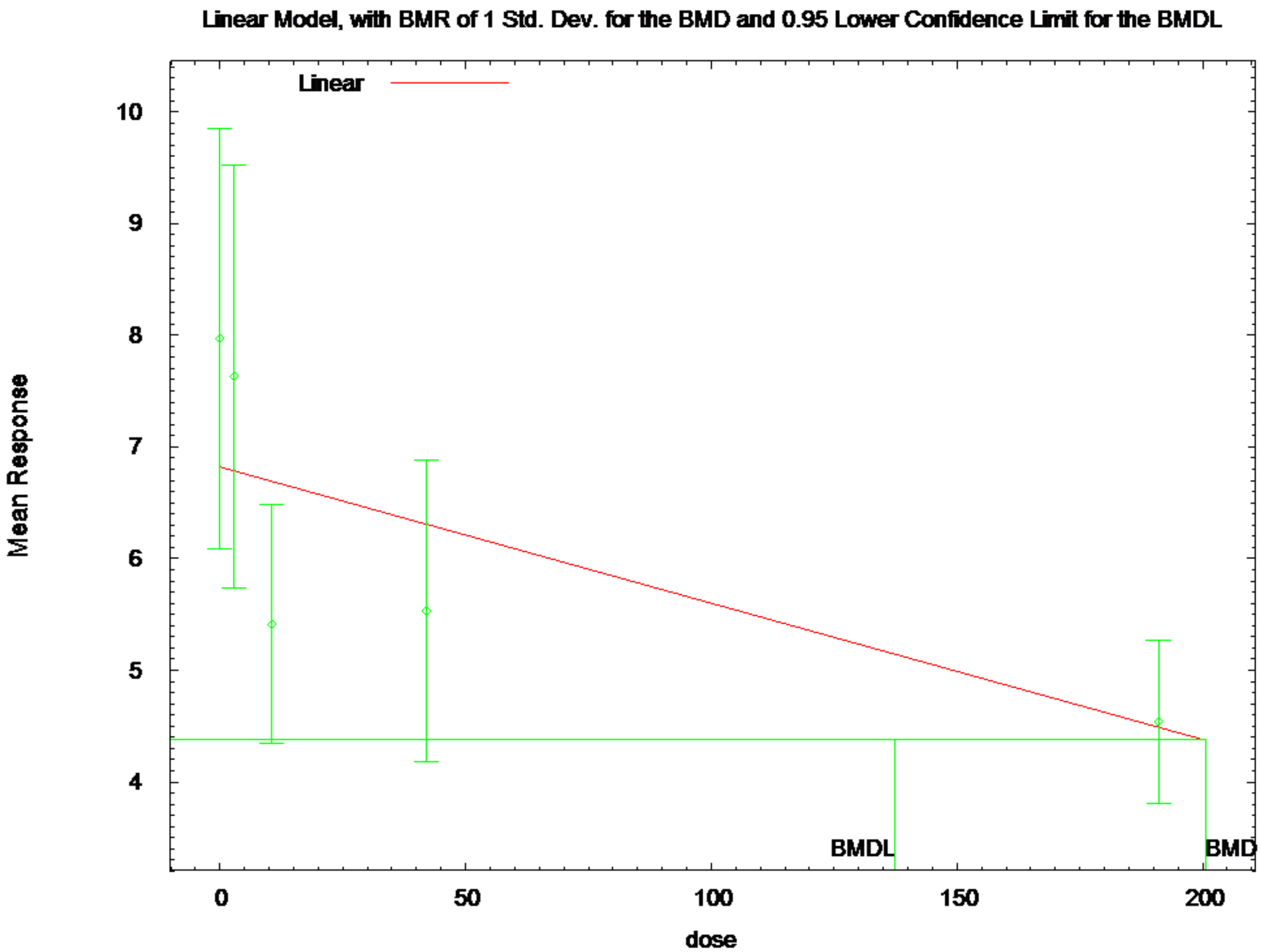
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 154.441

BMDL = 101.242



12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:44:58 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      6.88046
                         beta_1 =   -0.0134724


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1           -1        0.046       -0.054
```

rho	-1	1	-0.046	0.055
beta_0	0.046	-0.046	1	-0.82
beta_1	-0.054	0.055	-0.82	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.96308	2.24713	-11.3674	-2.55879
rho	4.55432	1.23325	2.1372	6.97144
beta_0	6.82487	0.406771	6.02761	7.62212
beta_1	-0.0121567	0.00273518	-0.0175175	-0.00679584

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.82	2.63	2.44	1.48
2.9	10	7.63	6.79	2.65	2.41	1.1
10.6	9	5.41	6.7	1.39	2.34	-1.65
42	9	5.53	6.31	1.76	2.04	-1.15
191.1	10	4.54	4.5	1.02	0.946	0.128

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-55.234090	4	118.468180
R	-64.896924	2	133.793848

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	12.0391	3	0.00725

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

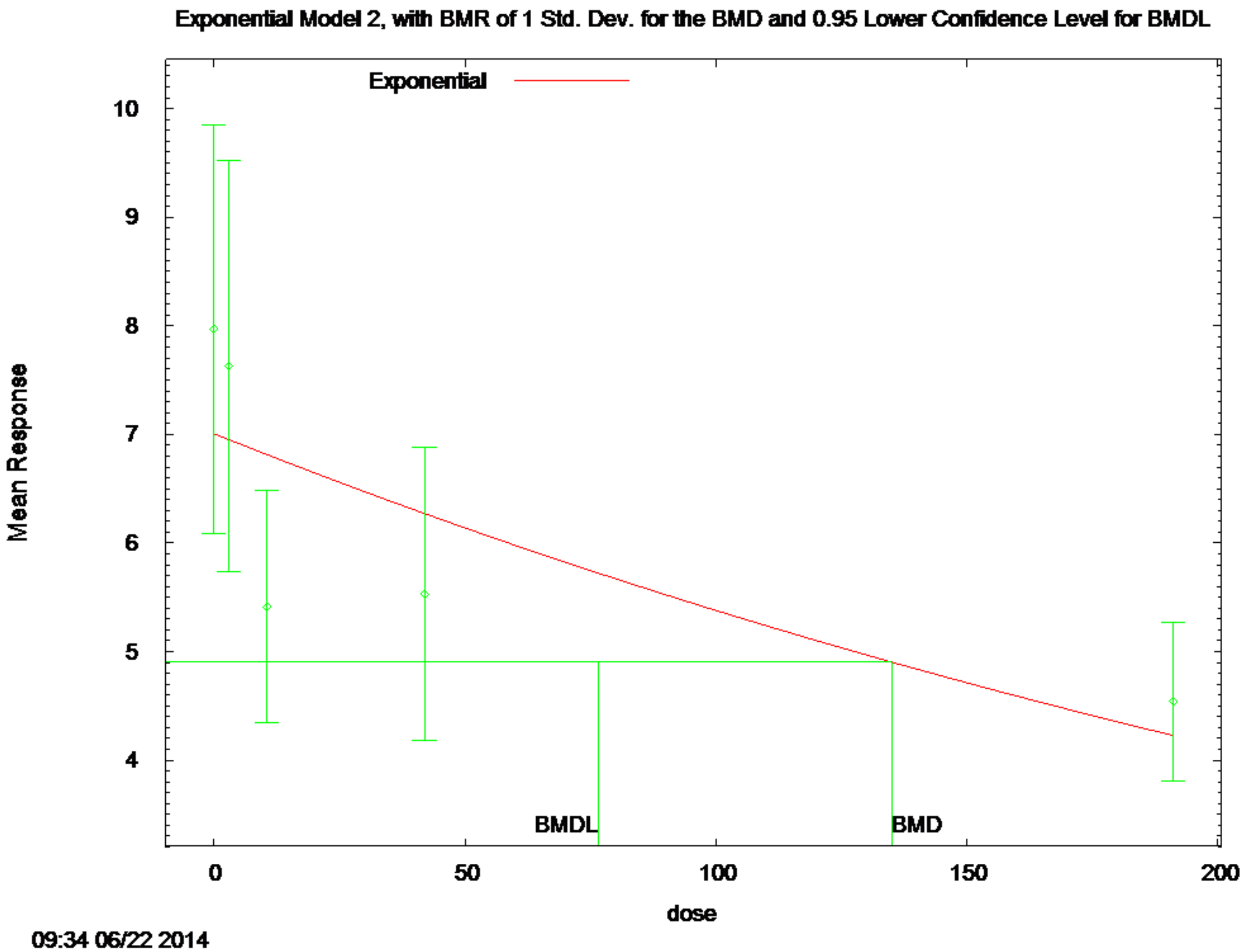
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.696

BMDL = 137.478



Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                          Sun Jun 22 09:34:40 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.29317
rho(S)	0
a	5.42664
b	0.00232433
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.48734
rho	0
a	7.00671
b	0.00264475
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.007	2.104	1.448
2.9	6.953	2.104	1.017
10.6	6.813	2.104	-2.001
42	6.27	2.104	-1.055
191.1	4.227	2.104	0.4707

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
2	-59.6961	3	125.3922

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

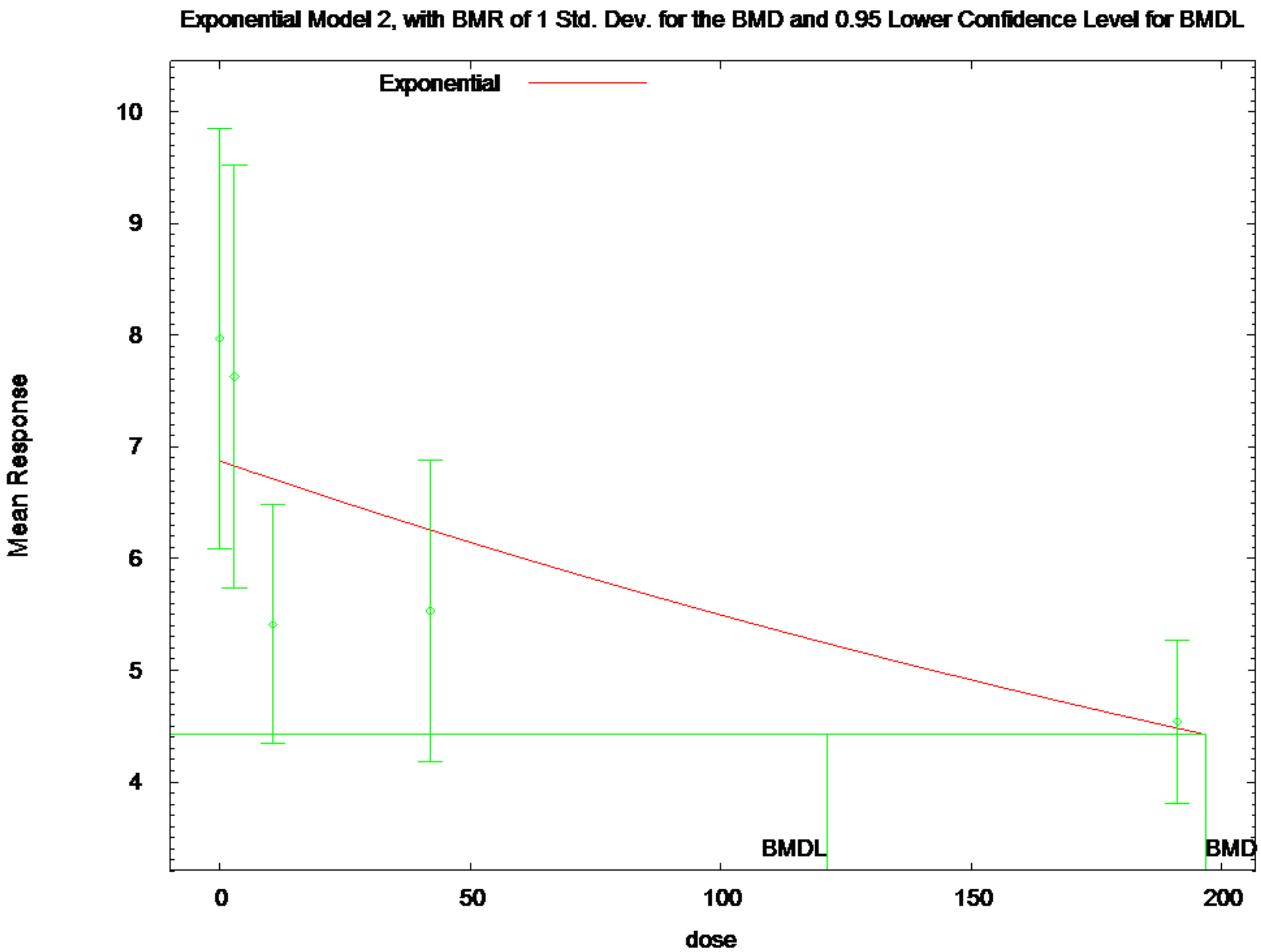
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	

```
0.0001017
     Test 2                              12.06            4
0.01687
     Test 3                              12.06            4
0.01687
     Test 4                               9.32            3
0.02533


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  Consider running
     a non-homogeneous variance model.

     The p-value for Test 3 is less than .1.  You may want to
     consider a different variance model.

     The p-value for Test 4 is less than .1.  Model 2 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      134.987

                 BMDL =      76.6345
```



09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sun Jun 22 09:34:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-4.88417
rho	3.3405
a	5.42664
b	0.00232433
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-6.78632
rho	4.44974
a	6.87236
b	0.00223755
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.872	2.448	1.418
2.9	6.828	2.413	1.051
10.6	6.711	2.322	-1.681
42	6.256	1.986	-1.096
191.1	4.481	0.9455	0.1963

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
2	-54.95966	4	117.9193

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017
Test 2	12.06	4	

0.01687

Test 3	0.4217	3	0.9357
Test 4	11.49	3	0.00935

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

Specified Effect = 1.000000

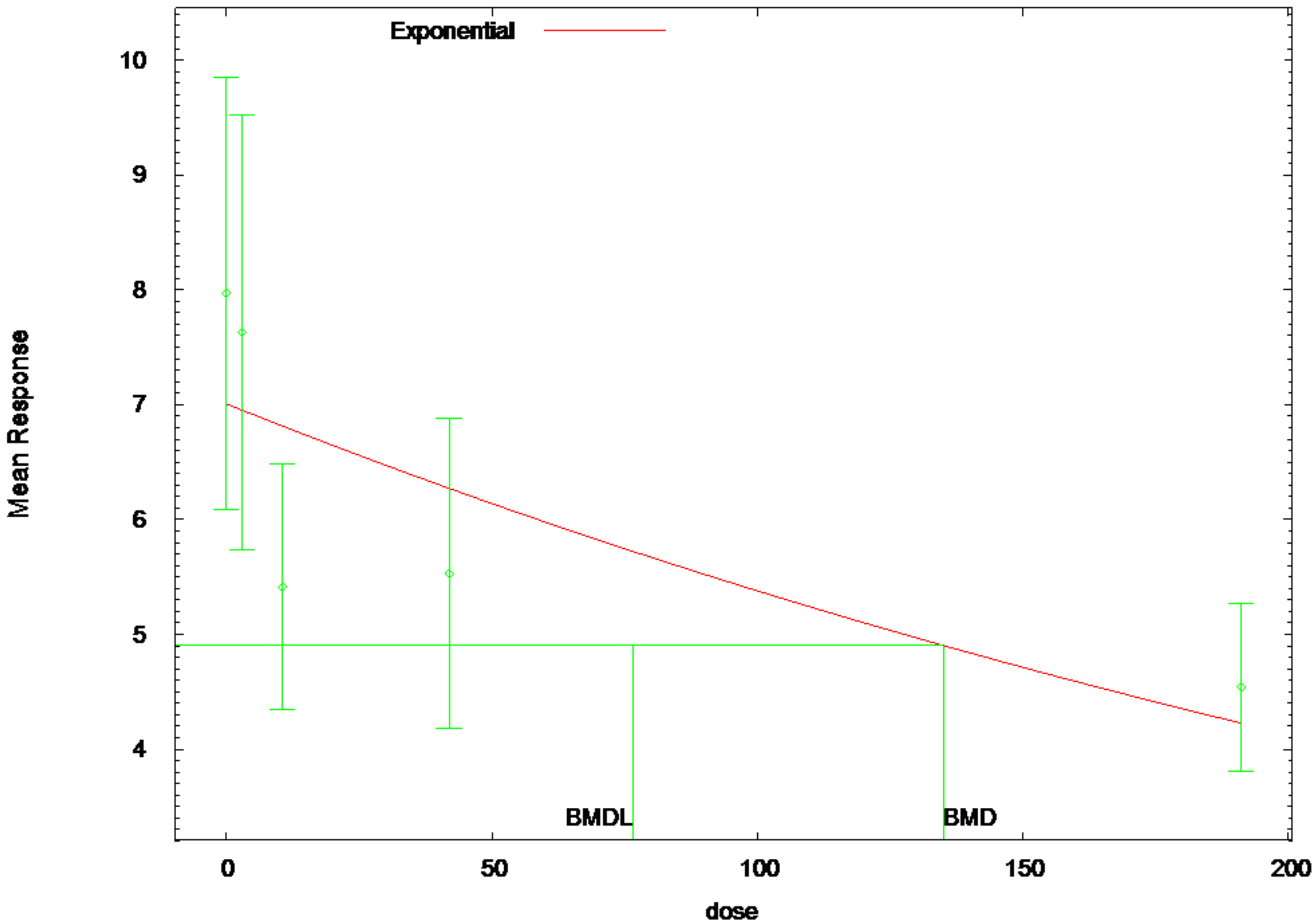
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 196.821

BMDL = 121.284

Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:34:40 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.29317
rho(S)	0
a	5.42664
b	0.00232433
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.48734
rho	0
a	7.00671
b	0.00264475
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.007	2.104	1.448
2.9	6.953	2.104	1.017
10.6	6.813	2.104	-2.001
42	6.27	2.104	-1.055
191.1	4.227	2.104	0.4707

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
3	-59.6961	3	125.3922

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 5a	9.32	3	0.02533

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

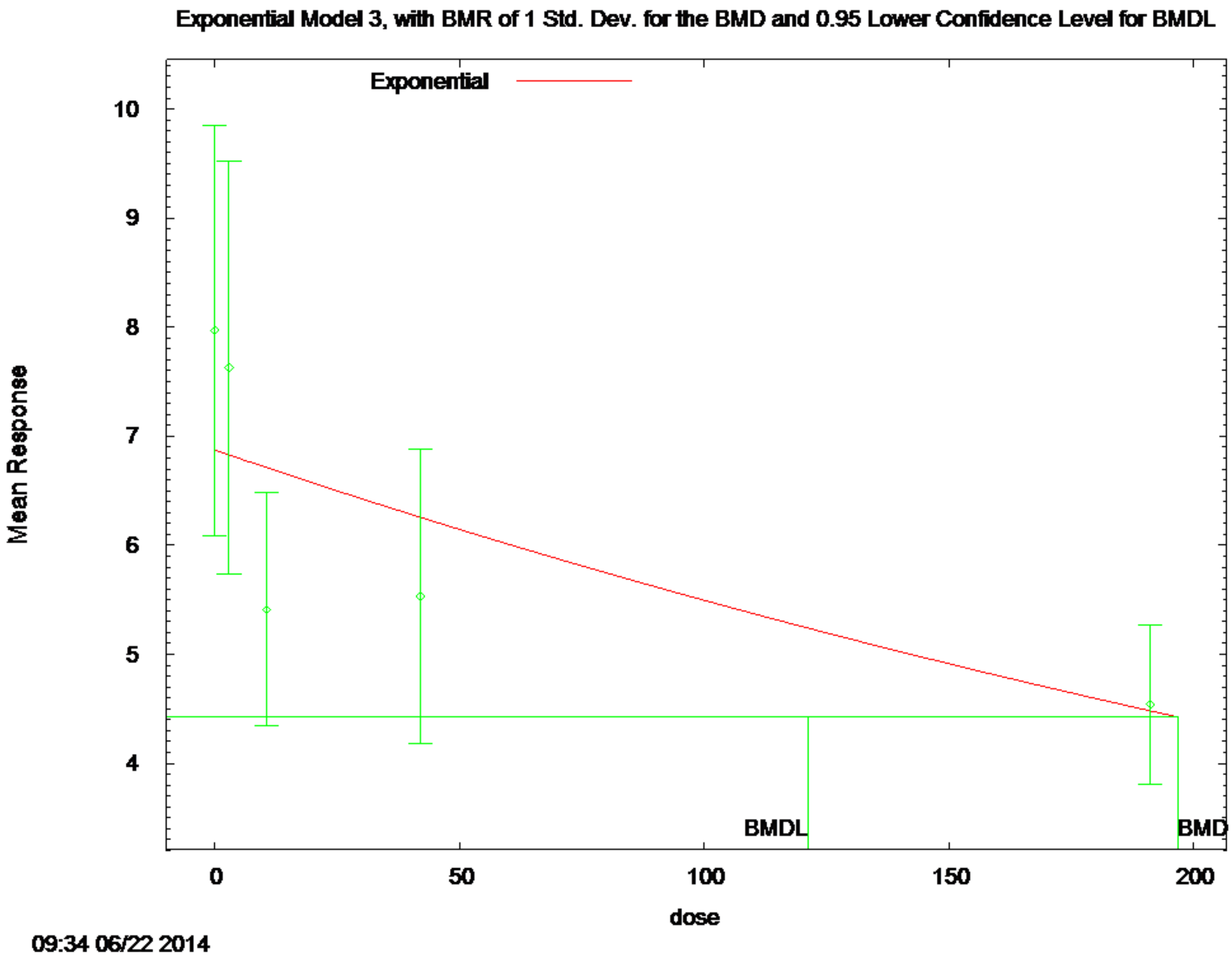
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 134.987

BMDL = 76.6345


Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:34:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-4.88417
rho	3.3405
a	5.42664
b	0.00232433
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-6.78632
rho	4.44974
a	6.87236
b	0.00223755
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.872	2.448	1.418
2.9	6.828	2.413	1.051
10.6	6.711	2.322	-1.681
42	6.256	1.986	-1.096
191.1	4.481	0.9455	0.1963

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
3	-54.95966	4	117.9193

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

Test 2	12.06	4	0.01687
Test 3	0.4217	3	0.9357
Test 5a	11.49	3	0.00935

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

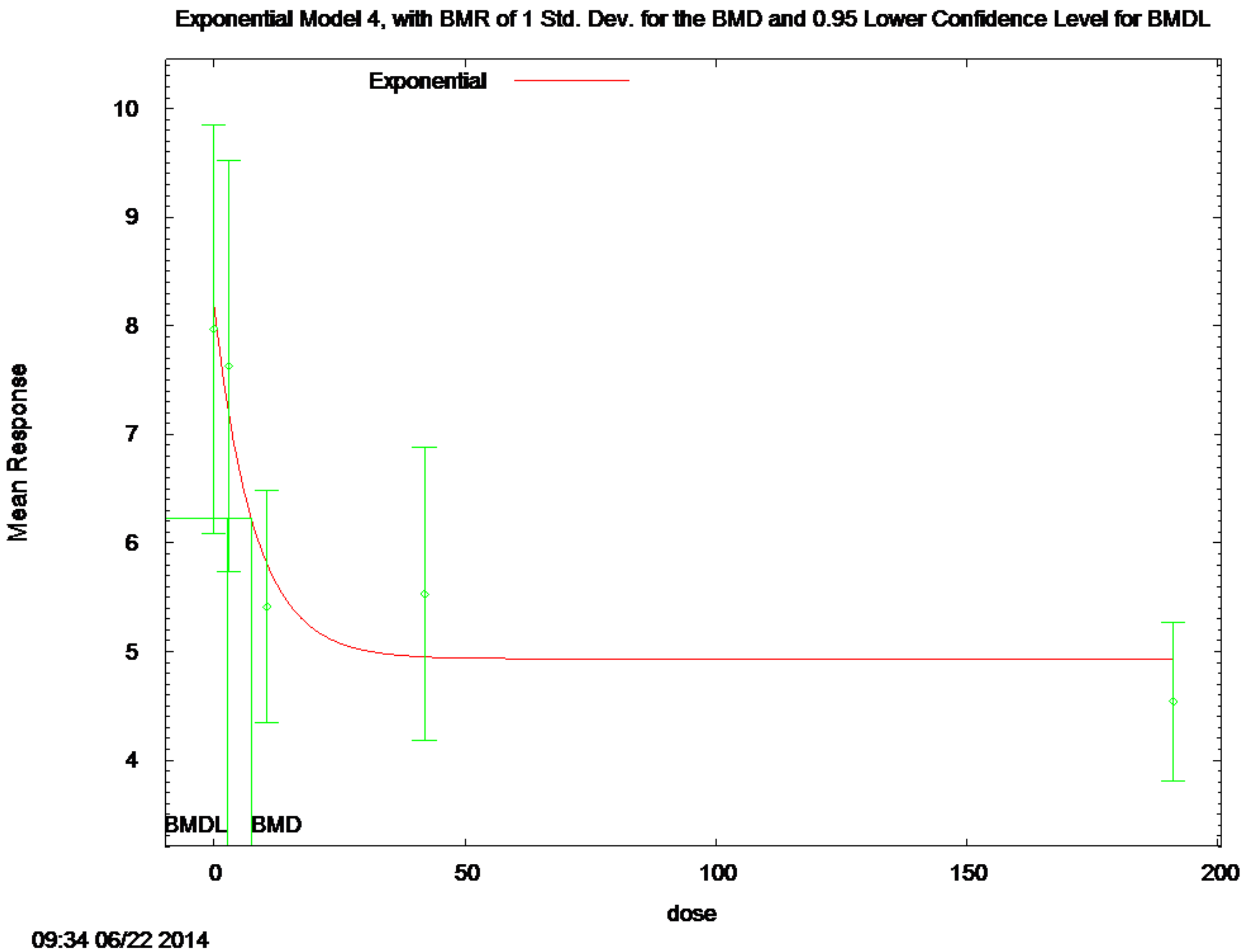
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 196.821

BMDL = 121.284


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:34:40 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.29317
rho(S)	0
a	8.3685
b	0.0162762
c	0.516677
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.33935
rho	0
a	8.1813
b	0.124602
c	0.602967
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.181	1.954	-0.342
2.9	7.196	1.954	0.7021
10.6	5.8	1.954	-0.599
42	4.95	1.954	0.8901
191.1	4.933	1.954	-0.6362

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
              Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
              Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
              Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
4	-56.1443	4	120.2886

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 6a	2.216	2	0.3302

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

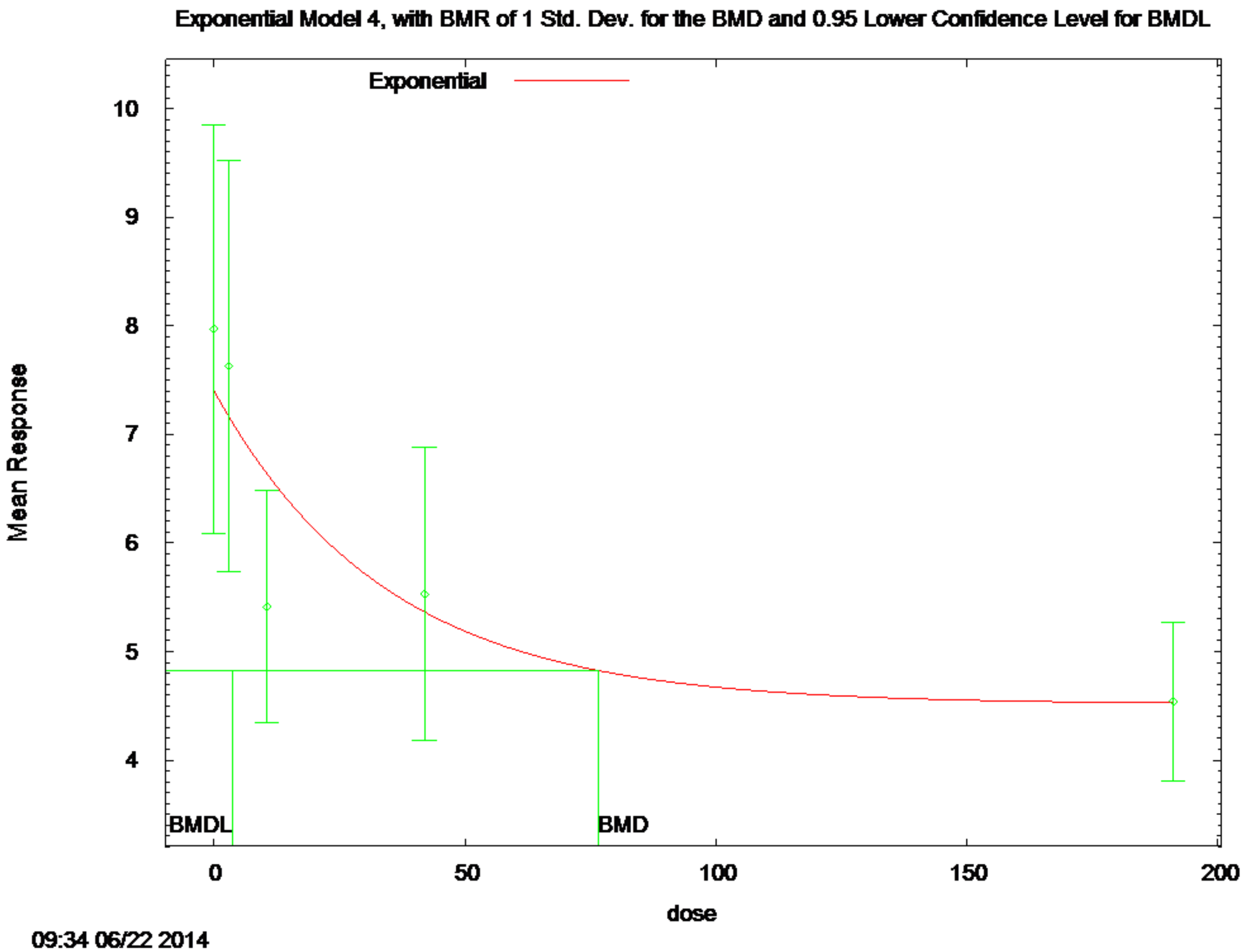
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 7.38252

BMDL = 2.78564


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:34:42 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~


   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-4.88417
rho	3.3405
a	8.3685
b	0.0162762
c	0.516677
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-5.39586
rho	3.64125
a	7.40123
b	0.0291784
c	0.610206
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.401	2.576	0.6982
2.9	7.167	2.43	0.6024
10.6	6.634	2.111	-1.739
42	5.363	1.433	0.3488
191.1	4.527	1.053	0.03843

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
4	-52.81813	5	115.6363

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

Test 2	12.06	4	0.01687
Test 3	0.4217	3	0.9357
Test 6a	7.207	2	0.02723

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

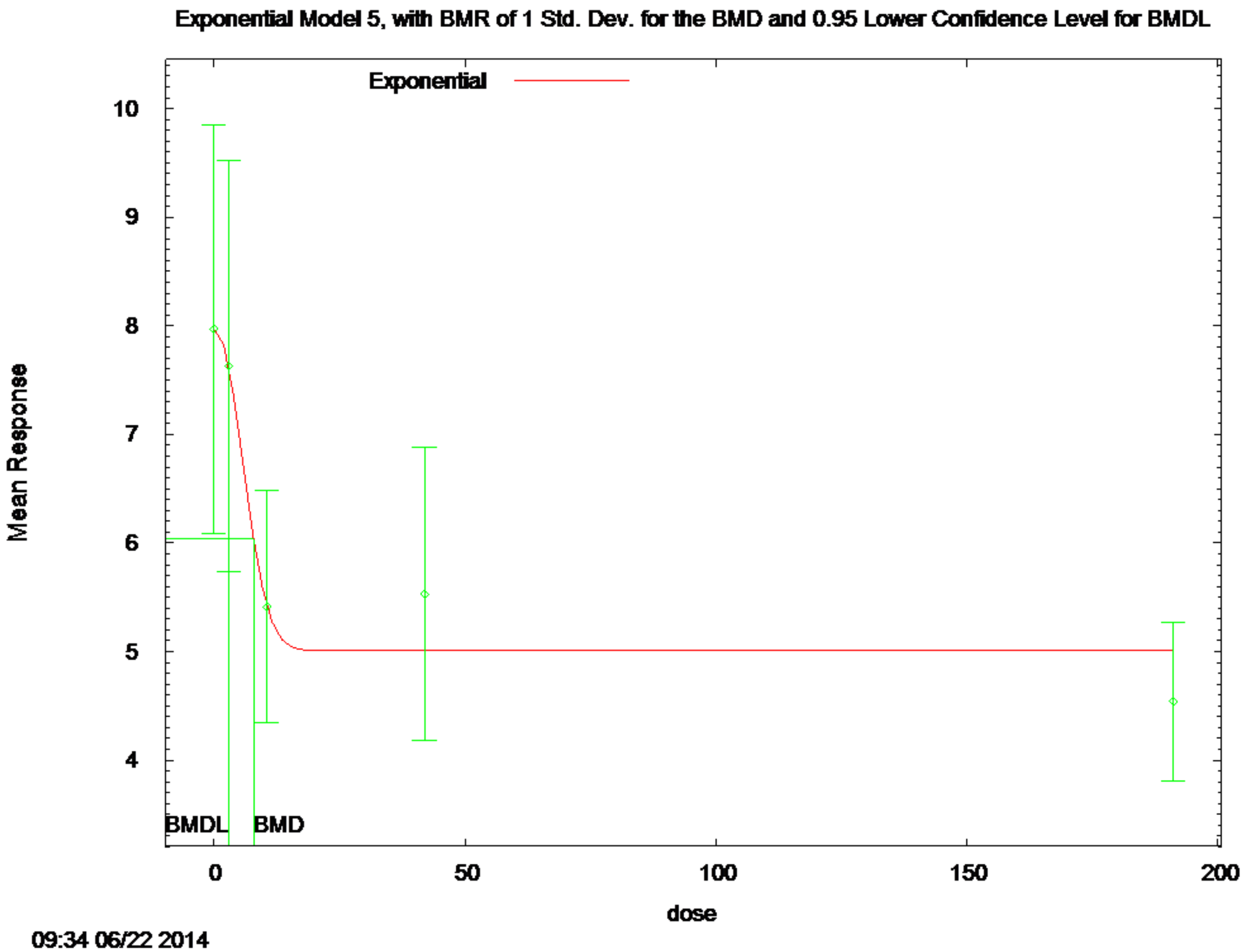
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 76.5897

BMDL = 3.58429


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:34:40 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.29317
rho(S)	0
a	8.3685
b	0.0162762
c	0.516677
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.31937
rho	0
a	7.97
b	0.130055
c	0.628475
d	2.15774

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.97	1.934	7.975e-007
2.9	7.63	1.934	-1.085e-006
10.6	5.41	1.934	-4.854e-007
42	5.009	1.934	0.8082
191.1	5.009	1.934	-0.7667

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
5	-55.66483	5	121.3297

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 7a	1.257	1	0.2622

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

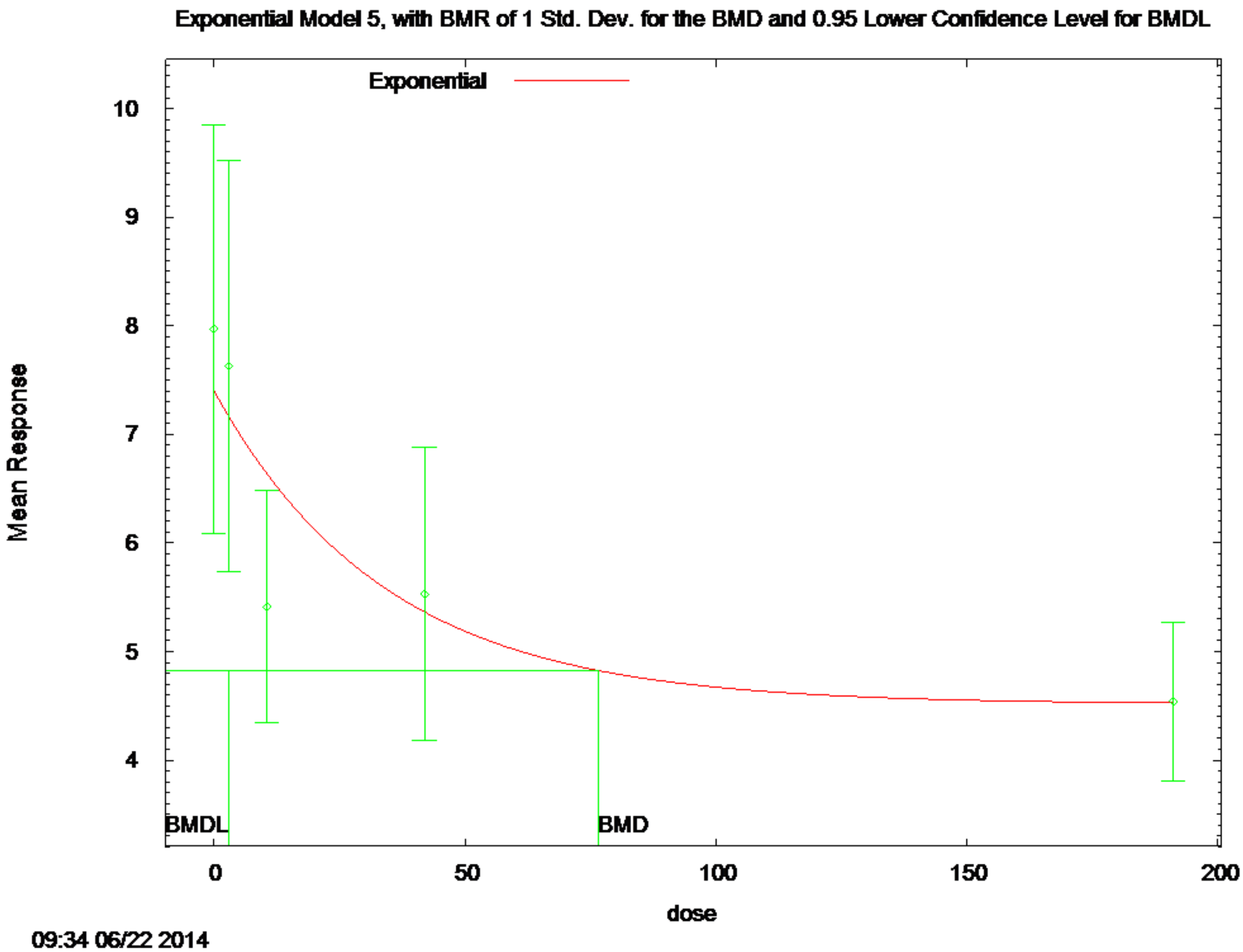
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 7.89619

BMDL = 2.93169


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:34:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~


   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-4.88417
rho	3.3405
a	8.3685
b	0.0162762
c	0.516677
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-5.39586
rho	3.64125
a	7.40123
b	0.0291784
c	0.610206
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
2.9	10	7.63	2.653
10.6	9	5.41	1.392
42	9	5.53	1.756
191.1	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.401	2.576	0.6982
2.9	7.167	2.43	0.6024
10.6	6.634	2.111	-1.739
42	5.363	1.433	0.3488
191.1	4.527	1.053	0.03844

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
5	-52.81813	5	115.6363

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

Test 2	12.06	4	0.01687
Test 3	0.4217	3	0.9357
Test 7a	7.207	2	0.02723

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

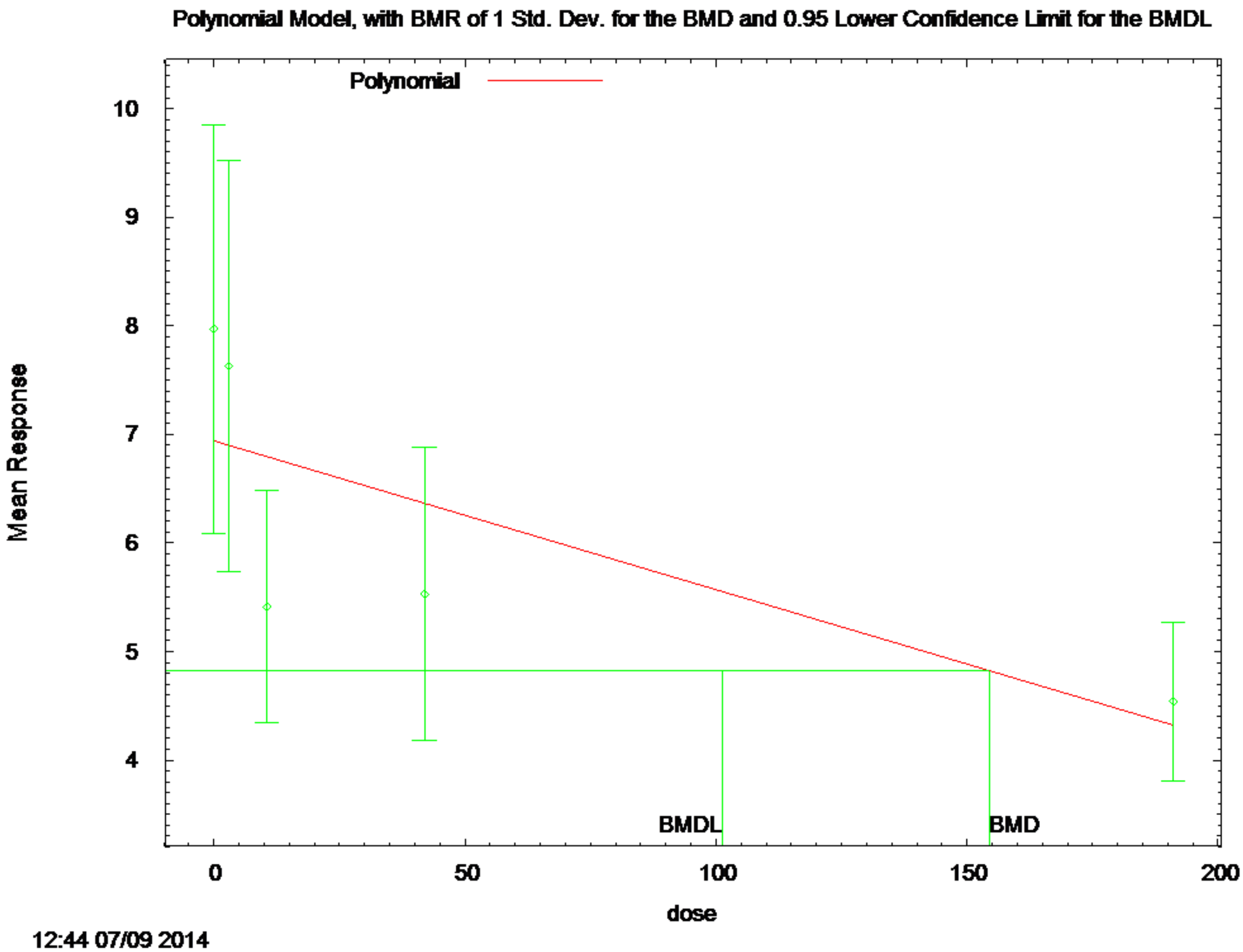
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 76.5897

BMDL = 2.94249


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:44:57 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      7.40214
                         beta_1 =   -0.0643244
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.8e-007	3.5e-007
beta_0	-1.8e-007	1	-0.56
beta_1	3.5e-007	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	4.47634	0.91373	2.68547	6.26722
beta_0	6.93587	0.369654	6.21136	7.66038
beta_1	-0.0136993	0.00414278	-0.021819	-0.0055796
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.63	2.12	1.55
2.9	10	7.63	6.9	2.65	2.12	1.1
10.6	9	5.41	6.79	1.39	2.12	-1.96
42	9	5.53	6.36	1.76	2.12	-1.18
191.1	10	4.54	4.32	1.02	2.12	0.332

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-59.971358	3	125.942715
R	-64.896924	2	133.793848

Explanation of Tests

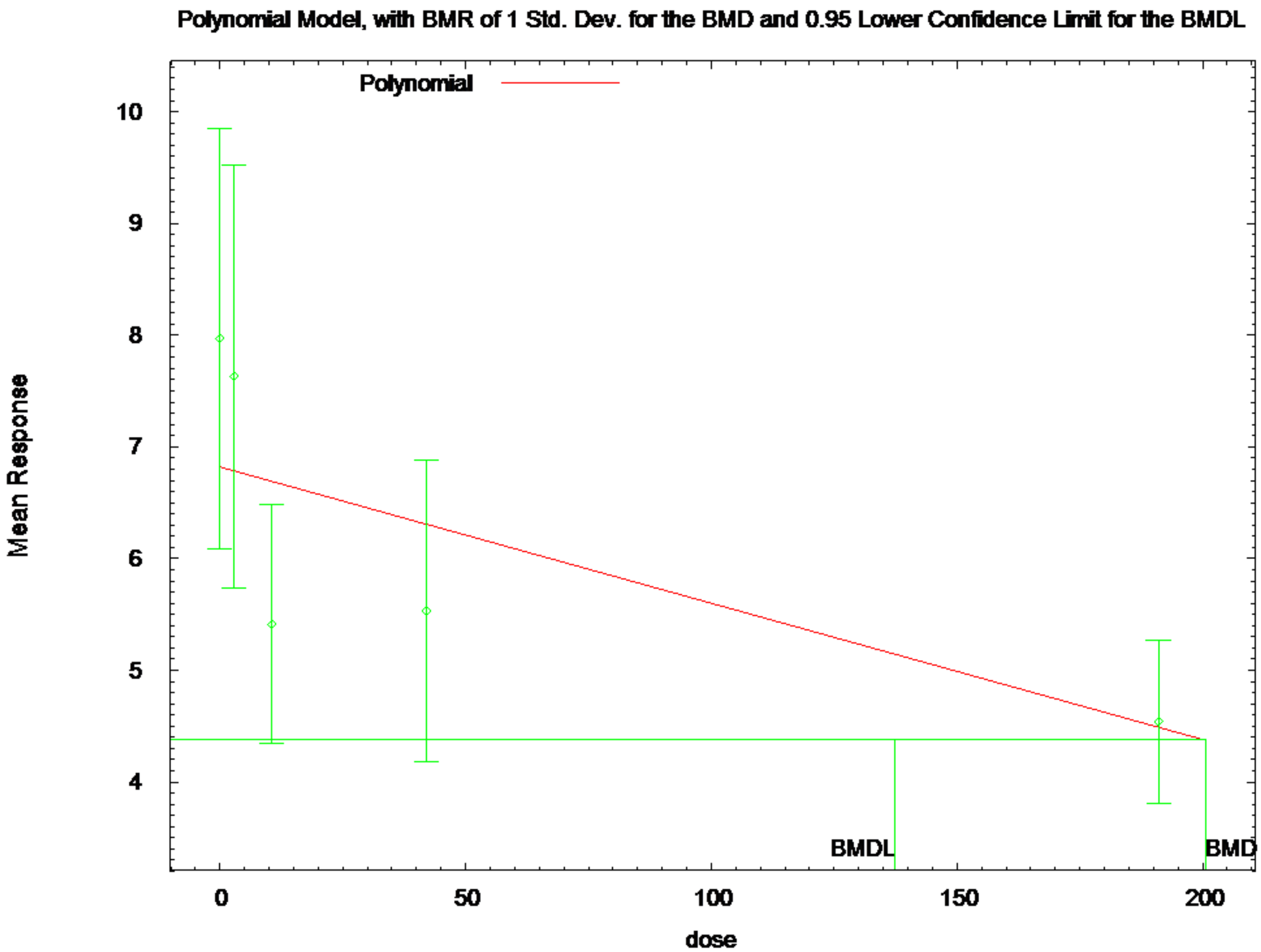
Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	9.87035	3	0.0197

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

```
The p-value for Test 2 is less than .1.  Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1.  You may want to consider
a
different variance model

The p-value for Test 4 is less than .1.  You may want to try a
different
model


             Benchmark Dose Computation

Specified effect =            1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =         0.95

             BMD =       154.441


            BMDL =       101.242
```



12:44 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly2NCV-1SD-5d.plt
                                       Wed Jul 09 12:44:58 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      7.40214
                         beta_1 =   -0.0643244
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.046	-0.054
rho	-1	1	-0.046	0.055
beta_0	0.046	-0.046	1	-0.82
beta_1	-0.054	0.055	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.96308	2.24713	-11.3674	-2.55879
rho	4.55432	1.23325	2.1372	6.97144
beta_0	6.82487	0.406771	6.02761	7.62212
beta_1	-0.0121567	0.00273518	-0.0175175	-0.00679584
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.82	2.63	2.44	1.48
2.9	10	7.63	6.79	2.65	2.41	1.1
10.6	9	5.41	6.7	1.39	2.34	-1.65
42	9	5.53	6.31	1.76	2.04	-1.15

191.1 10 4.54 4.5 1.02 0.946
0.128

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-55.234090	4	118.468180
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	12.0391	3	0.00725

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

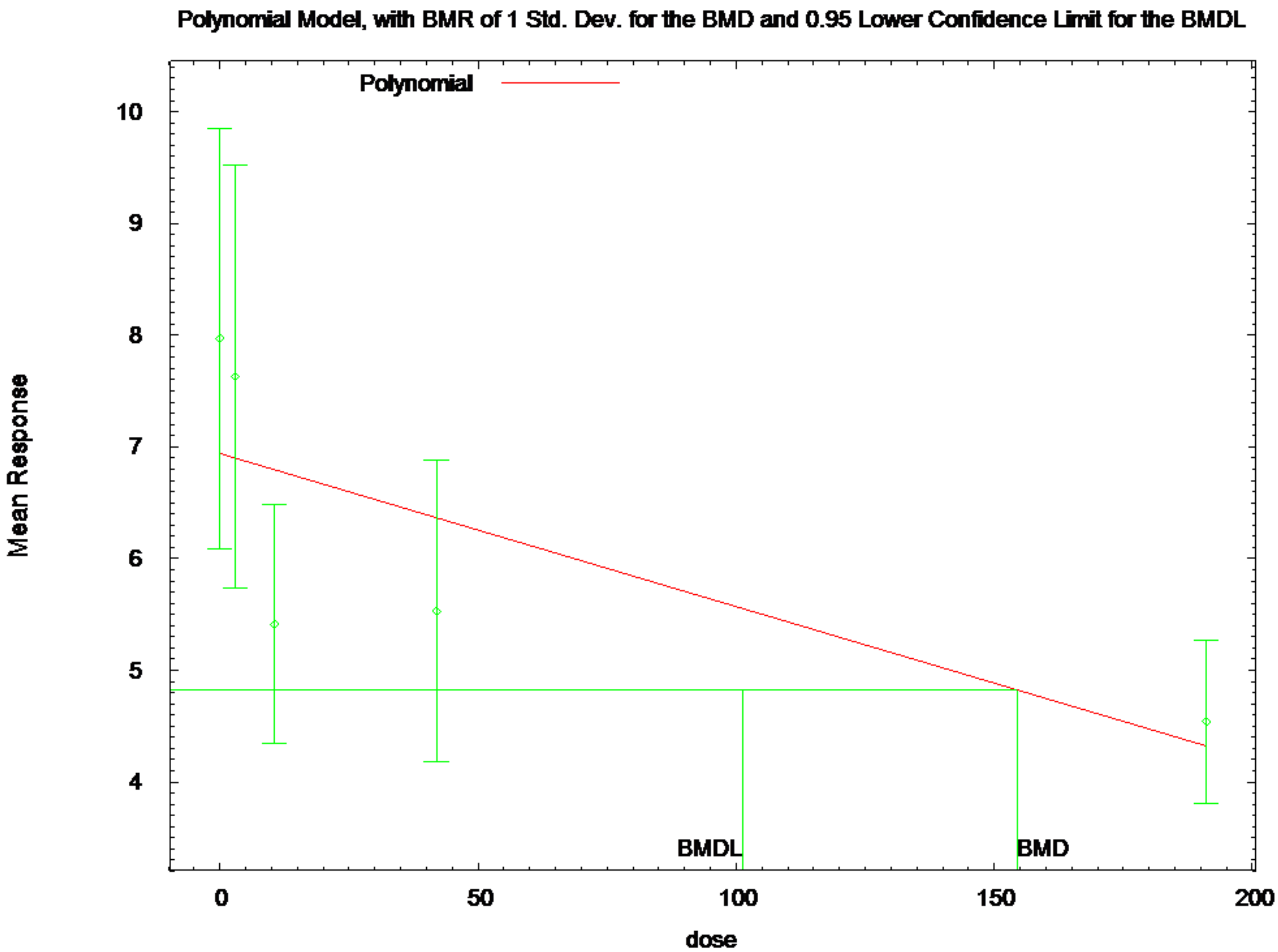
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.696

BMDL = 137.478



12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:44:57 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      8.18961
                         beta_1 =    -0.328545
                         beta_2 =            0
                         beta_3 = -3.14654e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-2.2e-008	-5.3e-008
beta_0	-2.2e-008	1	-0.56
beta_1	-5.3e-008	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	4.47634	0.91373	2.68547	6.26722
beta_0	6.93587	0.369654	6.21136	7.66038
beta_1	-0.0136993	0.00414278	-0.021819	-0.00557961
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.63	2.12	1.55
2.9	10	7.63	6.9	2.65	2.12	1.1
10.6	9	5.41	6.79	1.39	2.12	-1.96
42	9	5.53	6.36	1.76	2.12	-1.18
191.1	10	4.54	4.32	1.02	2.12	

0.332

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-59.971358	3	125.942715
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	9.87035	3	0.0197

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

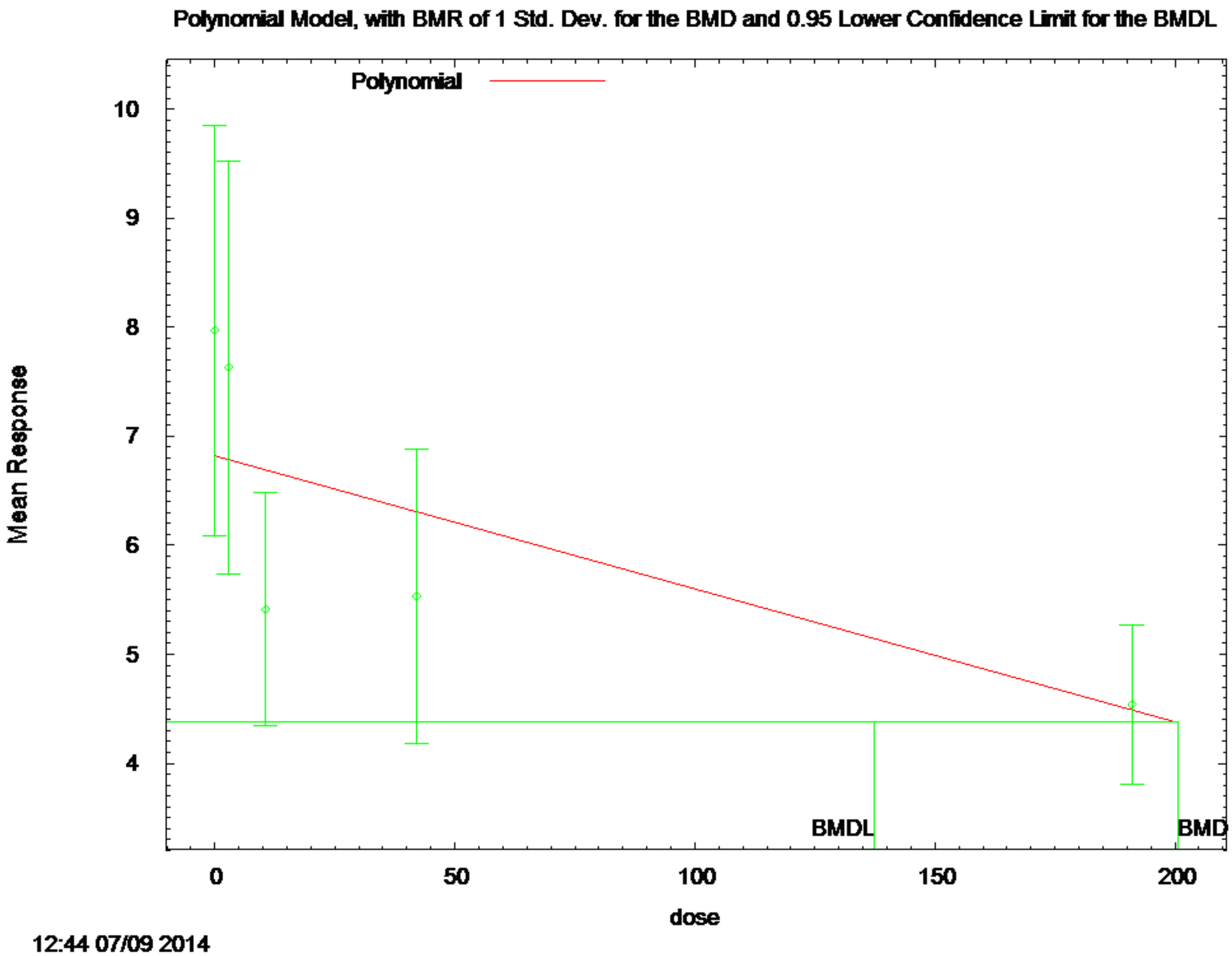
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 154.441

BMDL = 101.242


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:44:58 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      8.18961
                         beta_1 =    -0.328545
                         beta_2 =            0
                         beta_3 = -3.14654e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.046	-0.054
rho	-1	1	-0.046	0.055
beta_0	0.046	-0.046	1	-0.82
beta_1	-0.054	0.055	-0.82	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.96308	2.24713	-11.3674	-2.55879
rho	4.55432	1.23325	2.1372	6.97144
beta_0	6.82487	0.406771	6.02761	7.62212
beta_1	-0.0121567	0.00273518	-0.0175175	-0.00679584
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.82	2.63	2.44	1.48
2.9	10	7.63	6.79	2.65	2.41	1.1
10.6	9	5.41	6.7	1.39	2.34	-1.65

```
  42     9       5.53         6.31         1.76         2.04
-1.15
191.1    10       4.54          4.5         1.02        0.946
0.128
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-55.234090	4	118.468180
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357

Test 4	12.0391	3	0.00725

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

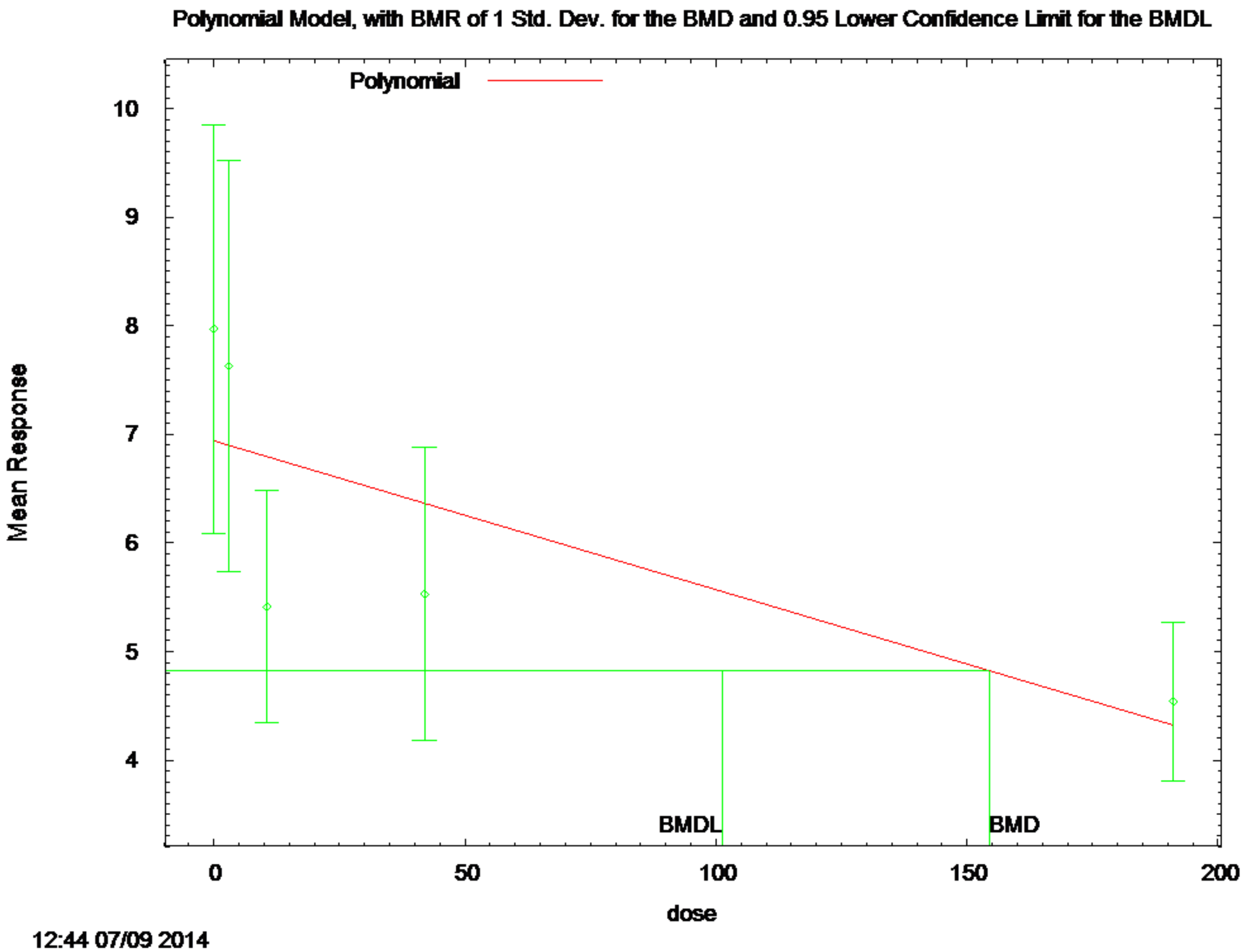
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.696

BMDL = 137.478


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
50
100
150
200
12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:44:56 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =         7.97
                         beta_1 =   -0.0490906
                         beta_2 =   -0.0256112
                         beta_3 =            0
                         beta_4 = -3.15099e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	5.3e-008	7.6e-009
beta_0	5.3e-008	1	-0.56
beta_1	7.6e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	4.47634	0.91373	2.68547	6.26722
beta_0	6.93587	0.369654	6.21136	7.66038
beta_1	-0.0136993	0.00414278	-0.021819	-0.00557961
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.63	2.12	1.55
2.9	10	7.63	6.9	2.65	2.12	1.1
10.6	9	5.41	6.79	1.39	2.12	-1.96
42	9	5.53	6.36	1.76	2.12	

-1.18						
191.1	10	4.54	4.32	1.02	2.12	
0.332						

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-59.971358	3	125.942715
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	9.87035	3	0.0197

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

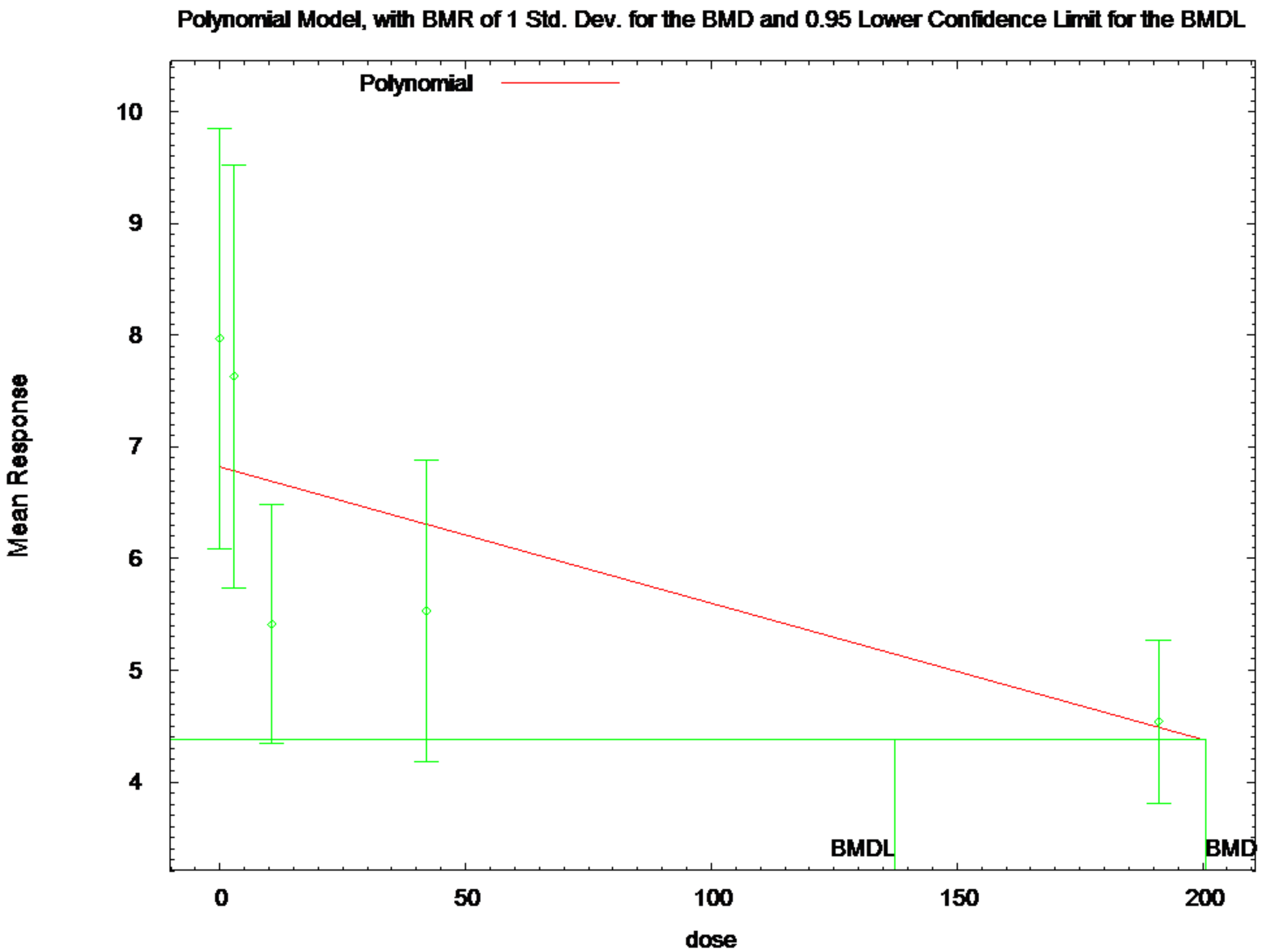
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 154.441

BMDL = 101.242



12:44 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical/WBC_Historical-HLS
2001-White Blood Cell Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:44:58 2014
=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =         7.97
                         beta_1 =   -0.0490906
                         beta_2 =   -0.0256112
                         beta_3 =            0
                         beta_4 = -3.15099e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-1	0.046	-0.054
rho	-1	1	-0.046	0.055
beta_0	0.046	-0.046	1	-0.82
beta_1	-0.054	0.055	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.96308	2.24713	-11.3674	-2.55879
rho	4.55432	1.23325	2.1372	6.97144
beta_0	6.82487	0.406771	6.02761	7.62213
beta_1	-0.0121567	0.00273517	-0.0175175	-0.00679584
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.82	2.63	2.44	1.48
2.9	10	7.63	6.79	2.65	2.41	

```
1.1
 10.6     9       5.41          6.7          1.39          2.34
-1.65
   42     9       5.53         6.31          1.76          2.04
-1.15
191.1    10       4.54          4.5          1.02         0.946
0.128
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

```
                       Likelihoods of Interest

           Model      Log(likelihood)   # Param's      AIC
            A1          -55.036182           6     122.072364
            A2          -49.003692          10     118.007385
            A3          -49.214548           7     112.429095
        fitted          -55.234090           4     118.468180
             R          -64.896924           2     133.793848
```

```
                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

```
                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	12.0391	3	0.00725

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

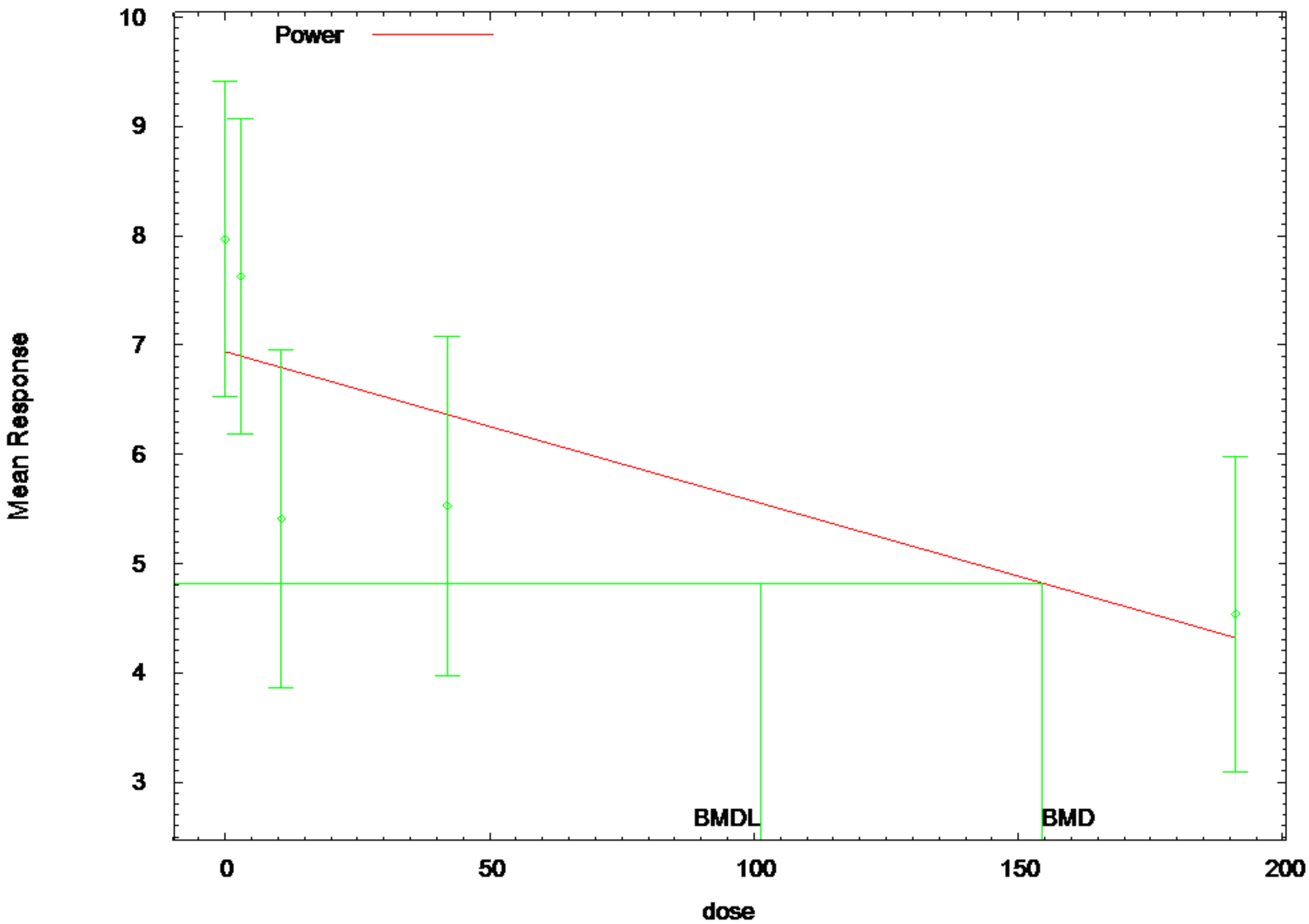
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.696

BMDL = 137.478

Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



09:34 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.plt
                                      Sun Jun 22 09:34:41 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                        control =         4.54
                          slope =       3.7818
                          power =    -0.420444


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	4e-009	-8.1e-010
control	4e-009	1	-0.56
slope	-8.1e-010	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	4.47634	0.91373	2.68547	6.26722
control	6.93587	0.369654	6.21136	7.66038
slope	-0.0136993	0.00414278	-0.021819	-0.00557961
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.94	2.63	2.12	1.55
2.9	10	7.63	6.9	2.65	2.12	1.1
10.6	9	5.41	6.79	1.39	2.12	-1.96
42	9	5.53	6.36	1.76	2.12	-1.18
191.1	10	4.54	4.32	1.02	2.12	0.332

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-59.971358	3	125.942715
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	9.87035	3	0.0197

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

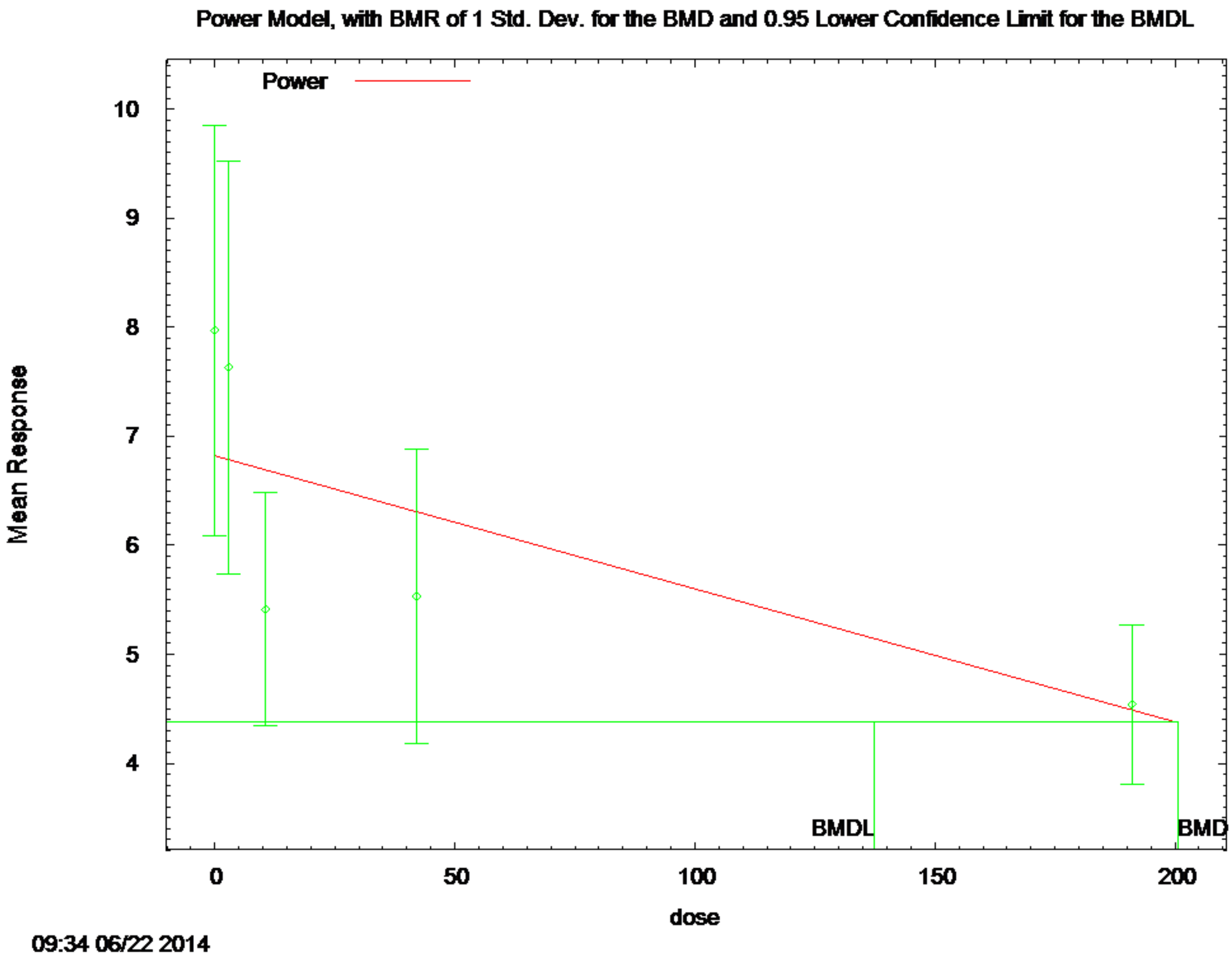
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 154.441

BMDL = 101.242


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
50
100
150
200
dose
09:34 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/WBC_Historical-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.plt
                                      Sun Jun 22 09:34:42 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                        control =         4.54
                          slope =       3.7818
                          power =    -0.420444


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-1	0.42	-0.64
rho	-1	1	-0.48	0.67
control	0.42	-0.48	1	-0.82
slope	-0.64	0.67	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-6.96308	2.98801	-12.8195	-1.10669
rho	4.55432	1.6721	1.27706	7.83158
control	6.82487	0.408449	6.02432	7.62541
slope	-0.0121567	0.00273251	-0.0175123	-0.00680106
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	6.82	2.63	2.44	1.48
2.9	10	7.63	6.79	2.65	2.41	1.1
10.6	9	5.41	6.7	1.39	2.34	-1.65
42	9	5.53	6.31	1.76	2.04	-1.15

191.1 10 4.54 4.5 1.02 0.946
0.128

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-55.234090	4	118.468180
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	12.0391	3	0.00725

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

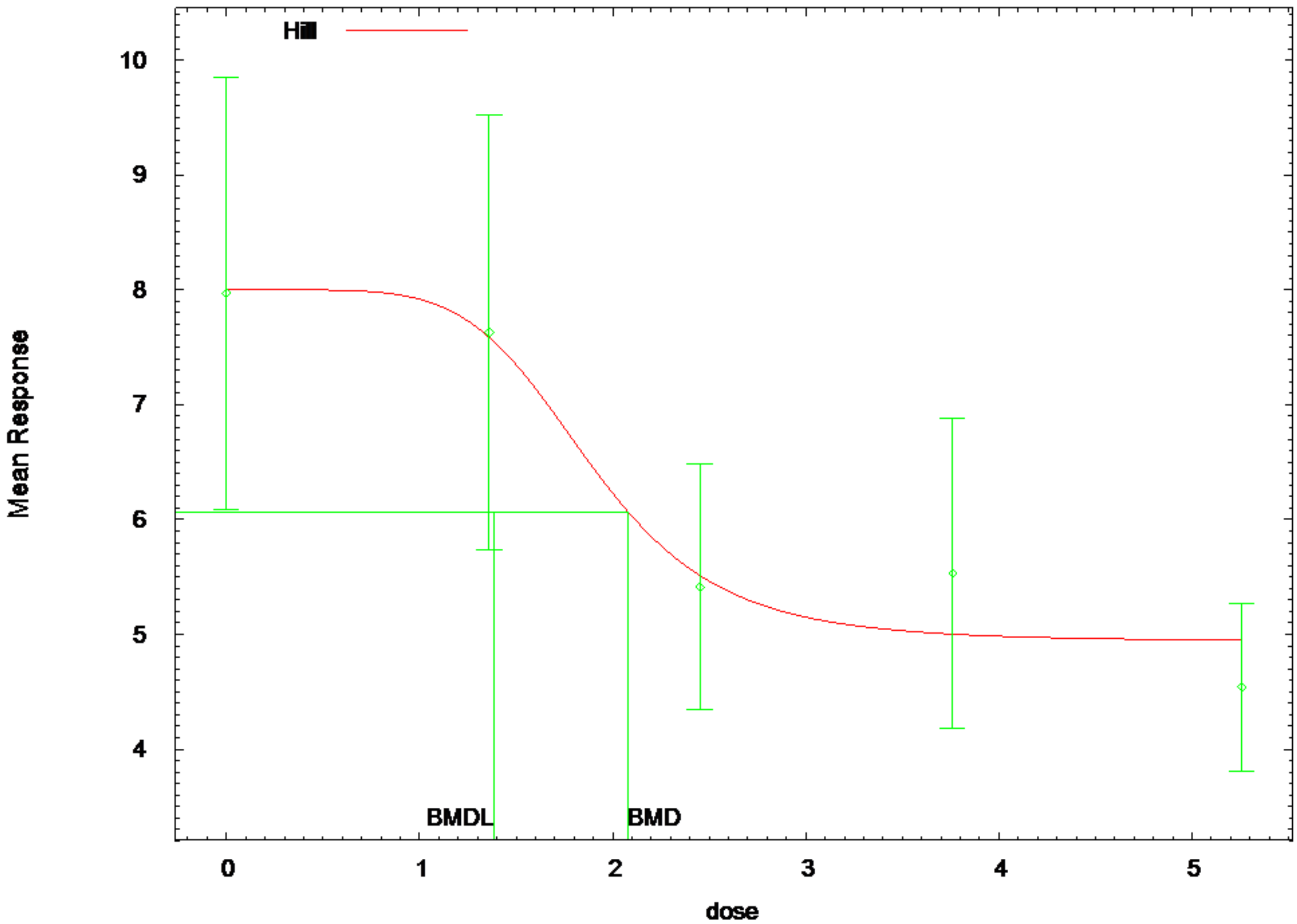
Confidence level = 0.95

BMD = 200.696

BMDL = 137.478

BMDS Model Results for White Blood Cell Count
(Log-transformed Doses, Historical Controls)

Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



09:40 06/22 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-HillCV-1SD-5d.plt
                                       Sun Jun 22 09:40:09 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                      intercept =         7.97
                              v =        -3.43
                              n =      4.25613
                              k =      2.03611


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-5.9e-008	7.1e-008	5.5e-008	6.7e-008
intercept	-5.9e-008	1	-0.78	-0.46	-0.4
v	7.1e-008	-0.78	1	0.68	-0.02
n	5.5e-008	-0.46	0.68	1	-0.1
k	6.7e-008	-0.4	-0.02	-0.1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.7342	0.76224	2.24023	5.22816
intercept	8.0005	0.601995	6.82061	9.18038
v	-3.06445	0.884065	-4.79718	-1.33171
n	5.65284	5.65725	-5.43517	16.7409
k	1.88908	0.468465	0.970902	2.80725

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	8	2.63	1.93	-0.0499

```
1.361    10       7.63         7.59         2.65         1.93
0.0731
2.451     9       5.41         5.51         1.39         1.93
-0.152
3.761     9       5.53            5         1.76         1.93
0.827
5.258    10       4.54         4.95         1.02         1.93
-0.663
```

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-55.620782	5	121.241565
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test -2*log(Likelihood Ratio) Test df p-value

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	1.1692	1	0.2796

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

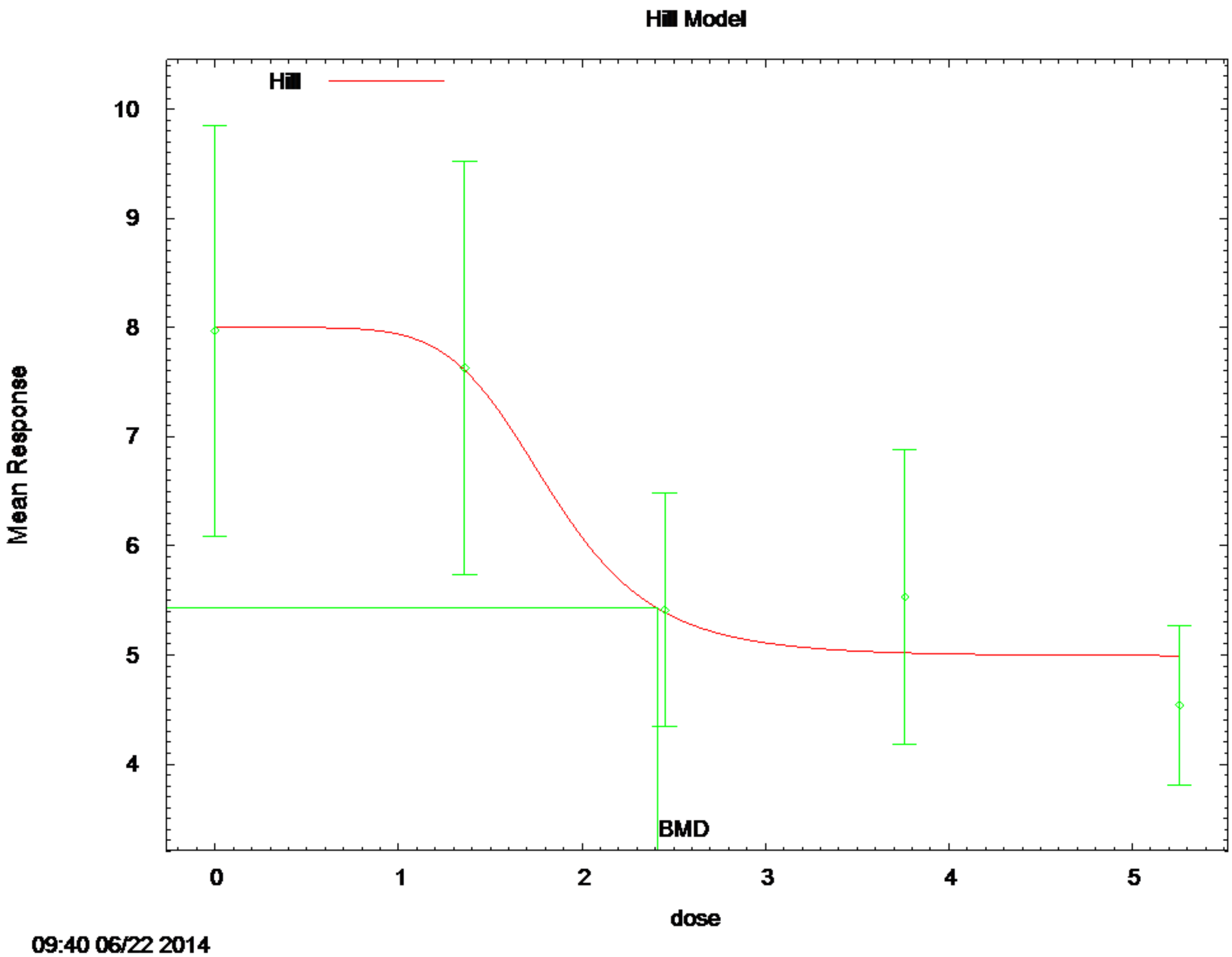
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.0765

BMDL = 1.38411



Hill Model
Hill
10
9
8
7
6
5
4
Mean Response
BMD
0
1
2
3
4
5
dose
09:40 06/22 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-HillNCV-1SD-5d.plt
                                    Sun Jun 22 09:40:10 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                      intercept =         7.97
                              v =        -3.43
                              n =      4.25613
                              k =      2.03611


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.3	-0.36	-0.054	0.024
rho	-0.99	1	-0.33	0.37	0.053	-0.023
intercept	0.3	-0.33	1	-0.92	-0.53	-0.45
v	-0.36	0.37	-0.92	1	0.7	0.27
n	-0.054	0.053	-0.53	0.7	1	0.17
k	0.024	-0.023	-0.45	0.27	0.17	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.7714	2.03099	-7.75207	0.209269
rho	2.72094	1.11924	0.527268	4.91461
intercept	8.00013	0.773538	6.48402	9.51624
v	-3.00709	0.97751	-4.92297	-1.09121
n	6.4198	7.51173	-8.30292	21.1425
k	1.83415	0.387095	1.07546	2.59284

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	8	2.63	2.57	-0.0371

```
1.361    10       7.63         7.61         2.65         2.4
0.0209
2.451     9       5.41          5.4         1.39         1.5
0.0246
3.761     9       5.53         5.02         1.76        1.36
1.12
5.258    10       4.54            5         1.02        1.35
-1.07
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.685936	6	115.371872
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	4.94278	1	0.0262

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

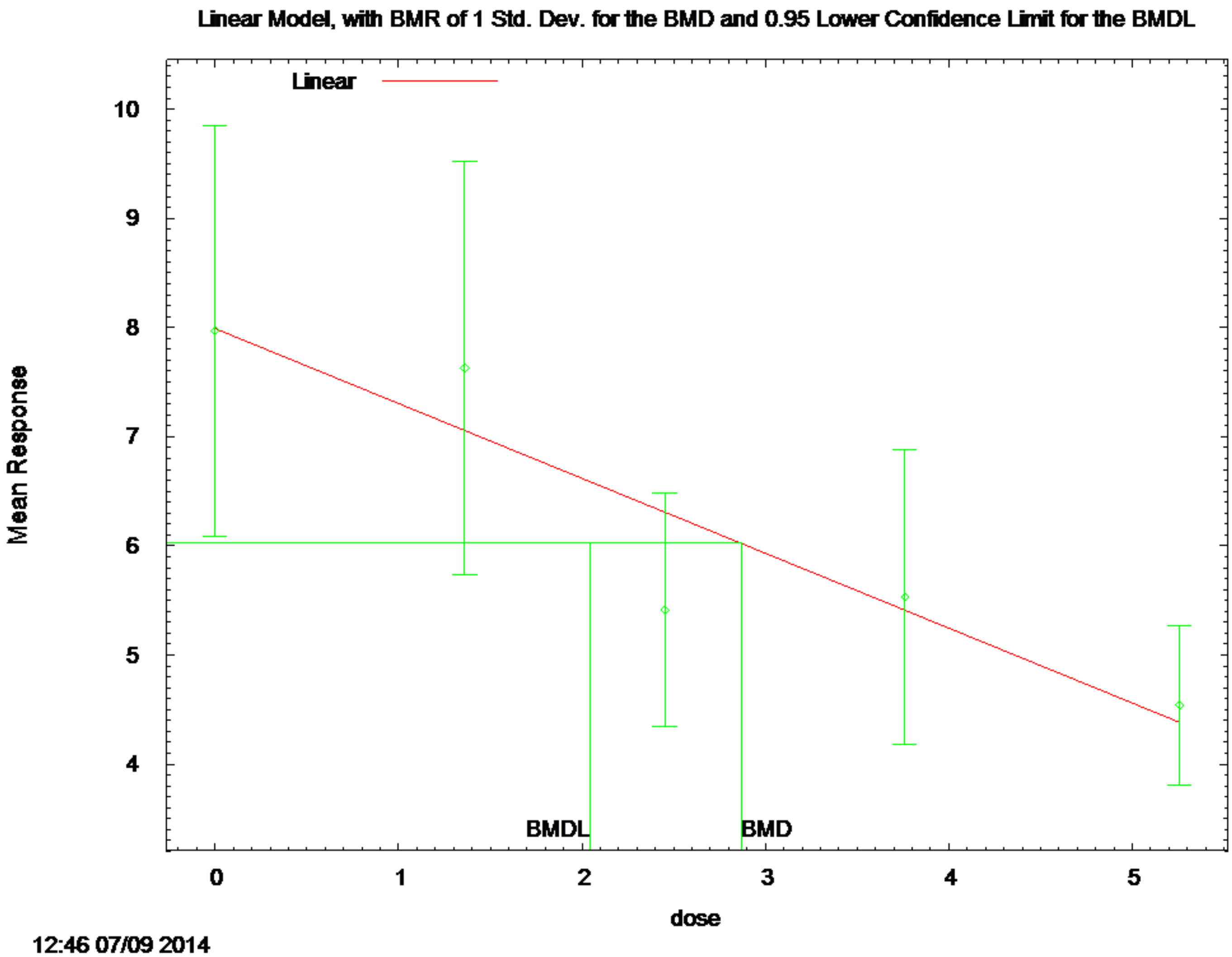
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.41554

BMDL computation failed.



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:46 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:46:34 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      7.97189
                         beta_1 =    -0.684236


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	2.1e-008	-8.7e-010
beta_0	2.1e-008	1	-0.81
beta_1	-8.7e-010	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.87222	0.790413	2.32303	5.4214
beta_0	7.9913	0.481462	7.04765	8.93494
beta_1	-0.685697	0.152832	-0.985242	-0.386152

Table of Data and Estimated Values of Interest

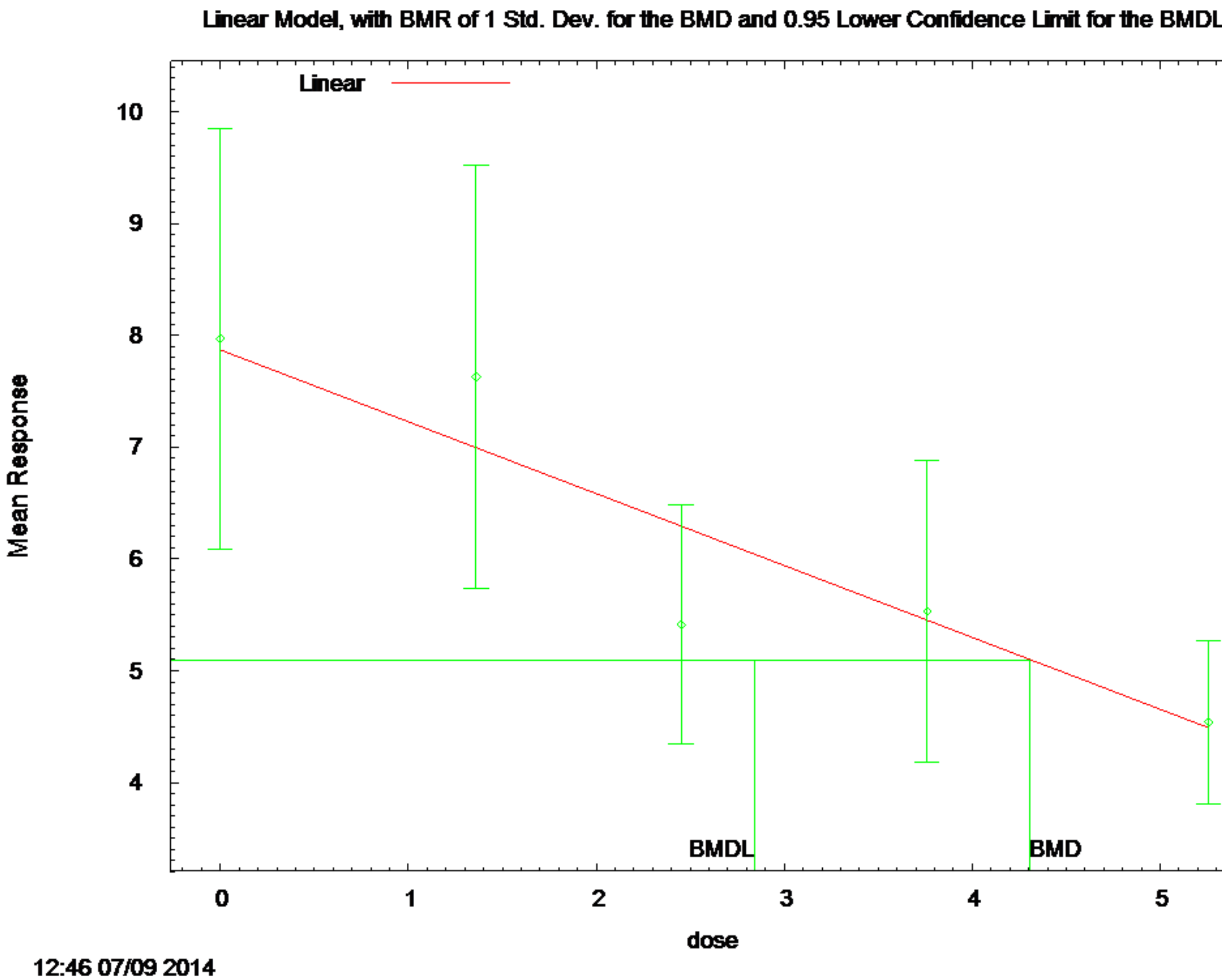
Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.63	1.97	-0.0342
1.361	10	7.63	7.06	2.65	1.97	0.919
2.451	9	5.41	6.31	1.39	1.97	-1.37
3.761	9	5.53	5.41	1.76	1.97	0.179
5.258	10	4.54	4.39	1.02	1.97	0.248

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -55.036182           6     122.072364
             A2          -49.003692          10     118.007385
             A3          -55.036182           6     122.072364
         fitted          -56.491842           3     118.983685
              R          -64.896924           2     133.793848


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              31.7865          8       0.0001017
   Test 2               12.065          4         0.01687
   Test 3               12.065          4         0.01687
   Test 4              2.91132          3          0.4055

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1.  You may want to consider
a
```

```
different variance model

The p-value for Test 4 is greater than .1.  The model chosen
seems
to adequately describe the data


             Benchmark Dose Computation

Specified effect =             1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =          0.95

             BMD =        2.86977


            BMDL =        2.04395
```



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
12:46 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:46:35 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      7.97189
                         beta_1 =    -0.684236


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99         0.13        -0.15
```

rho	-0.99	1	-0.13	0.15
beta_0	0.13	-0.13	1	-0.91
beta_1	-0.15	0.15	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.14645	1.9704	-9.00836	-1.28454
rho	3.48317	1.08261	1.3613	5.60504
beta_0	7.86568	0.562534	6.76313	8.96823
beta_1	-0.643285	0.134966	-0.907813	-0.378757

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.87	2.63	2.77	0.119
1.361	10	7.63	6.99	2.65	2.26	0.897
2.451	9	5.41	6.29	1.39	1.88	-1.41
3.761	9	5.53	5.45	1.76	1.46	0.172
5.258	10	4.54	4.48	1.02	1.04	0.172

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.789349	4	111.578698
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	5.1496	3	0.1612

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance
appears

to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

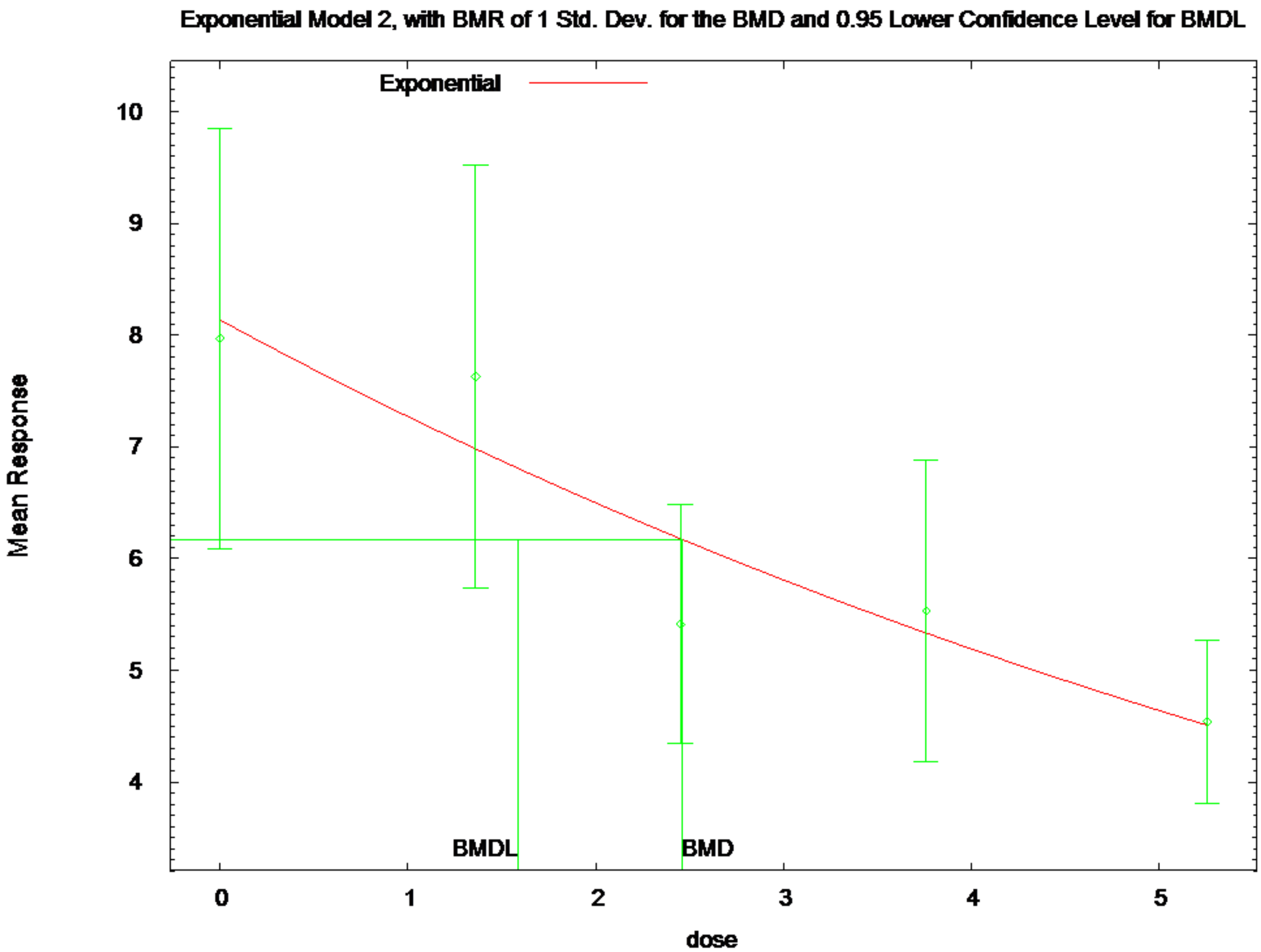
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.30585

BMDL = 2.84002



09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.29317
rho(S)	0
a	4.59625
b	0.111233
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.3495
rho	0
a	8.1349
b	0.112266
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.135	1.964	-0.2656
1.361	6.982	1.964	1.043
2.451	6.178	1.964	-1.173
3.761	5.333	1.964	0.3008
5.258	4.508	1.964	0.05142

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
2	-56.38802	3	118.776

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	

```
0.0001017
     Test 2                          12.06          4
0.01687
     Test 3                          12.06          4
0.01687
     Test 4                          2.704          3
0.4396
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

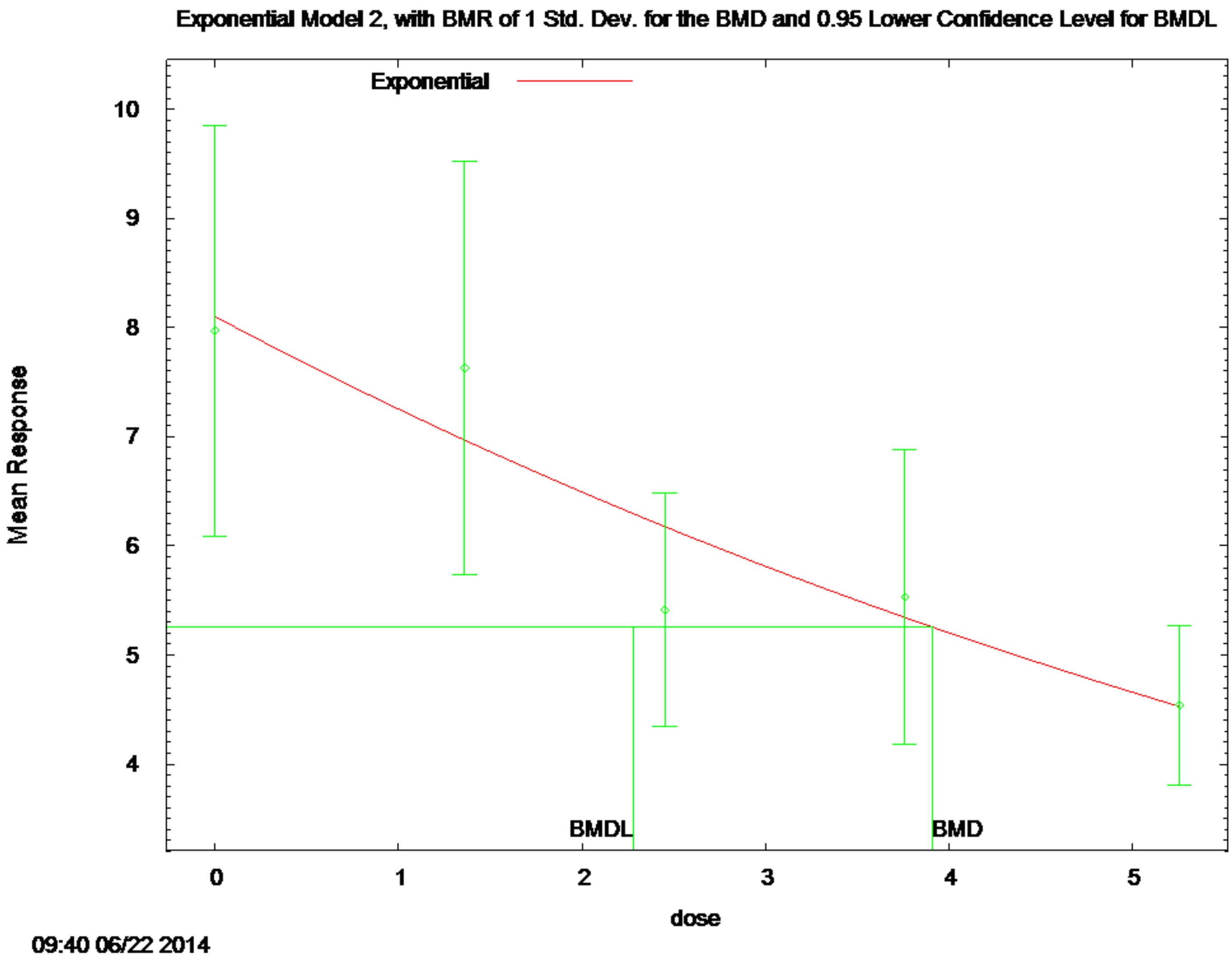
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.46063

BMDL = 1.58483


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
09:40 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:09 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-4.88417
rho	3.3405
a	4.59625
b	0.111233
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-4.84136
rho	3.31356
a	8.10018
b	0.110606
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.1	2.844	-0.1448
1.361	6.968	2.216	0.9445
2.451	6.177	1.815	-1.267
3.761	5.344	1.427	0.3918
5.258	4.528	1.085	0.03447

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
2	-51.79089	4	111.5818

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017
Test 2	12.06	4	

0.01687
Test 3 0.4217 3
0.9357
Test 4 5.153 3
0.161

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

Specified Effect = 1.000000

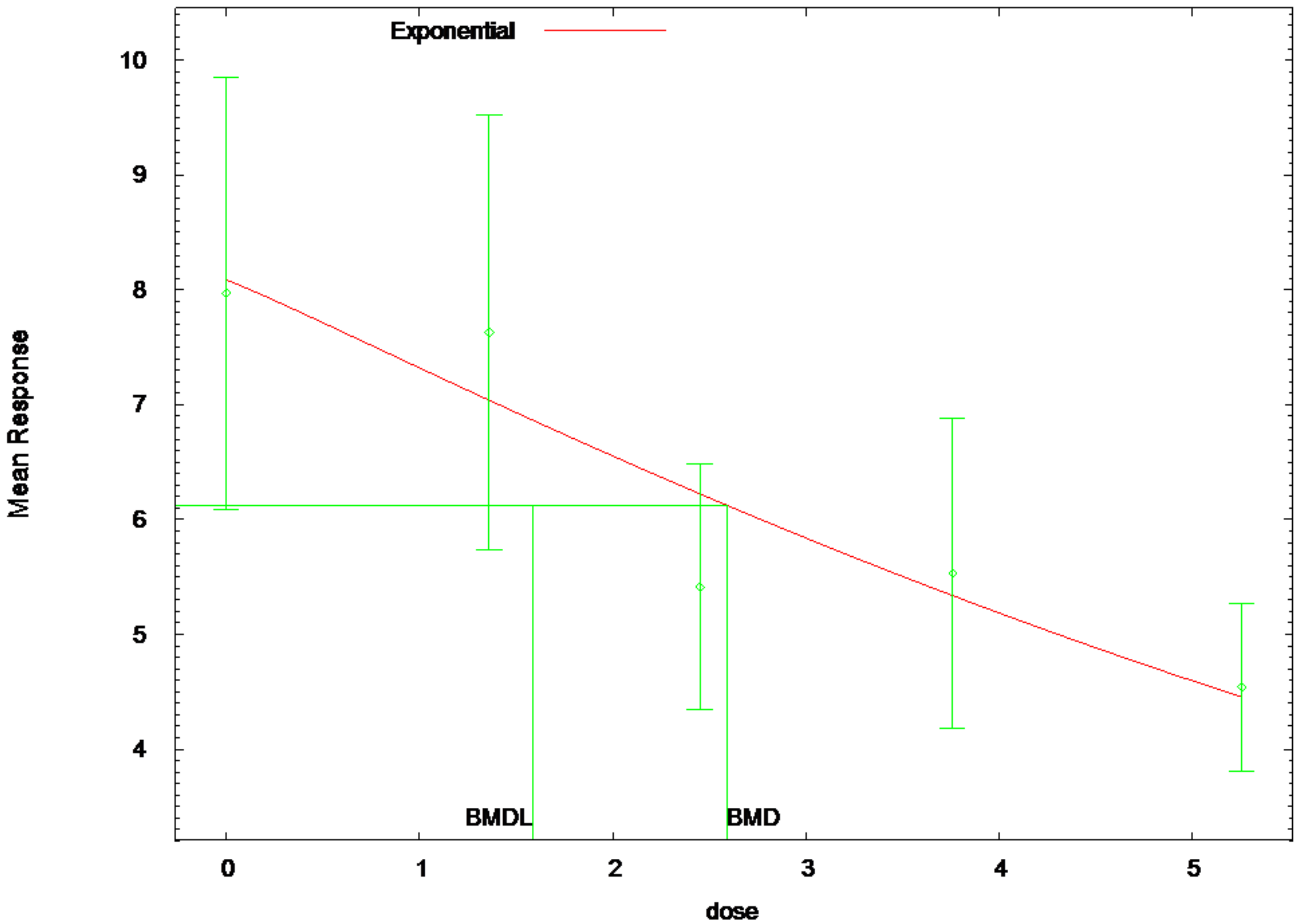
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.90961

BMDL = 2.28044

Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:40:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.29317
rho(S)	0
a	4.59625
b	0.111233
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.34879
rho	0
a	8.0841
b	0.117784
c	0
d	1.07945

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.084	1.963	-0.1838
1.361	7.038	1.963	0.9541
2.451	6.224	1.963	-1.243
3.761	5.337	1.963	0.295
5.258	4.454	1.963	0.1391

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
3	-56.37095	4	120.7419

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 5a	2.67	2	0.2632

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

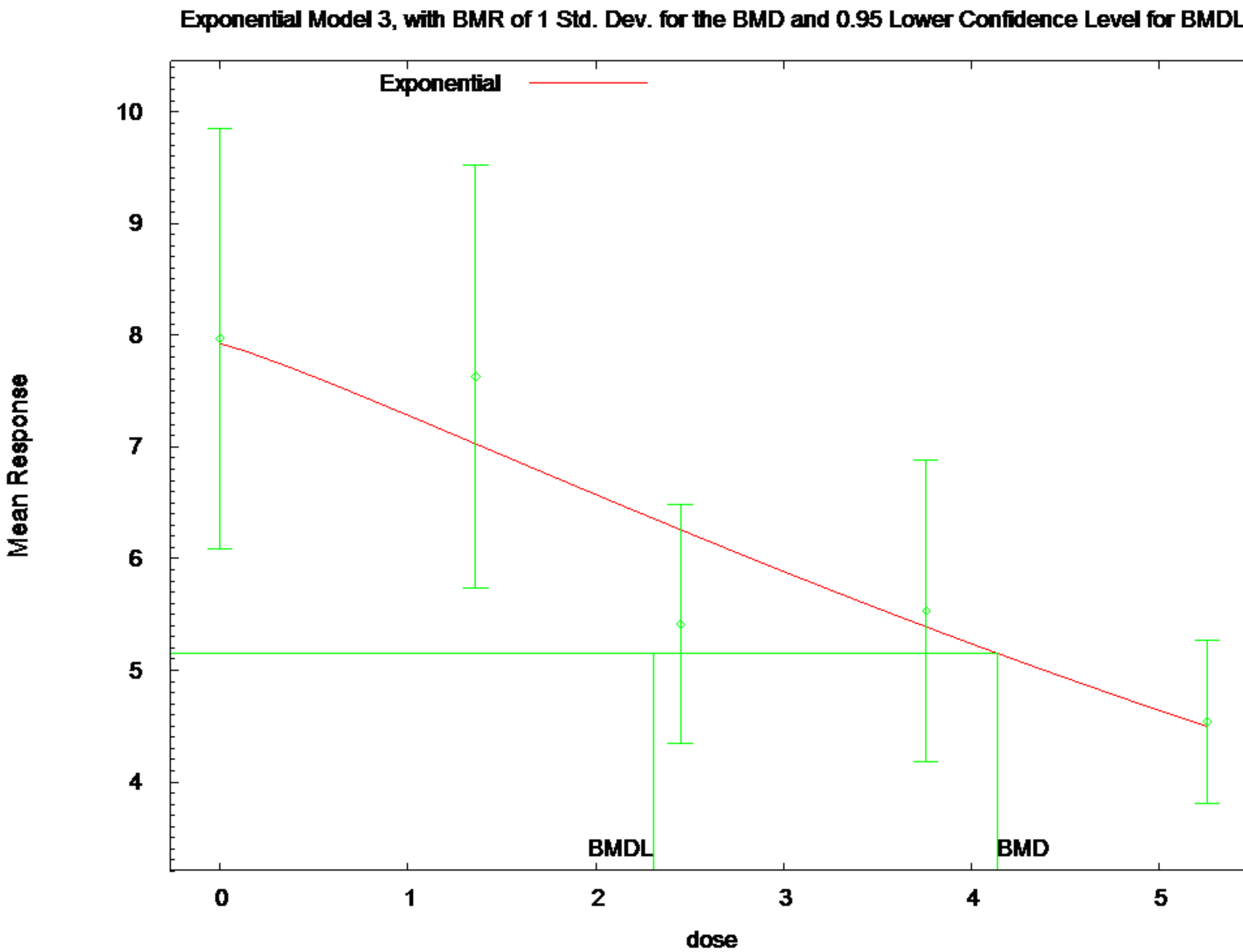
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.59459

BMDL = 1.58867



09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-4.88417
rho	3.3405
a	4.59625
b	0.111233
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-4.99941
rho	3.39998
a	7.92142
b	0.115959
c	0
d	1.14918

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.921	2.769	0.05548
1.361	7.027	2.259	0.8443
2.451	6.259	1.855	-1.372
3.761	5.388	1.438	0.2956
5.258	4.496	1.057	0.1309

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)

```
              Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
              Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
              Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
3	-51.72531	5	113.4506

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

Test 2	12.06	4	0.01687
Test 3	0.4217	3	0.9357
Test 5a	5.022	2	0.08121

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

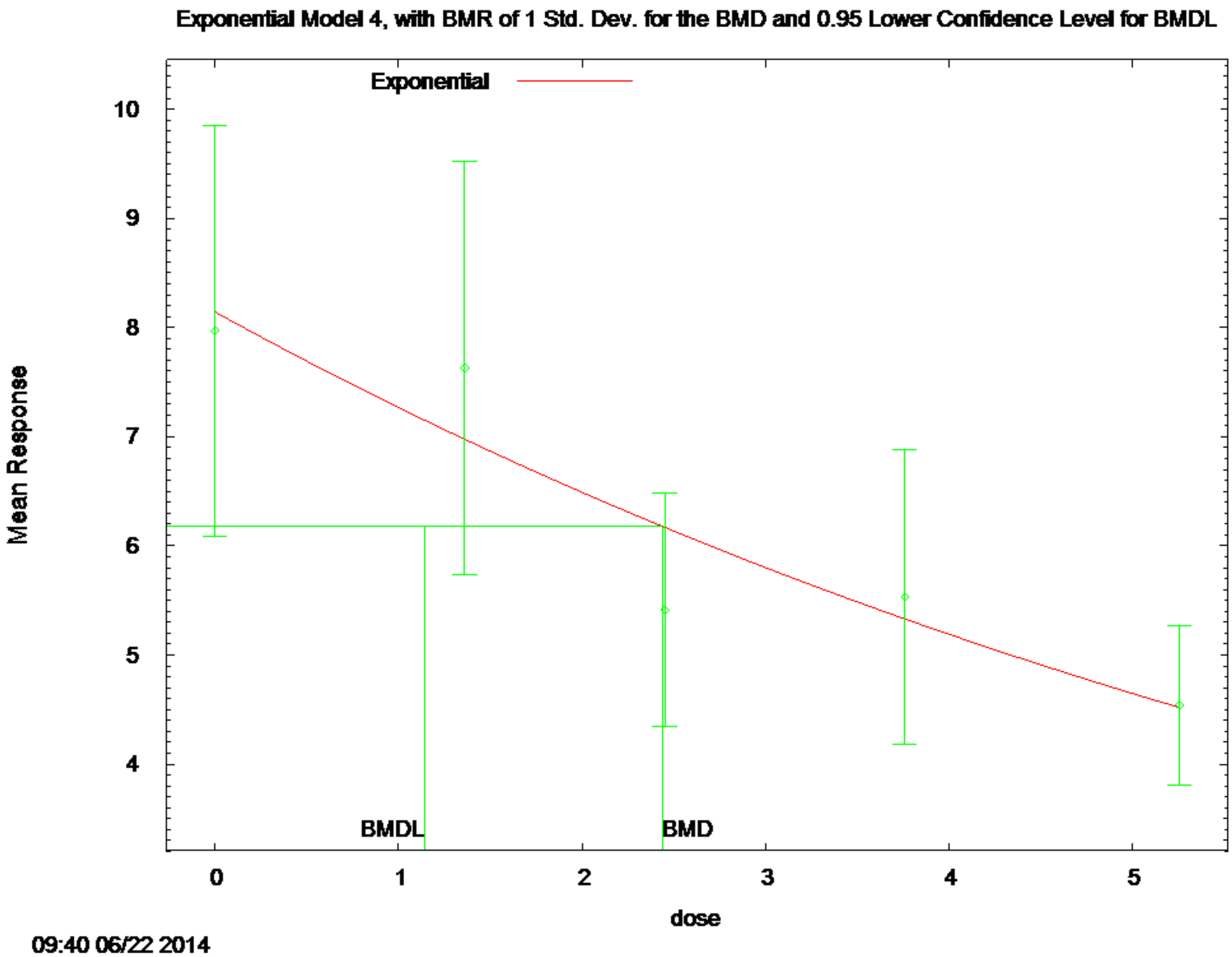
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 4.13868

BMDL = 2.30726


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.29317
rho(S)	0
a	8.3685
b	0.188405
c	0.271255
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.34948
rho	0
a	8.14254
b	0.119801
c	0.0476544
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.143	1.964	-0.2779
1.361	6.976	1.964	1.053
2.451	6.169	1.964	-1.16
3.761	5.33	1.964	0.306
5.258	4.518	1.964	0.03482

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
4	-56.3876	4	120.7752

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 6a	2.703	2	0.2589

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

Specified Effect = 1.000000

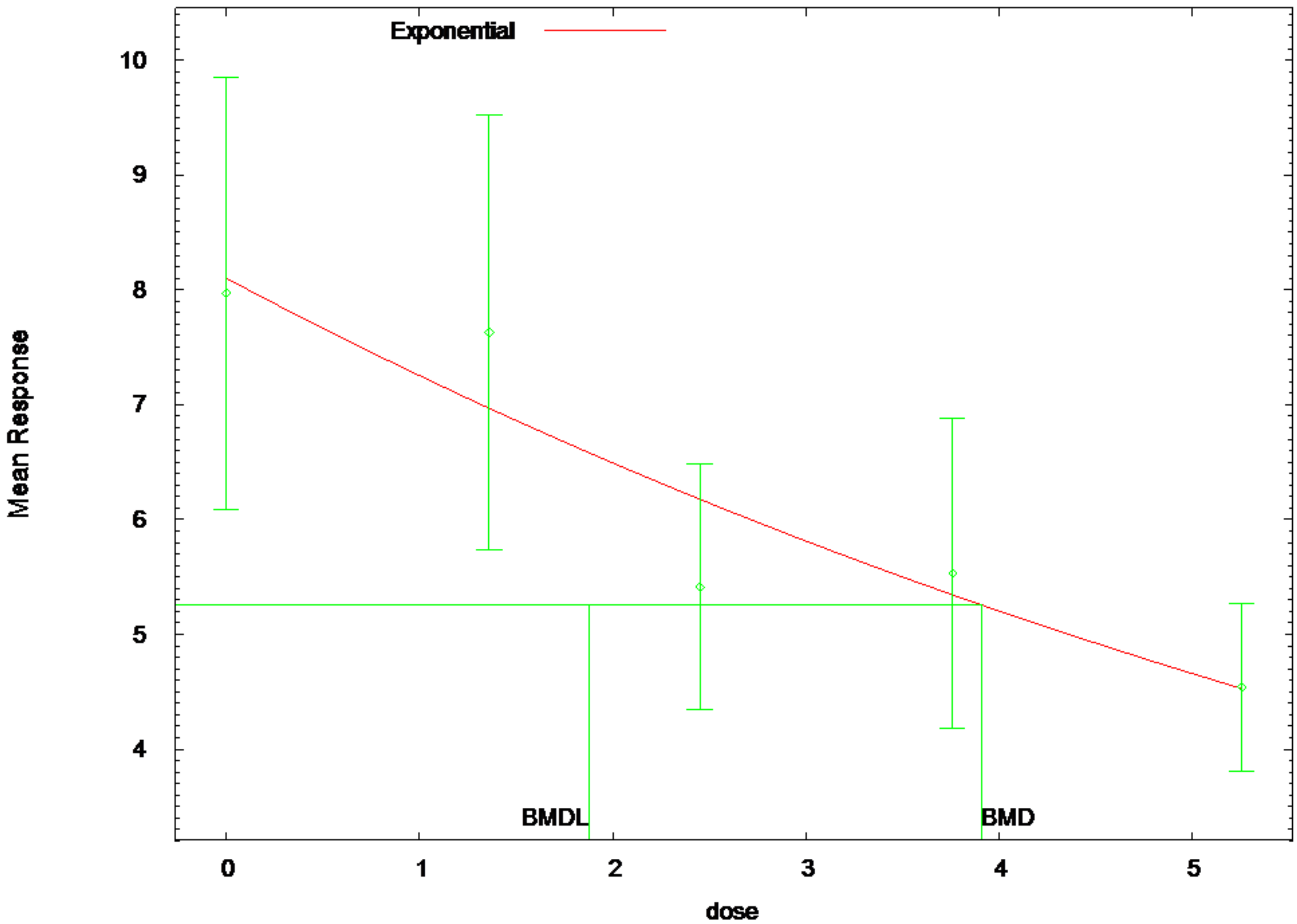
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.43714

BMDL = 1.14153

Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-4.88417
rho	3.3405
a	8.3685
b	0.140289
c	0.108502
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-4.84136
rho	3.31356
a	8.10018
b	0.110606
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	8.1	2.844	-0.1448
1.361	6.968	2.216	0.9445
2.451	6.177	1.815	-1.267
3.761	5.344	1.427	0.3918
5.258	4.528	1.085	0.03447

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
4	-51.79089	4	111.5818

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

Test 2	12.06	4	0.01687
Test 3	0.4217	3	0.9357
Test 6a	5.153	3	0.161

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

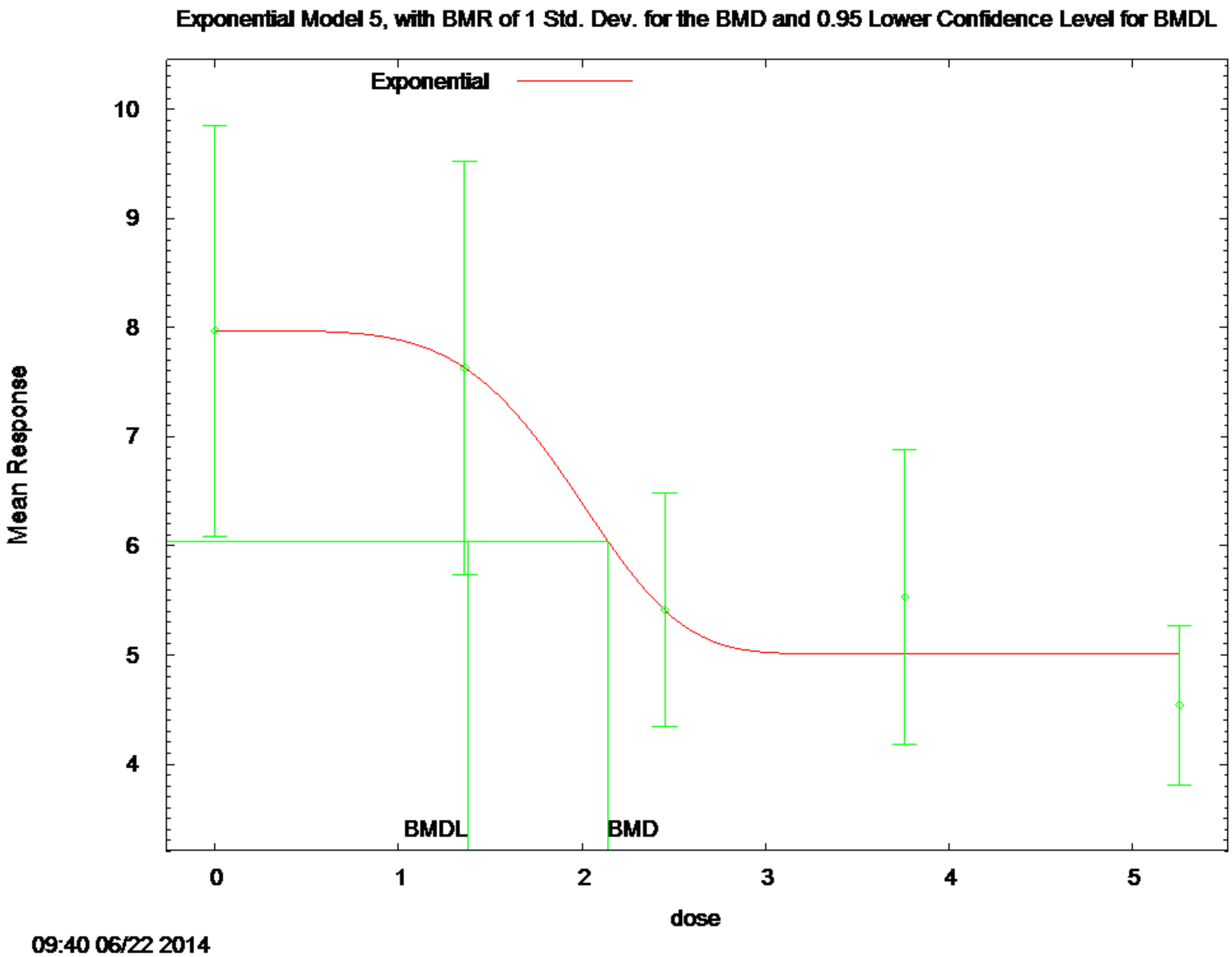
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.90961

BMDL = 1.87854


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
09:40 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.29317
rho(S)	0
a	8.3685
b	0.188405
c	0.271255
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.31937
rho	0
a	7.97001
b	0.471998
c	0.628474
d	4.754

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.97	1.934	-1.275e-005
1.361	7.63	1.934	1.8e-005
2.451	5.41	1.934	-1.795e-005
3.761	5.009	1.934	0.8082
5.258	5.009	1.934	-0.7667

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-55.03618	6	122.0724
R	-64.89692	2	133.7938
5	-55.66483	5	121.3297

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.79	8	0.0001017
Test 2	12.06	4	0.01687
Test 3	12.06	4	0.01687
Test 7a	1.257	1	0.2622

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

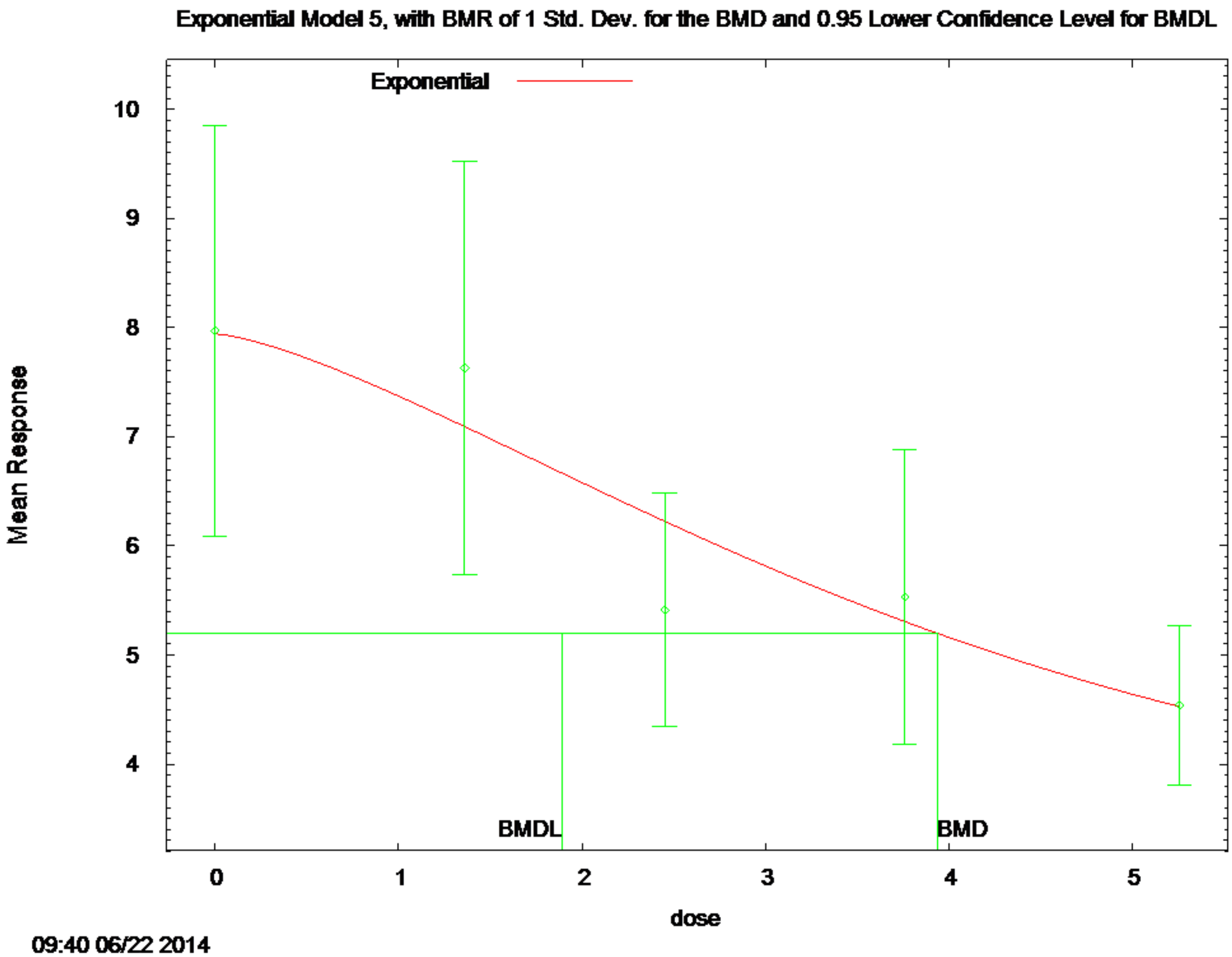
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.14436

BMDL = 1.37587



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
09:40 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:40:09 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-4.88417
rho	3.3405
a	8.3685
b	0.140289
c	0.108502
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-4.83301
rho	3.30719
a	7.94216
b	0.240307
c	0.427483
d	1.40851

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	7.97	2.626
1.361	10	7.63	2.653
2.451	9	5.41	1.392
3.761	9	5.53	1.756
5.258	10	4.54	1.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.942	2.746	0.03206
1.361	7.091	2.277	0.7483
2.451	6.224	1.835	-1.331
3.761	5.305	1.409	0.4781
5.258	4.527	1.084	0.03666

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-55.03618	6	122.0724
A2	-49.00369	10	118.0074
A3	-49.21455	7	112.4291
R	-64.89692	2	133.7938
5	-51.68357	6	115.3671

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

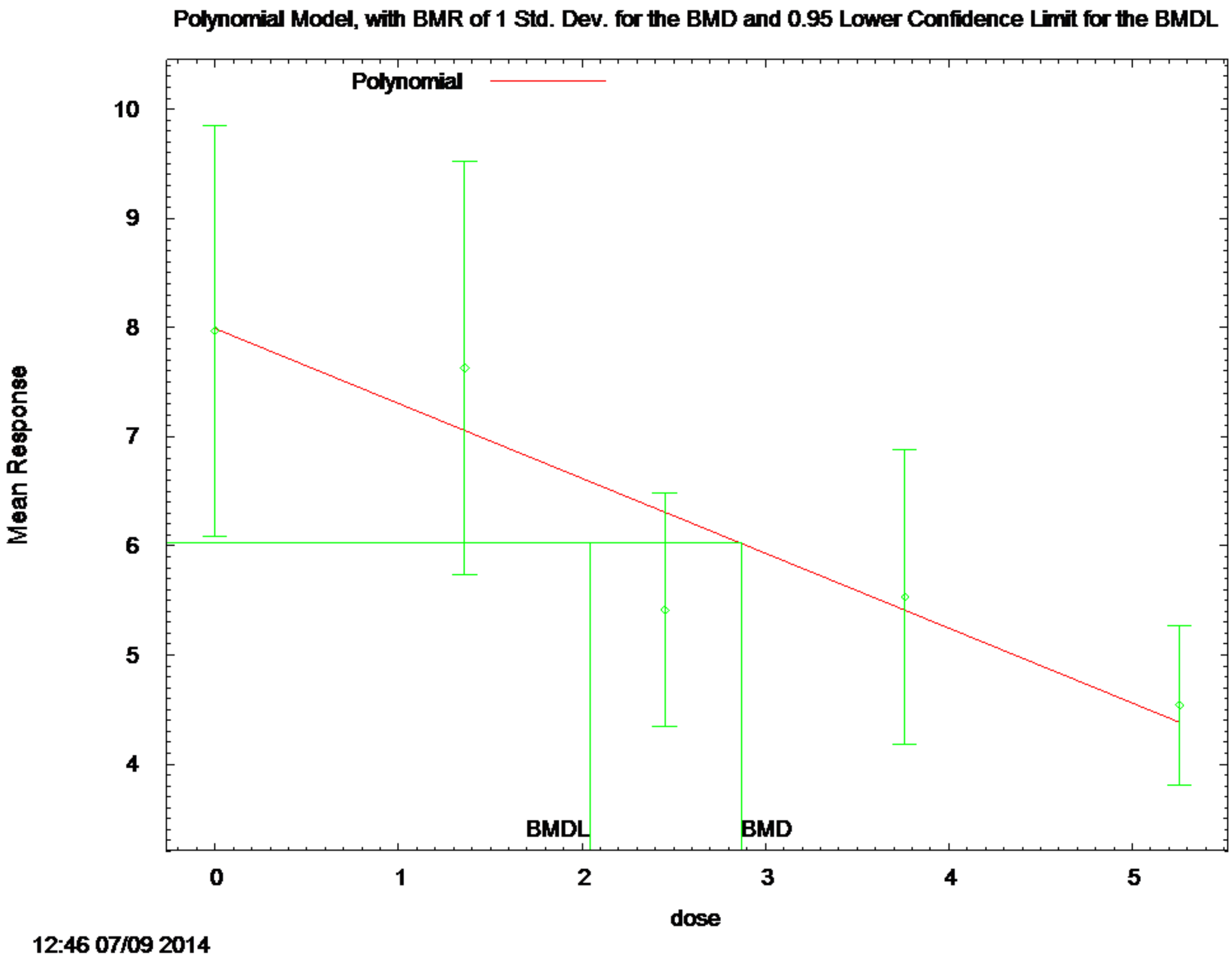
Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.79	8	0.0001017

```
     Test 2                          12.06          4
0.01687
     Test 3                         0.4217          3
0.9357
    Test 7a                          4.938          1
0.02627


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 7a is less than .1.  Model 5 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =       3.9402

                 BMDL =       1.8945
```


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
10
9
8
7
6
5
4
Mean Response
BMDL
BMD
0
1
2
3
4
5
dose
12:46 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:46:34 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      8.15662
                         beta_1 =    -0.952983
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	6.3e-008	-5.3e-008
beta_0	6.3e-008	1	-0.81
beta_1	-5.3e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.87221	0.790412	2.32303	5.42139
beta_0	7.9913	0.481462	7.04765	8.93494
beta_1	-0.685697	0.152832	-0.985242	-0.386152
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.63	1.97	-0.0342
1.361	10	7.63	7.06	2.65	1.97	0.919
2.451	9	5.41	6.31	1.39	1.97	-1.37
3.761	9	5.53	5.41	1.76	1.97	0.179
5.258	10	4.54	4.39	1.02	1.97	0.248

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-56.491842	3	118.983685
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	2.91132	3	0.4055

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

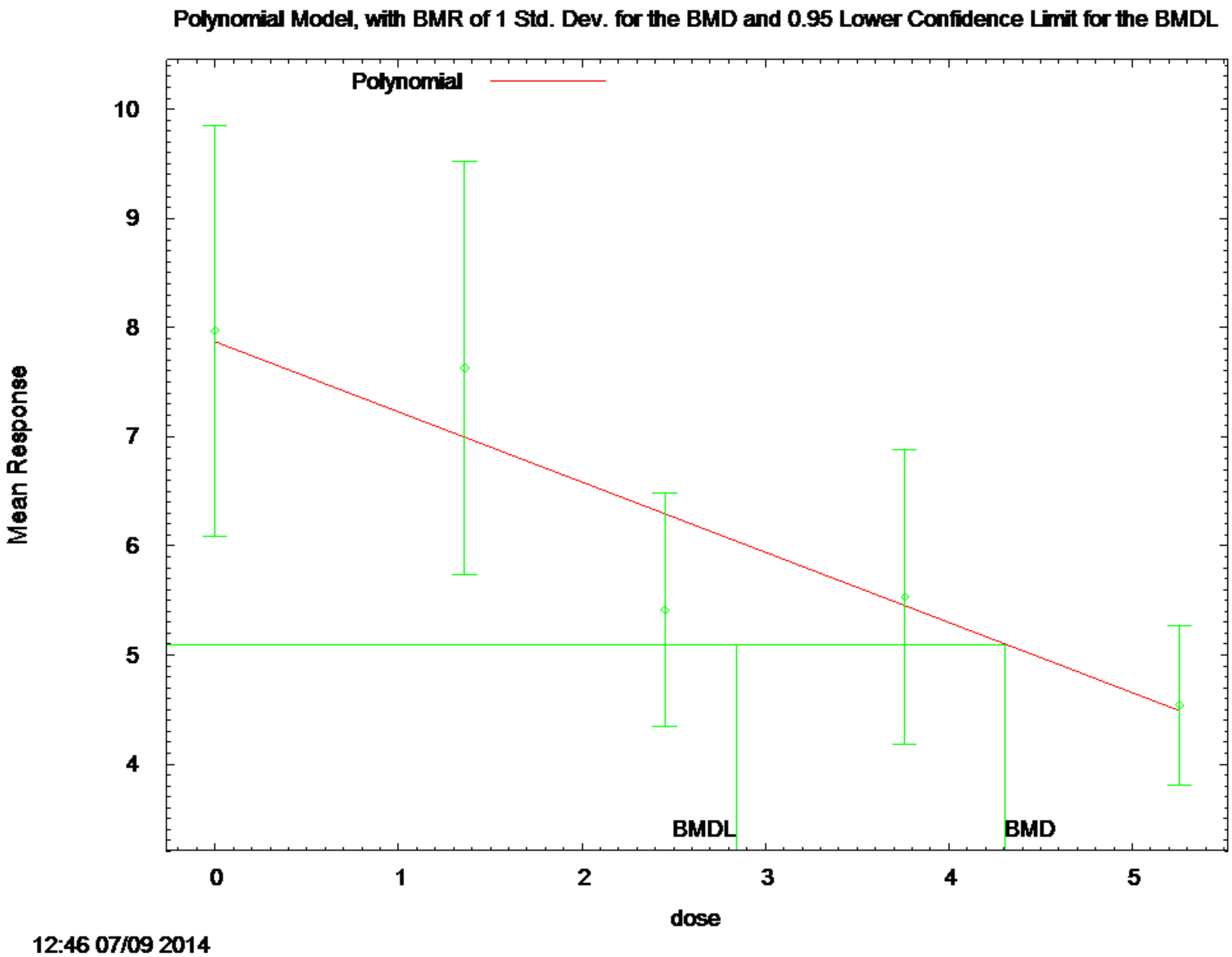
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.86977

BMDL = 2.04395


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
12:46 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:46:35 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      8.15662
                         beta_1 =    -0.952983
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.13	-0.15
rho	-0.99	1	-0.13	0.15
beta_0	0.13	-0.13	1	-0.91
beta_1	-0.15	0.15	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.14645	1.9704	-9.00836	-1.28454
rho	3.48317	1.08261	1.3613	5.60504
beta_0	7.86568	0.562534	6.76313	8.96823
beta_1	-0.643285	0.134966	-0.907813	-0.378757
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.87	2.63	2.77	0.119
1.361	10	7.63	6.99	2.65	2.26	0.897
2.451	9	5.41	6.29	1.39	1.88	-1.41
3.761	9	5.53	5.45	1.76	1.46	0.172

5.258 10 4.54 4.48 1.02 1.04
0.172

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.789349	4	111.578698
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	5.1496	3	0.1612

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

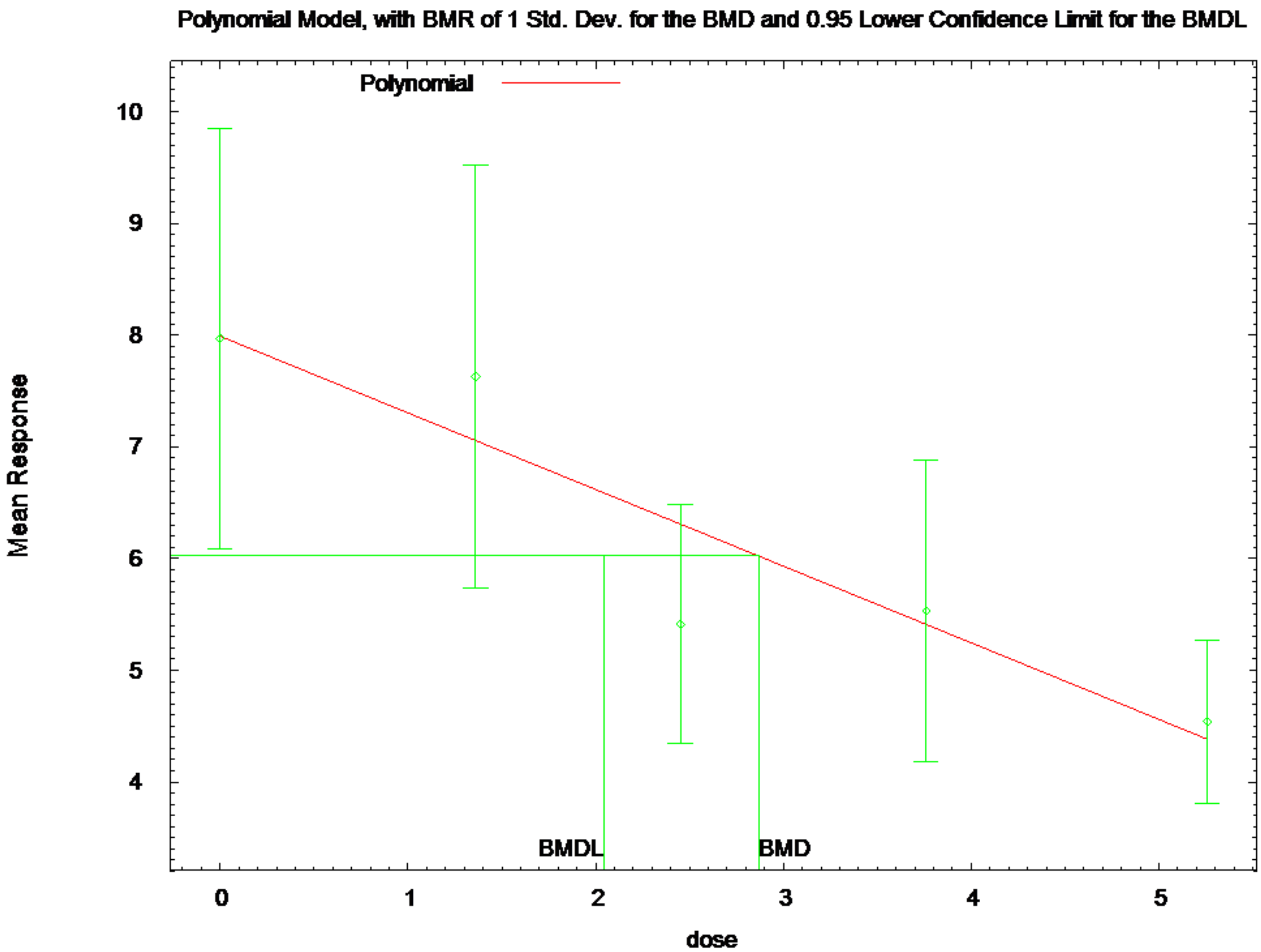
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.30585

BMDL = 2.84002



12:46 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:46:34 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =      8.07952
                         beta_1 =    -0.517572
                         beta_2 =    -0.184335
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.5e-008	-2.4e-008
beta_0	1.5e-008	1	-0.81
beta_1	-2.4e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.87222	0.790413	2.32303	5.4214
beta_0	7.9913	0.481462	7.04765	8.93494
beta_1	-0.685697	0.152832	-0.985242	-0.386152
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.63	1.97	-0.0342
1.361	10	7.63	7.06	2.65	1.97	0.919
2.451	9	5.41	6.31	1.39	1.97	-1.37
3.761	9	5.53	5.41	1.76	1.97	0.179
5.258	10	4.54	4.39	1.02	1.97	

0.248

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-56.491842	3	118.983685
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	2.91132	3	0.4055

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

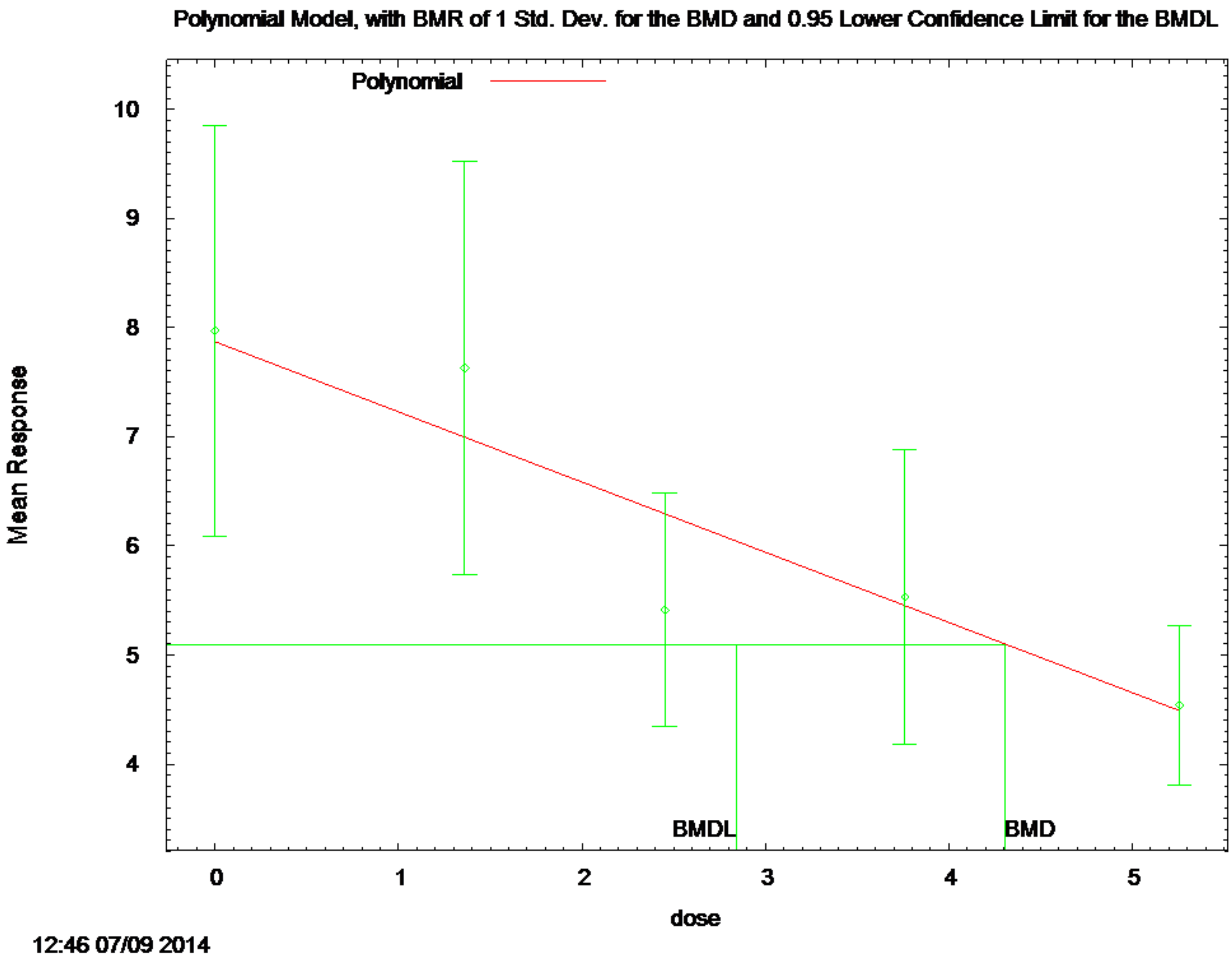
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.86977

BMDL = 2.04395



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:46 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:46:35 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =      8.07952
                         beta_1 =    -0.517572
                         beta_2 =    -0.184335
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.13	-0.15
rho	-0.99	1	-0.13	0.15
beta_0	0.13	-0.13	1	-0.91
beta_1	-0.15	0.15	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.14645	1.9704	-9.00836	-1.28453
rho	3.48317	1.08261	1.3613	5.60504
beta_0	7.86568	0.562534	6.76313	8.96823
beta_1	-0.643285	0.134966	-0.907813	-0.378757
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.87	2.63	2.77	0.119
1.361	10	7.63	6.99	2.65	2.26	0.897
2.451	9	5.41	6.29	1.39	1.88	-1.41

3.761	9	5.53	5.45	1.76	1.46	0.172
5.258	10	4.54	4.48	1.02	1.04	0.172

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.789349	4	111.578698
R	-64.896924	2	133.793848

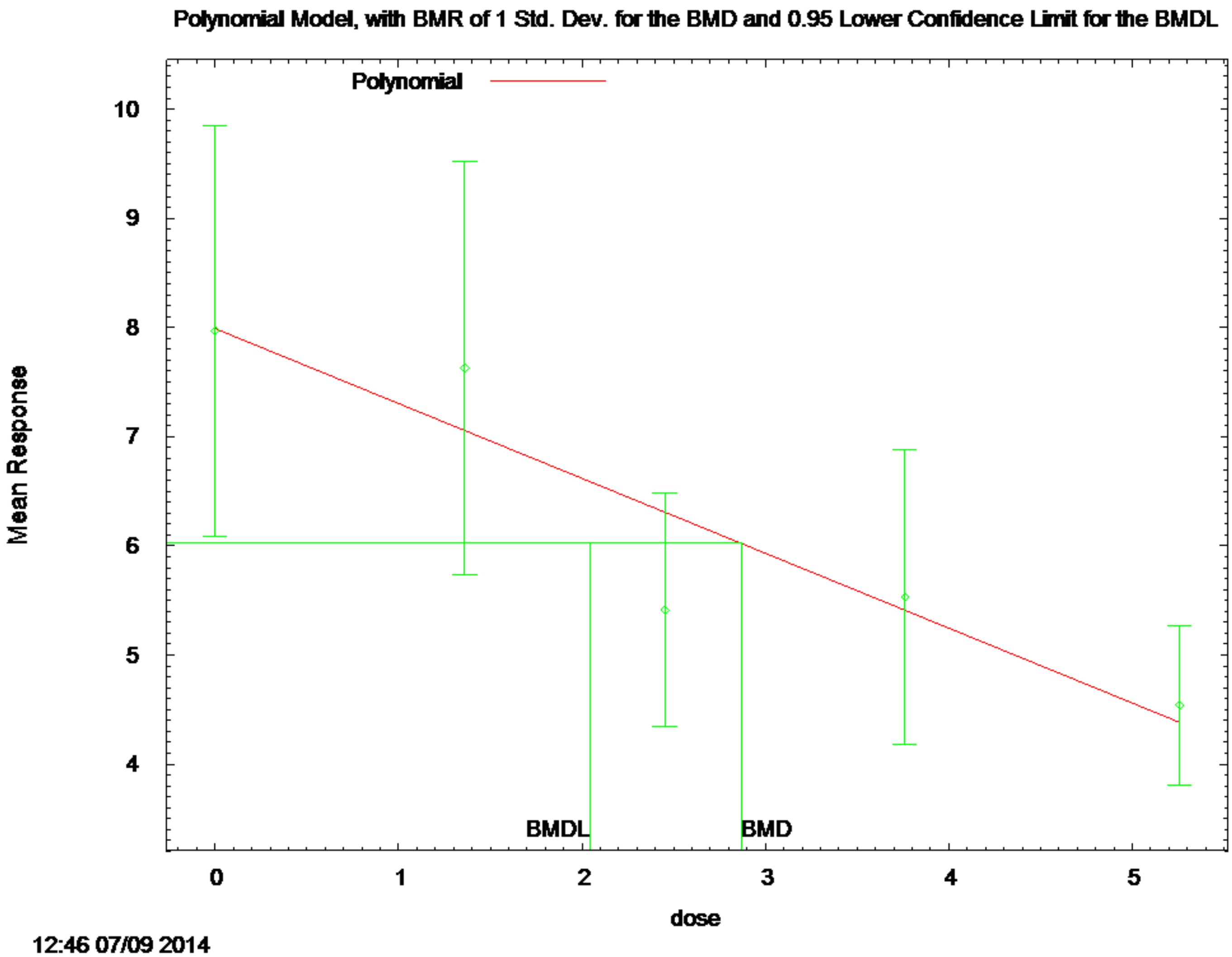
Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357

```
   Test 4              5.1496          3          0.1612

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance
appears
 to be appropriate here

The p-value for Test 4 is greater than .1.  The model chosen
seems
to adequately describe the data


             Benchmark Dose Computation

Specified effect =            1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =         0.95

             BMD =        4.30585


            BMDL =        2.84002
```


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
1
2
3
4
5
dose
12:46 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:46:34 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                         beta_0 =         7.97
                         beta_1 =            0
                         beta_2 =     -4.80701
                         beta_3 =            0
                         beta_4 =    -0.138078


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-9.6e-009	-1.9e-009
beta_0	-9.6e-009	1	-0.81
beta_1	-1.9e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.87222	0.790413	2.32303	5.4214
beta_0	7.9913	0.481462	7.04765	8.93494
beta_1	-0.685697	0.152832	-0.985242	-0.386152
beta_2	-1.61465e-138	NA		
beta_3	-1.41684e-143	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.63	1.97	-0.0342
1.361	10	7.63	7.06	2.65	1.97	0.919
2.451	9	5.41	6.31	1.39	1.97	-1.37
3.761	9	5.53	5.41	1.76	1.97	

0.179
5.258   10   4.54   4.39   1.02   1.97
0.248

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-56.491842	3	118.983685
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	2.91132	3	0.4055

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

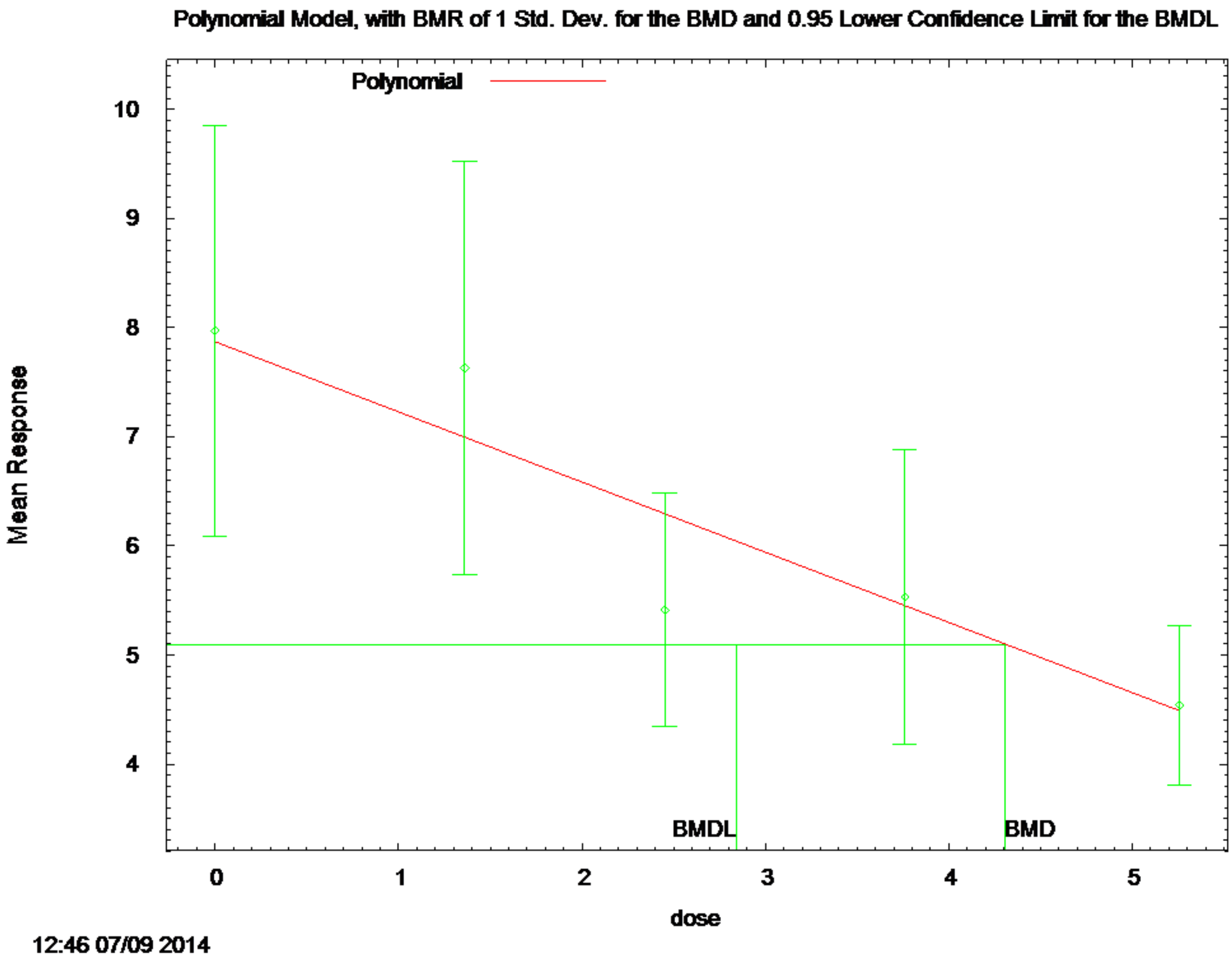
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.86977

BMDL = 2.04395



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
10
9
8
7
6
5
4
0
1
2
3
4
5
12:46 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_WBC_Historical_Ln/WBC_Historical_L
n-HLS 2001-White Blood Cell Count-Poly4NCV-1SD-5d.plt
                                        Wed Jul 09 12:46:35 2014
====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                         beta_0 =         7.97
                         beta_1 =            0
                         beta_2 =     -4.80701
                         beta_3 =            0
                         beta_4 =    -0.138078


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.13	-0.15
rho	-0.99	1	-0.13	0.15
beta_0	0.13	-0.13	1	-0.91
beta_1	-0.15	0.15	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.14645	1.9704	-9.00837	-1.28453
rho	3.48317	1.08261	1.3613	5.60505
beta_0	7.86568	0.562535	6.76313	8.96823
beta_1	-0.643285	0.134966	-0.907814	-0.378757
beta_2	0	NA		
beta_3	0	NA		
beta_4	-6.97218e-107	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.87	2.63	2.77	0.119
1.361	10	7.63	6.99	2.65	2.26	

```
0.897
2.451     9       5.41         6.29         1.39         1.88
-1.41
3.761     9       5.53         5.45         1.76         1.46
0.172
5.258    10       4.54         4.48         1.02         1.04
0.172
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.789349	4	111.578698
R	-64.896924	2	133.793848

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	5.1496	3	0.1612

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

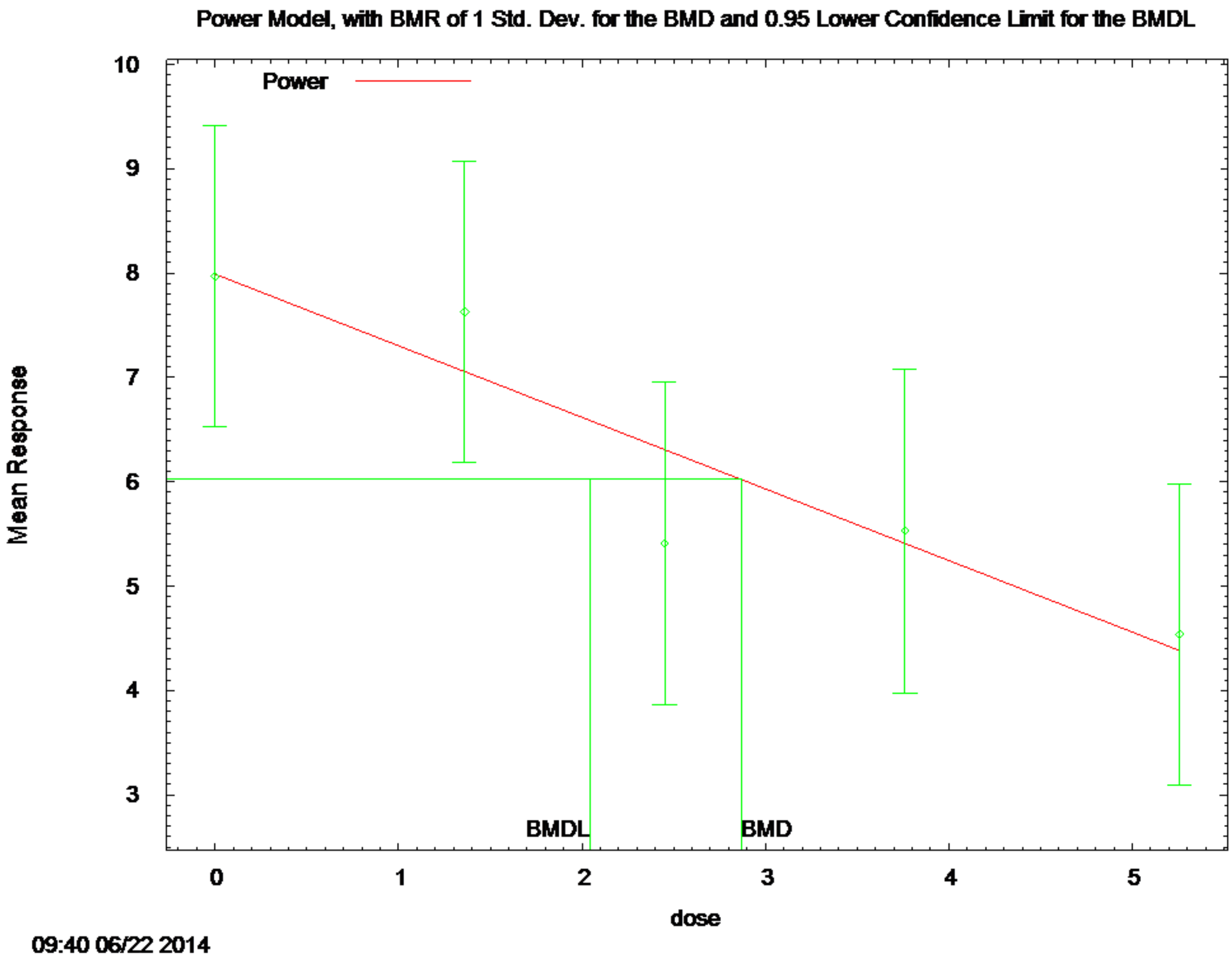
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.30586

BMDL = 2.84002



Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
10
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
09:40 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-PowerCV-1SD-5d.plt
                                       Sun Jun 22 09:40:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       4.0681
                            rho =            0   Specified
                        control =         4.54
                          slope =      3.75463
                          power =     -1.18214


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-2.6e-010	-1.7e-010
control	-2.6e-010	1	-0.81
slope	-1.7e-010	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.87222	0.790413	2.32303	5.4214
control	7.9913	0.481462	7.04765	8.93494
slope	-0.685697	0.152832	-0.985242	-0.386152
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.99	2.63	1.97	-0.0342
1.361	10	7.63	7.06	2.65	1.97	0.919
2.451	9	5.41	6.31	1.39	1.97	-1.37
3.761	9	5.53	5.41	1.76	1.97	0.179
5.258	10	4.54	4.39	1.02	1.97	0.248

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-55.036182	6	122.072364
fitted	-56.491842	3	118.983685
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	12.065	4	0.01687
Test 4	2.91132	3	0.4055

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

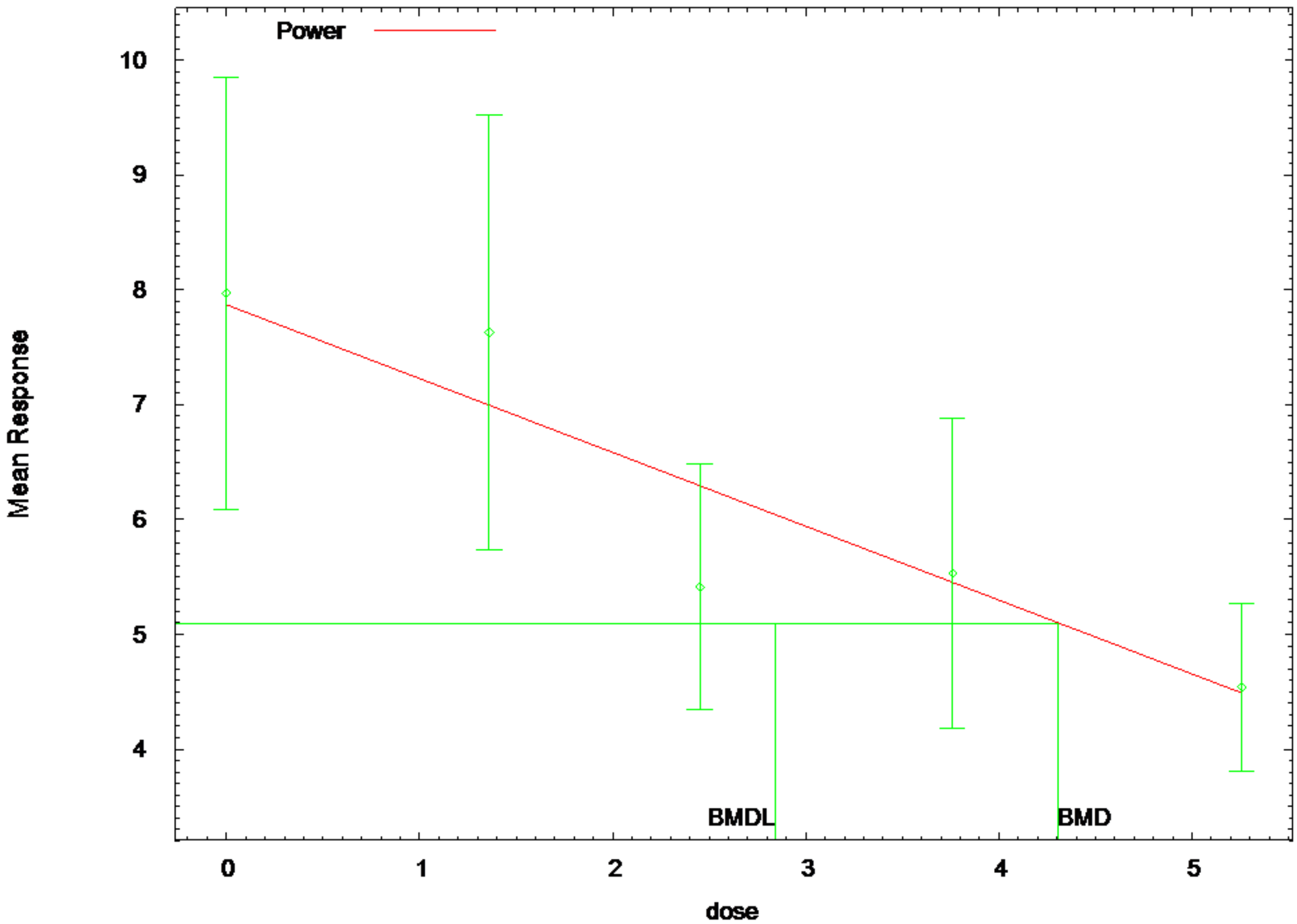
Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.86977

BMDL = 2.04395

Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



09:40 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/WBC_Historical_Ln-HLS 2001-White
Blood Cell Count-PowerNCV-1SD-5d.plt
                                      Sun Jun 22 09:40:10 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.40318
                            rho =            0
                        control =         4.54
                          slope =      3.75463
                          power =     -1.18214


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-0.99	0.44	-0.56
rho	-0.99	1	-0.49	0.58
control	0.44	-0.49	1	-0.92
slope	-0.56	0.58	-0.92	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.14645	2.39809	-9.84662	-0.446281
rho	3.48317	1.33215	0.872197	6.09414
control	7.86568	0.565523	6.75728	8.97409
slope	-0.643285	0.135832	-0.90951	-0.37706
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	7.97	7.87	2.63	2.77	0.119
1.361	10	7.63	6.99	2.65	2.26	0.897
2.451	9	5.41	6.29	1.39	1.88	-1.41
3.761	9	5.53	5.45	1.76	1.46	0.172

5.258 10 4.54 4.48 1.02 1.04
0.172

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-55.036182	6	122.072364
A2	-49.003692	10	118.007385
A3	-49.214548	7	112.429095
fitted	-51.789349	4	111.578698
R	-64.896924	2	133.793848

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7865	8	0.0001017
Test 2	12.065	4	0.01687
Test 3	0.421711	3	0.9357
Test 4	5.1496	3	0.1612

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

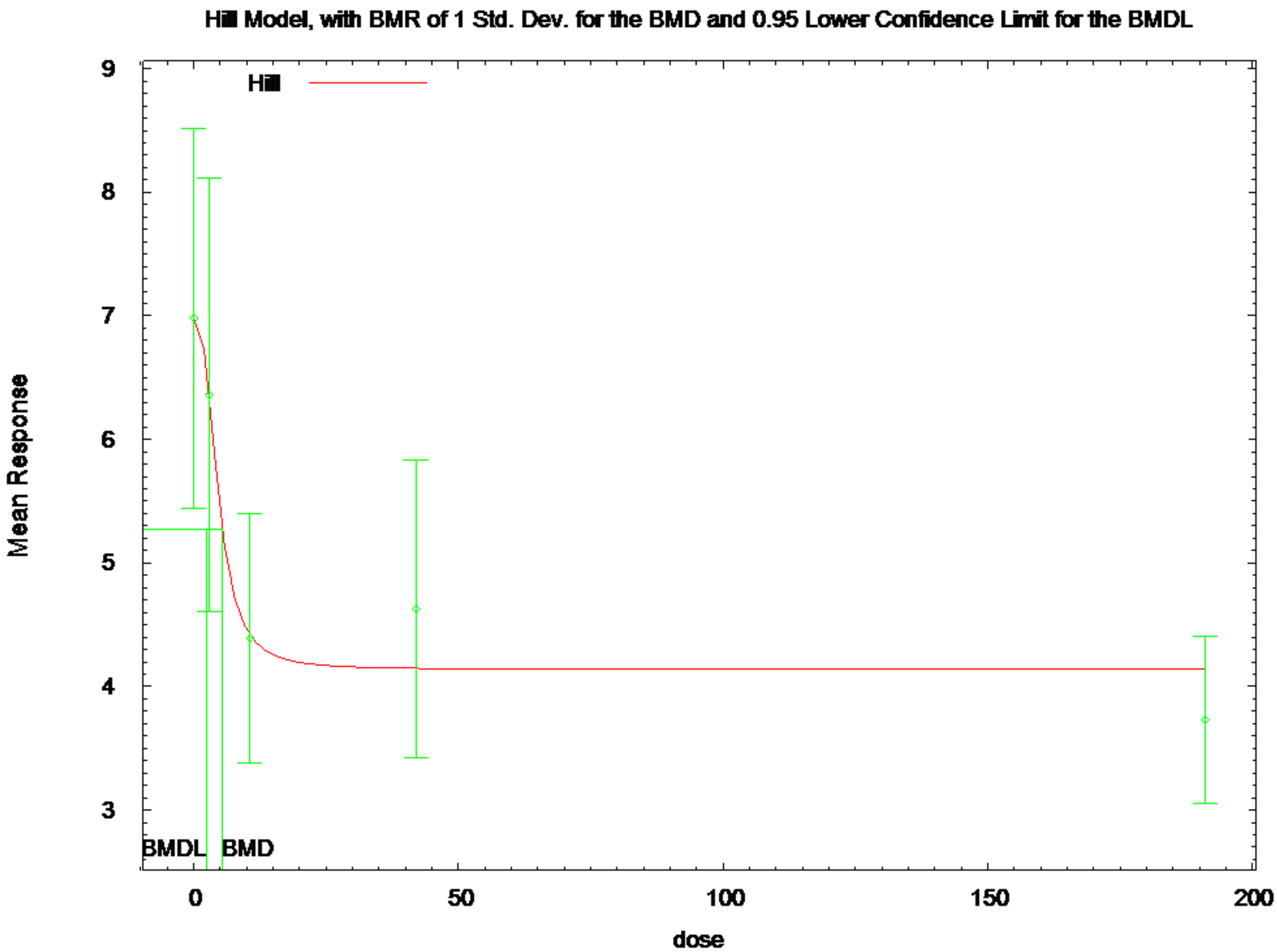
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.30585

BMDL = 2.84002

BMDS Model Results for Lymphocyte Count (Untransformed Doses, Concurrent Controls)



14:54 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.plt
                                       Sat Jun 21 14:54:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                      intercept =         6.98
                              v =        -3.25
                              n =       1.7748
                              k =      6.82817


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-4.7e-009	8.9e-009	5.4e-008	-1.5e-008
intercept	-4.7e-009	1	-0.8	-0.24	-0.39
v	8.9e-009	-0.8	1	0.5	0.0044
n	5.4e-008	-0.24	0.5	1	-0.45
k	-1.5e-008	-0.39	0.0044	-0.45	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	2.92849	0.597775	1.75687	4.1001
intercept	6.98398	0.540843	5.92395	8.04402
v	-2.84388	0.694315	-4.20471	-1.48305
n	2.6779	2.57223	-2.36358	7.71939
k	4.63333	2.49765	-0.261967	9.52864

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.98	2.15	1.71	-0.00736

2.9	10	6.36	6.35	2.45	1.71	0.0129
10.6	9	4.39	4.42	1.31	1.71	-0.052
42	9	4.63	4.15	1.56	1.71	0.845
191.1	10	3.73	4.14	0.941	1.71	-0.758

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-49.787657	5	109.575313
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	1.30976	1	0.2524

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

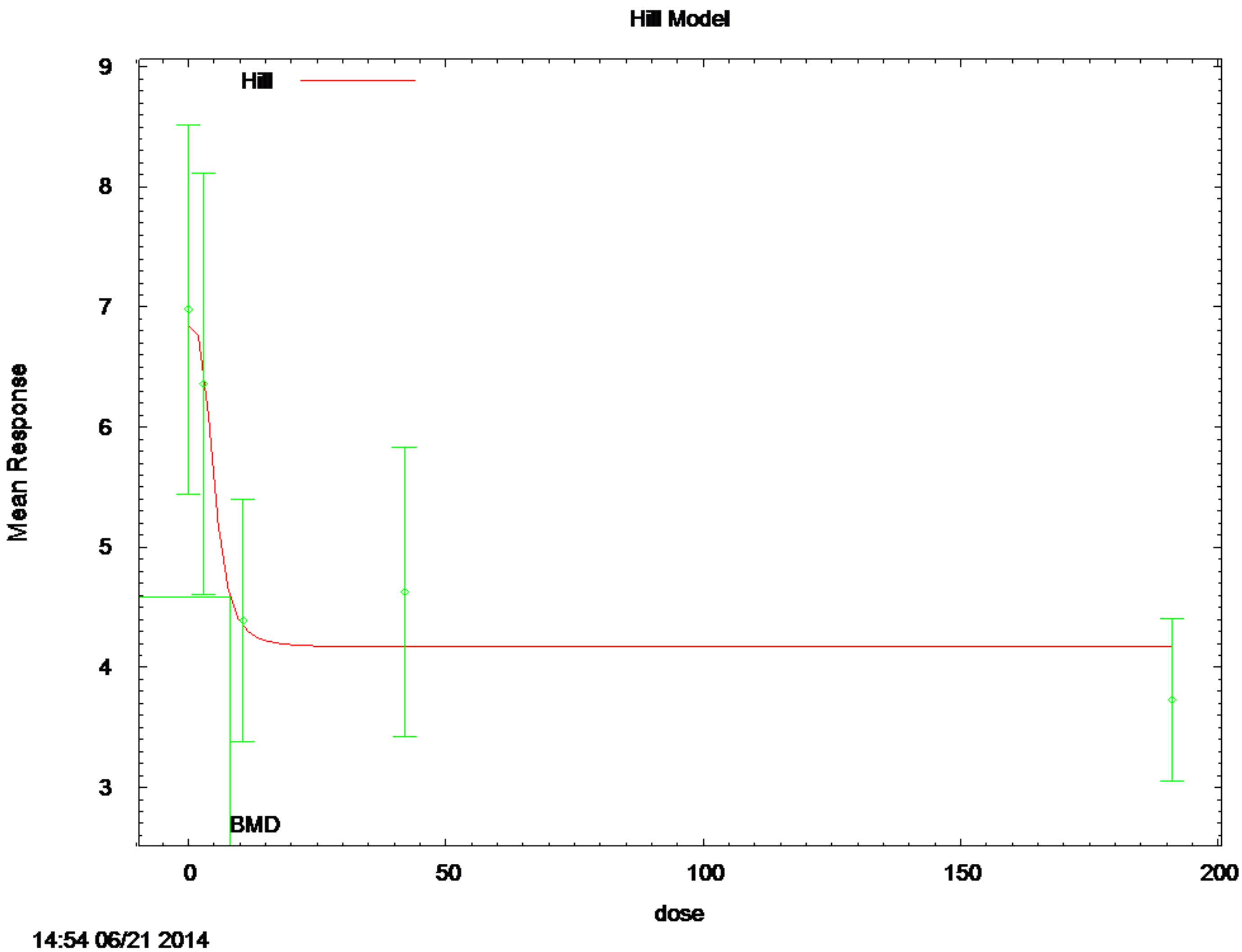
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 5.40541

BMDL = 2.33184



Hill Model
Hill
9
8
7
6
5
4
3
Mean Response
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.plt
                                      Sat Jun 21 14:54:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                      intercept =         6.98
                              v =        -3.25
                              n =       1.7748
                              k =      6.82817


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.33	-0.42	-0.12	-0.068
rho	-0.99	1	-0.36	0.44	0.12	0.068
intercept	0.33	-0.36	1	-0.92	-0.44	-0.52
v	-0.42	0.44	-0.92	1	0.55	0.36
n	-0.12	0.12	-0.44	0.55	1	0.11
k	-0.068	0.068	-0.52	0.36	0.11	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-2.89915	1.69974	-6.23058	0.432275
rho	2.3509	1.03442	0.323471	4.37834
intercept	6.83523	0.682559	5.49744	8.17302
v	-2.66512	0.760963	-4.15658	-1.17366
n	3.59728	3.28848	-2.84803	10.0426
k	5.0554	2.93561	-0.698289	10.8091

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.84	2.15	2.25	0.204

2.9	10	6.36	6.52	2.45	2.12	-0.234
10.6	9	4.39	4.34	1.31	1.32	0.105
42	9	4.63	4.17	1.56	1.26	1.09
191.1	10	3.73	4.17	0.941	1.26	-1.11

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-46.479307	6	104.958615
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	4.60357	1	0.03191

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

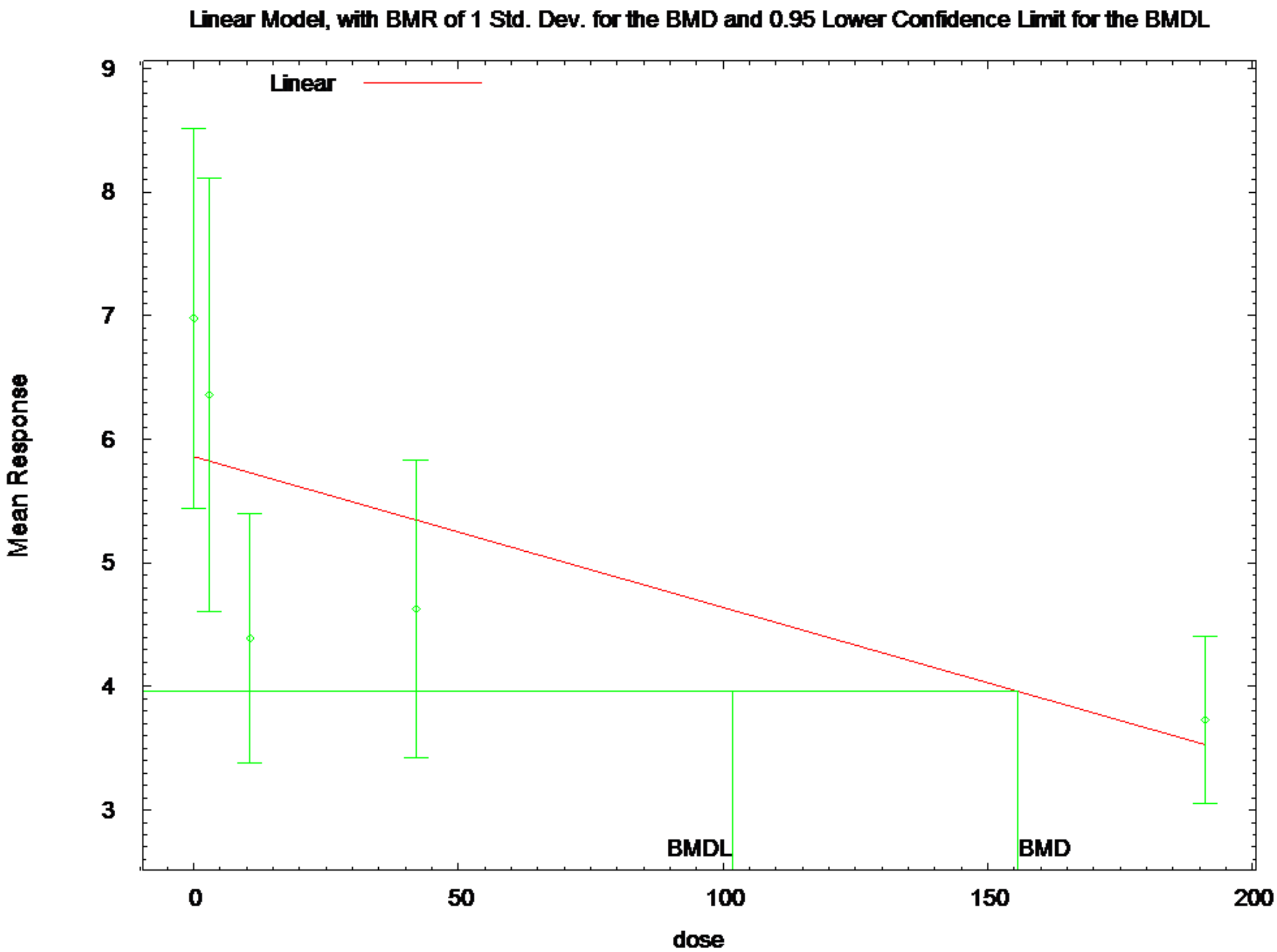
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 8.07024

BMDL computation failed.



12:47 07/09 2014

```
================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:47:23 2014

================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =       3.18101
                            rho =             0   Specified
                         beta_0 =       5.80912
                         beta_1 =    -0.0119854


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	5.7e-008	-1.1e-007
beta_0	5.7e-008	1	-0.56
beta_1	-1.1e-007	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.61273	0.737445	2.16736	5.05809
beta_0	5.86108	0.332087	5.2102	6.51196
beta_1	-0.0122035	0.00372175	-0.019498	-0.00490895

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.15	1.9	1.86
2.9	10	6.36	5.83	2.45	1.9	0.889
10.6	9	4.39	5.73	1.31	1.9	-2.12
42	9	4.63	5.35	1.56	1.9	-1.13
191.1	10	3.73	3.53	0.941	1.9	0.334

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-54.827112	3	115.654225
R	-59.677903	2	123.355807

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	11.3887	3	0.0098

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

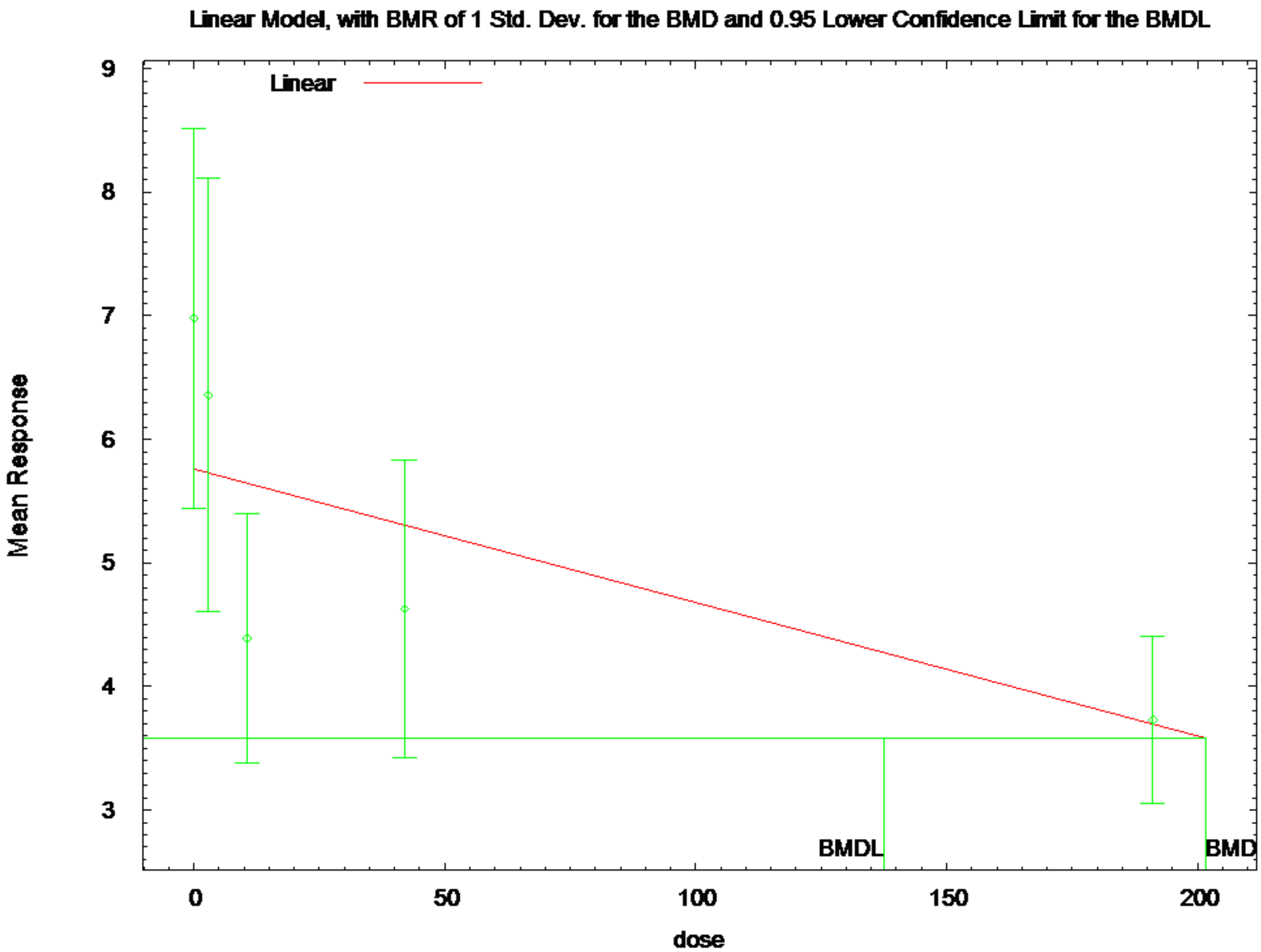
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 155.752

BMDL = 101.835



12:47 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.plt
                                       Wed Jul 09 12:47:25 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      5.80912
                         beta_1 =   -0.0119854


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99        0.046       -0.055
```

rho	-0.99	1	-0.047	0.056
beta_0	0.046	-0.047	1	-0.81
beta_1	-0.055	0.056	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.65714	1.90045	-9.38195	-1.93233
rho	4.12209	1.15309	1.86209	6.3821
beta_0	5.76447	0.365011	5.04907	6.47988
beta_1	-0.0108344	0.00248095	-0.015697	-0.00597185

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.15	2.19	1.76
2.9	10	6.36	5.73	2.45	2.16	0.917
10.6	9	4.39	5.65	1.31	2.1	-1.8
42	9	4.63	5.31	1.56	1.84	-1.1
191.1	10	3.73	3.69	0.941	0.873	0.13

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-50.343208	4	108.686416
R	-59.677903	2	123.355807

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	12.3314	3	0.00633

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance
appears

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

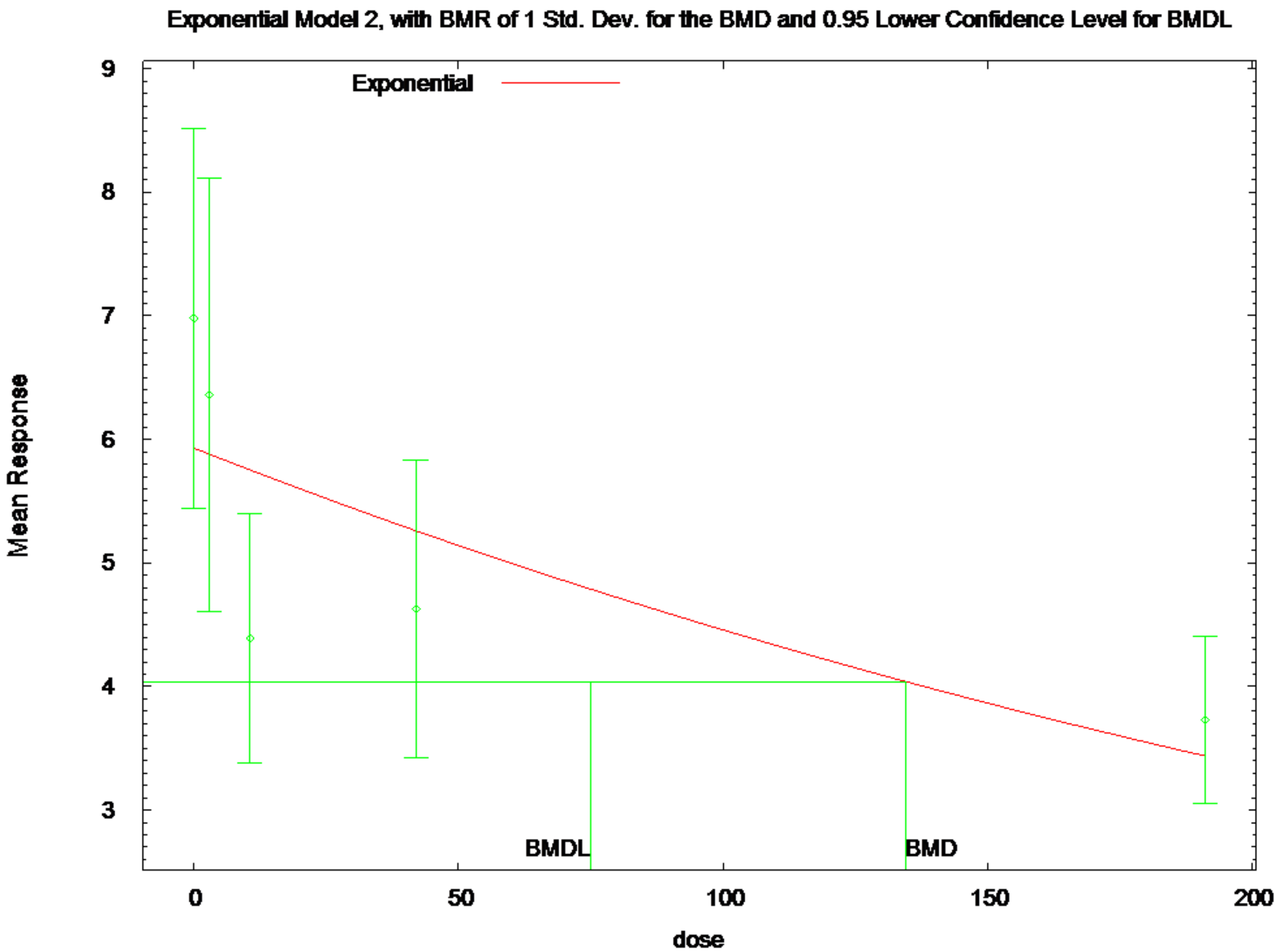
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 201.708

BMDL = 137.467



14:54 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 14:54:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.0472
rho(S)	0
a	4.506
b	0.00246217
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.27198
rho	0
a	5.93021
b	0.00285331
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.93	1.889	1.757
2.9	5.881	1.889	0.8013
10.6	5.754	1.889	-2.166
42	5.26	1.889	-1.001
191.1	3.438	1.889	0.4894

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
2	-54.52762	3	115.0552

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	

0.0001029

Test 2	10.67	4

0.03055

Test 3	10.67	4

0.03055

Test 4	10.79	3

0.01292

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

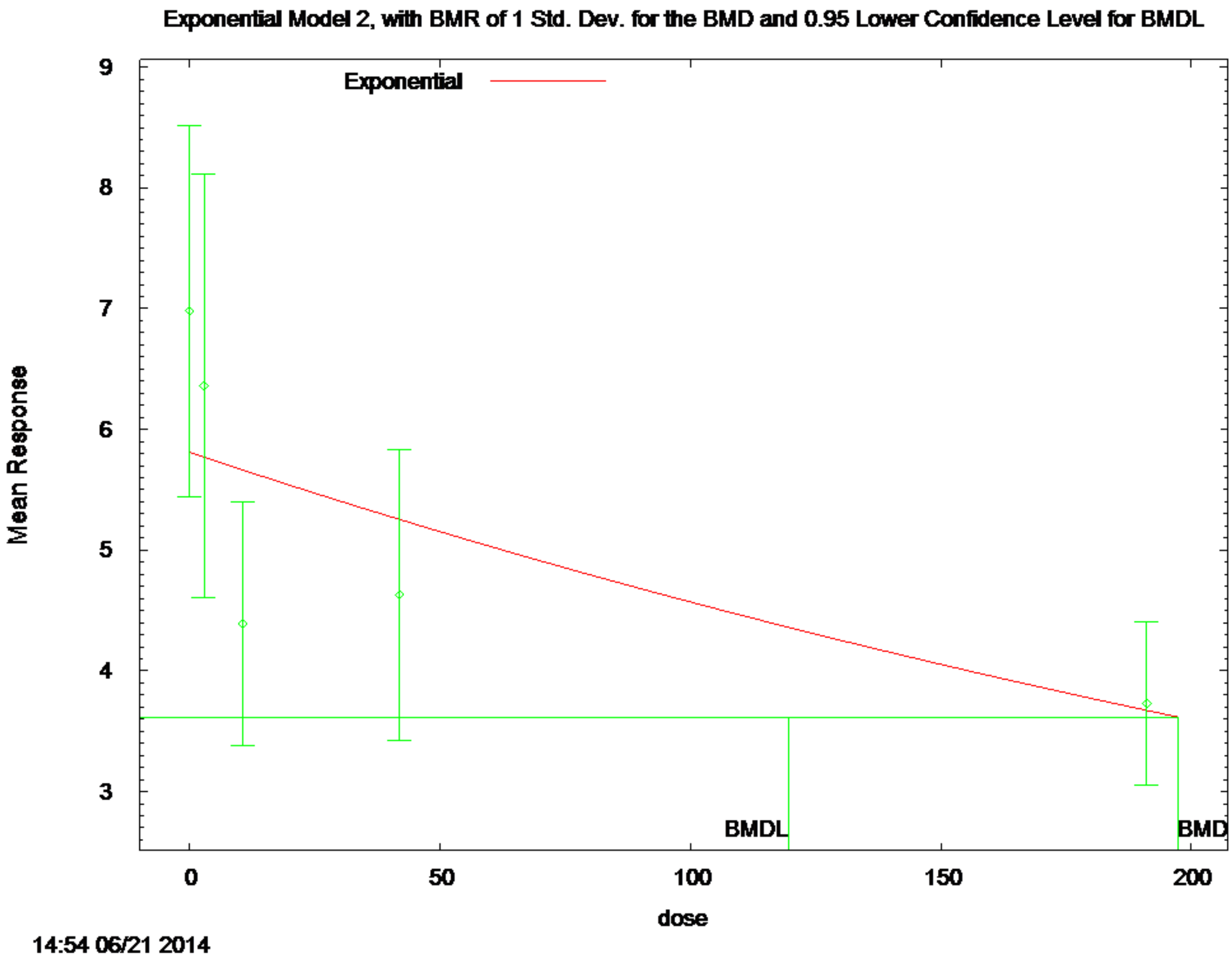
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 134.402

BMDL = 74.8756



Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 14:54:13 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-3.58873
rho	2.77965
a	4.506
b	0.00246217
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-5.4971
rho	4.01629
a	5.81037
b	0.00239974
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.81	2.193	1.687
2.9	5.77	2.162	0.8628
10.6	5.664	2.083	-1.835
42	5.253	1.791	-1.044
191.1	3.673	0.873	0.2059

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
2	-50.053	4	108.106

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029
Test 2	10.67	4	

```
0.03055
     Test 3                          0.7586           3
0.8593
     Test 4                           11.75           3
0.008287
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

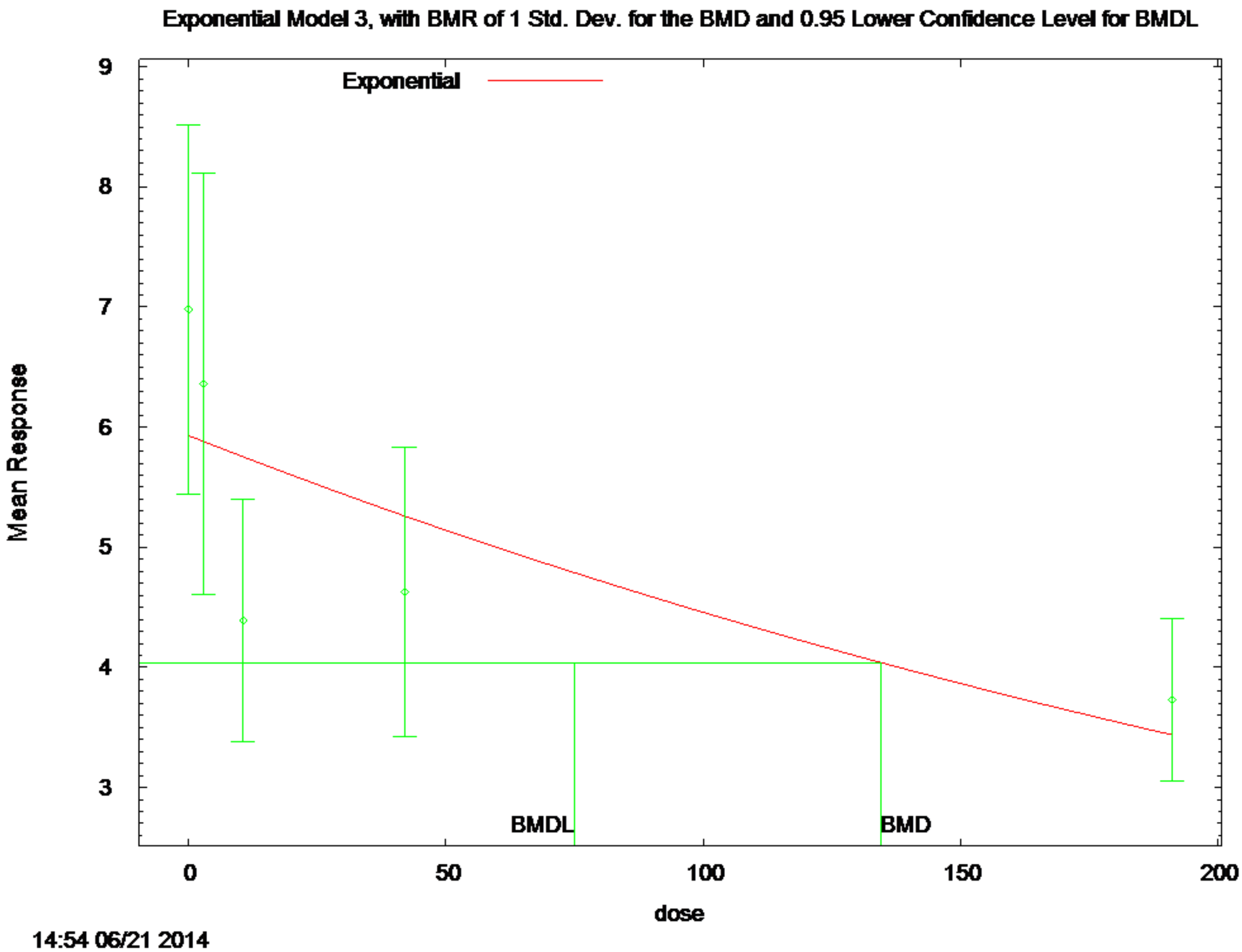
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 197.427

BMDL = 119.645



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 14:54:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.0472
rho(S)	0
a	4.506
b	0.00246217
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.27198
rho	0
a	5.93021
b	0.00285331
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.93	1.889	1.757
2.9	5.881	1.889	0.8013
10.6	5.754	1.889	-2.166
42	5.26	1.889	-1.001
191.1	3.438	1.889	0.4894

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
3	-54.52762	3	115.0552

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 5a	10.79	3	0.01292

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

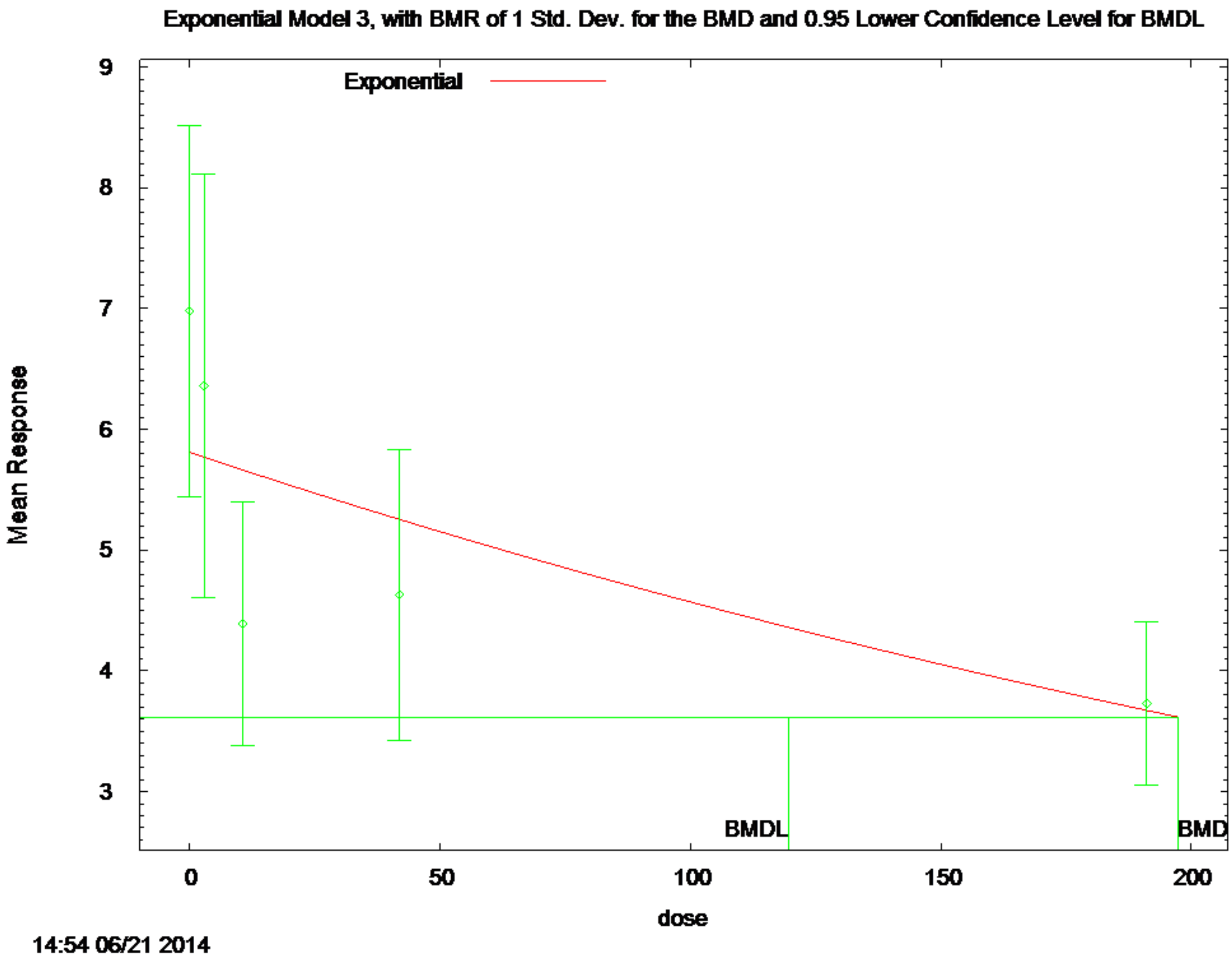
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 134.402

BMDL = 74.8756



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sat Jun 21 14:54:13 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-3.58873
rho	2.77965
a	4.506
b	0.00246217
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-5.4971
rho	4.01629
a	5.81037
b	0.00239974
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.81	2.193	1.687
2.9	5.77	2.162	0.8628
10.6	5.664	2.083	-1.835
42	5.253	1.791	-1.044
191.1	3.673	0.873	0.2059

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
3	-50.053	4	108.106

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029

Test 2	10.67	4	0.03055
Test 3	0.7586	3	0.8593
Test 5a	11.75	3	0.008287

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

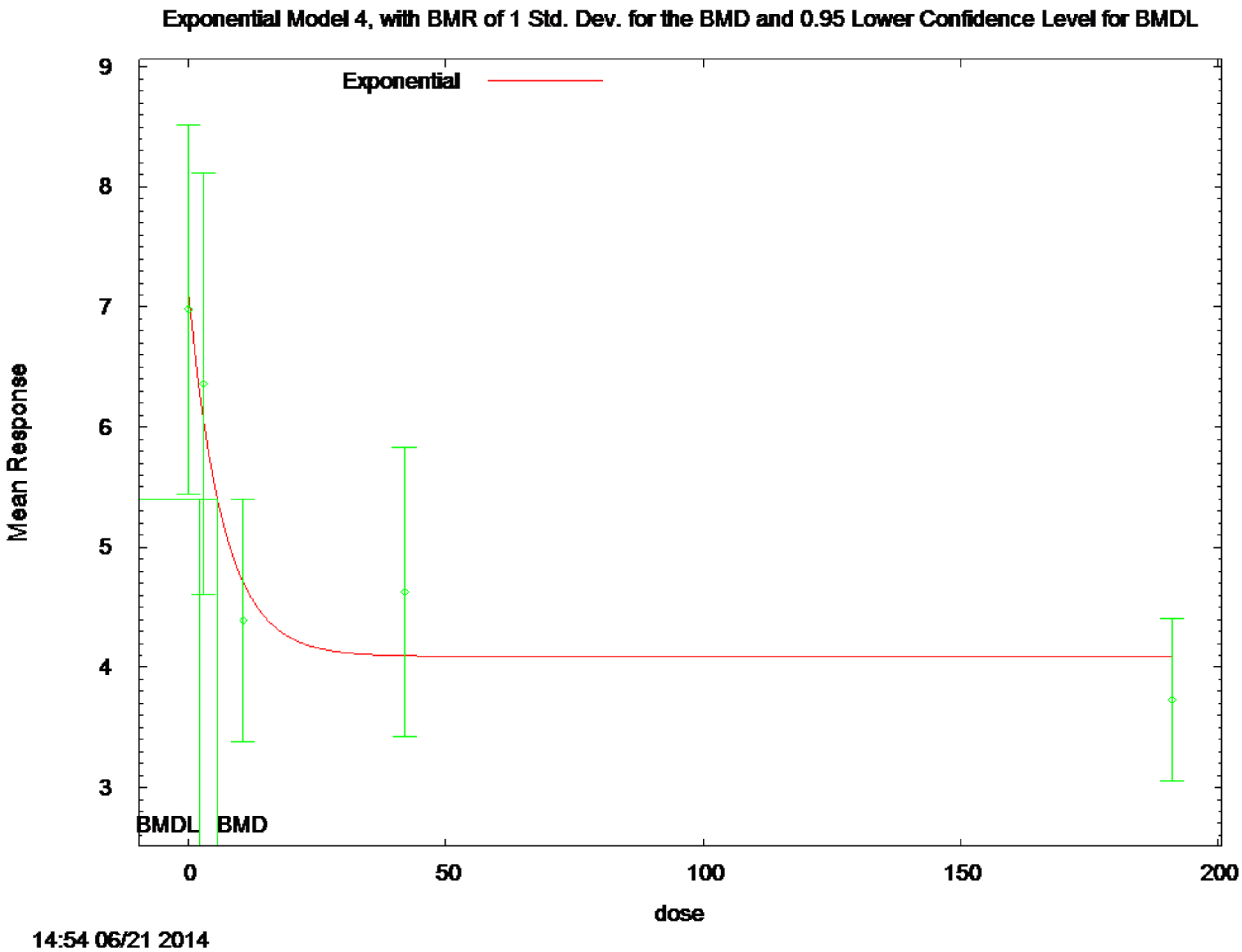
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 197.427

BMDL = 119.645



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
9
8
7
6
5
4
3
0
50
100
150
200
BMDL
BMD
14:54 06/21 2014

```
================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 14:54:11 2014

================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.0472
rho(S)	0
a	7.329
b	0.0170211
c	0.484702
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.08961
rho	0
a	7.12238
b	0.150285
c	0.574374
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.122	1.724	-0.2611
2.9	6.051	1.724	0.5659
10.6	4.707	1.724	-0.5519
42	4.096	1.724	0.9284
191.1	4.091	1.724	-0.6619

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
4	-50.15058	4	108.3012

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 6a	2.036	2	0.3614

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

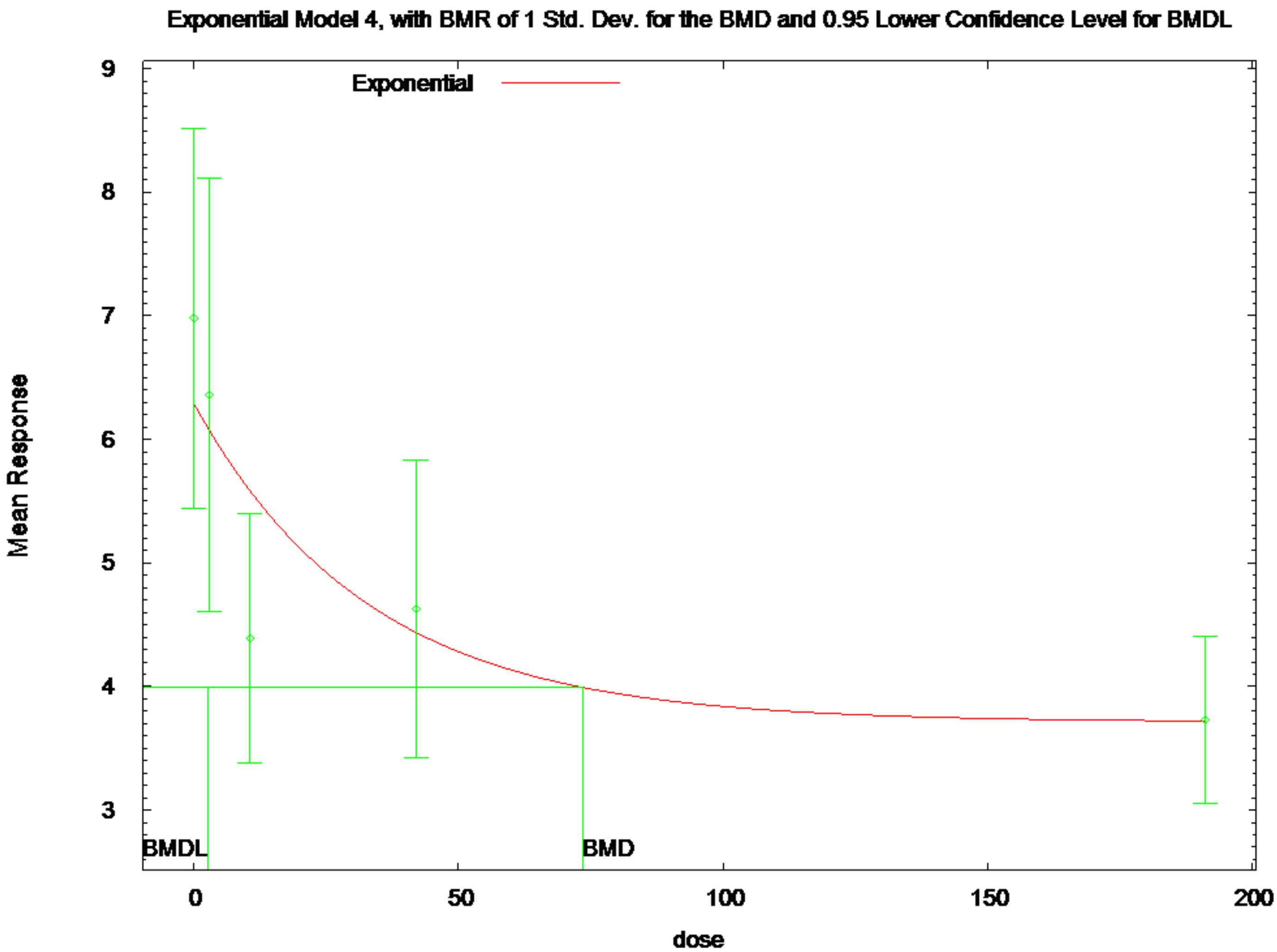
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 5.59708

BMDL = 2.23698



14:54 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sat Jun 21 14:54:13 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-3.58873
rho	2.77965
a	7.329
b	0.0170211
c	0.484702
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-4.3478
rho	3.2691
a	6.29097
b	0.0302436
c	0.590321
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.291	2.298	0.948
2.9	6.075	2.171	0.4159
10.6	5.584	1.892	-1.894
42	4.437	1.299	0.445
191.1	3.722	0.9745	0.02708

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
4	-47.90566	5	105.8113

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029

Test 2	10.67	4	0.03055
Test 3	0.7586	3	0.8593
Test 6a	7.456	2	0.02404

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

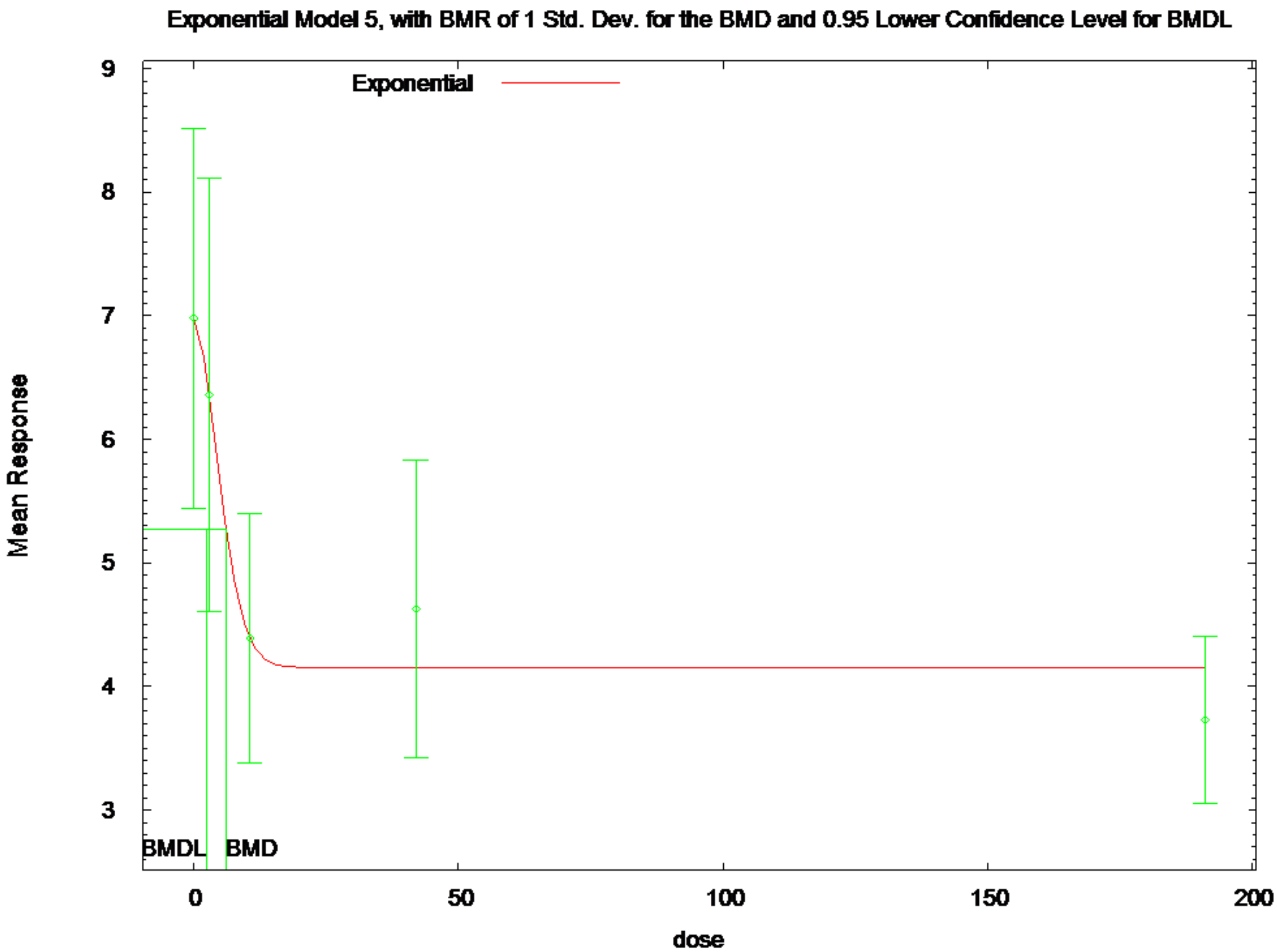
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 73.5309

BMDL = 2.76278



14:54 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 14:54:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.0472
rho(S)	0
a	7.329
b	0.0170211
c	0.484702
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.07486
rho	0
a	6.98
b	0.157544
c	0.595461
d	1.78043

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.98	1.712	-4.535e-007
2.9	6.36	1.712	-4.619e-007
10.6	4.39	1.712	6.233e-007
42	4.156	1.712	0.8302
191.1	4.156	1.712	-0.7876

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
5	-49.79672	5	109.5934

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 7a	1.328	1	0.2492

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

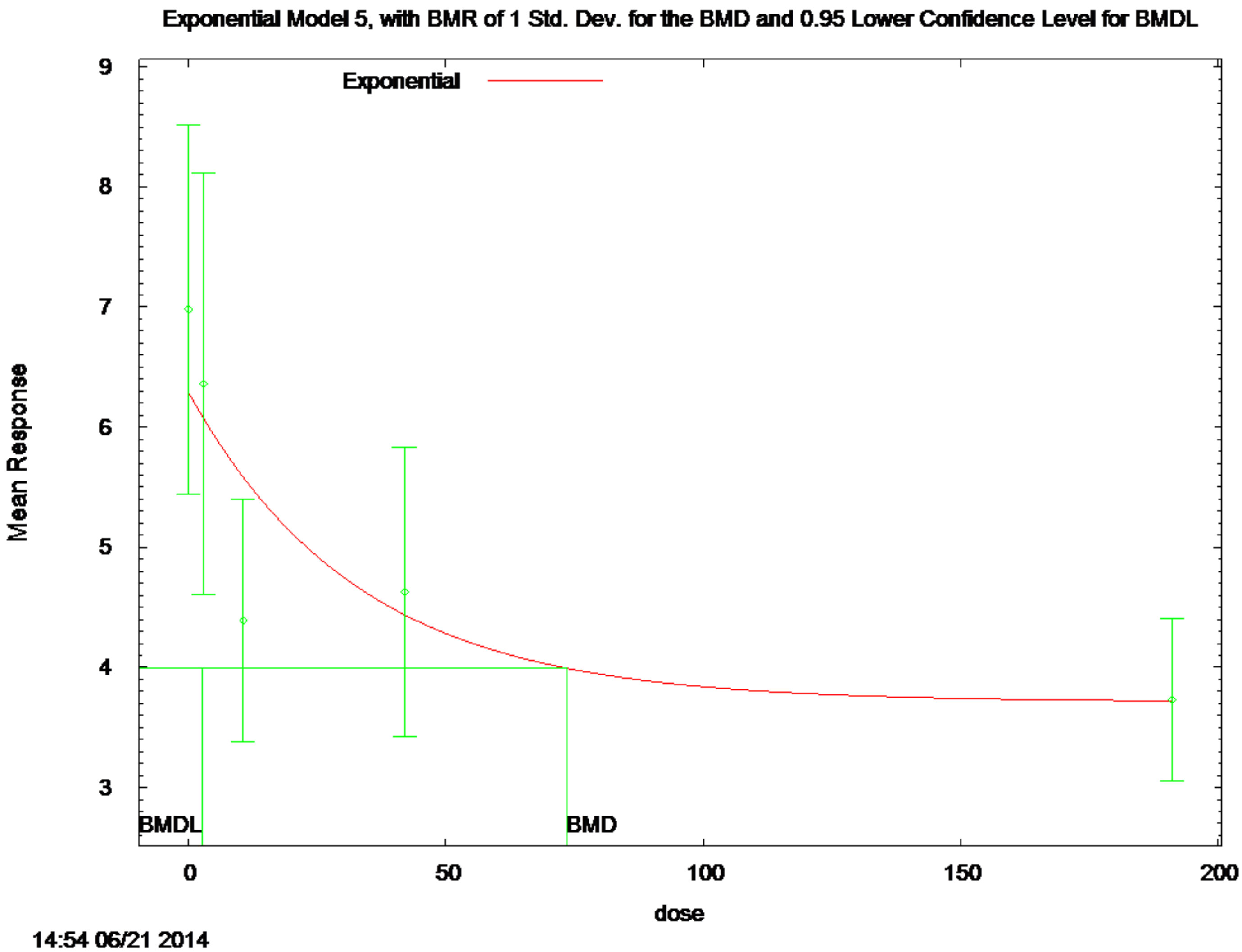
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 6.10056

BMDL = 2.52044


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 14:54:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-3.58873
rho	2.77965
a	7.329
b	0.0170211
c	0.484702
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-4.3478
rho	3.2691
a	6.29097
b	0.0302436
c	0.590321
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.291	2.298	0.948
2.9	6.075	2.171	0.4159
10.6	5.584	1.892	-1.894
42	4.437	1.299	0.445
191.1	3.722	0.9745	0.02708

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2


                                Likelihoods of Interest

                          Model      Log(likelihood)      DF
AIC
                         -------    -----------------    ----
------------
                             A1       -49.13278            6
110.2656
                             A2       -43.79823           10
107.5965
                             A3       -44.17752            7
102.355
                              R        -59.6779            2
123.3558
                              5       -47.90566            5
105.8113


   Additive constant for all log-likelihoods =     -44.11.  This
constant added to the
   above values gives the log-likelihood including the term that
does not
   depend on the model parameters.


                                 Explanation of Tests

   Test 1:  Does response and/or variances differ among Dose
levels? (A2 vs. R)
   Test 2:  Are Variances Homogeneous? (A2 vs. A1)
   Test 3:  Are variances adequately modeled? (A2 vs. A3)

   Test 7a: Does Model 5 fit the data? (A3 vs 5)


                             Tests of Interest

     Test          -2*log(Likelihood Ratio)       D. F.
p-value
   --------        ------------------------      ------
--------------
     Test 1                        31.76           8
0.0001029
```

Test 2	10.67	4	0.03055
Test 3	0.7586	3	0.8593
Test 7a	7.456	2	0.02404

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

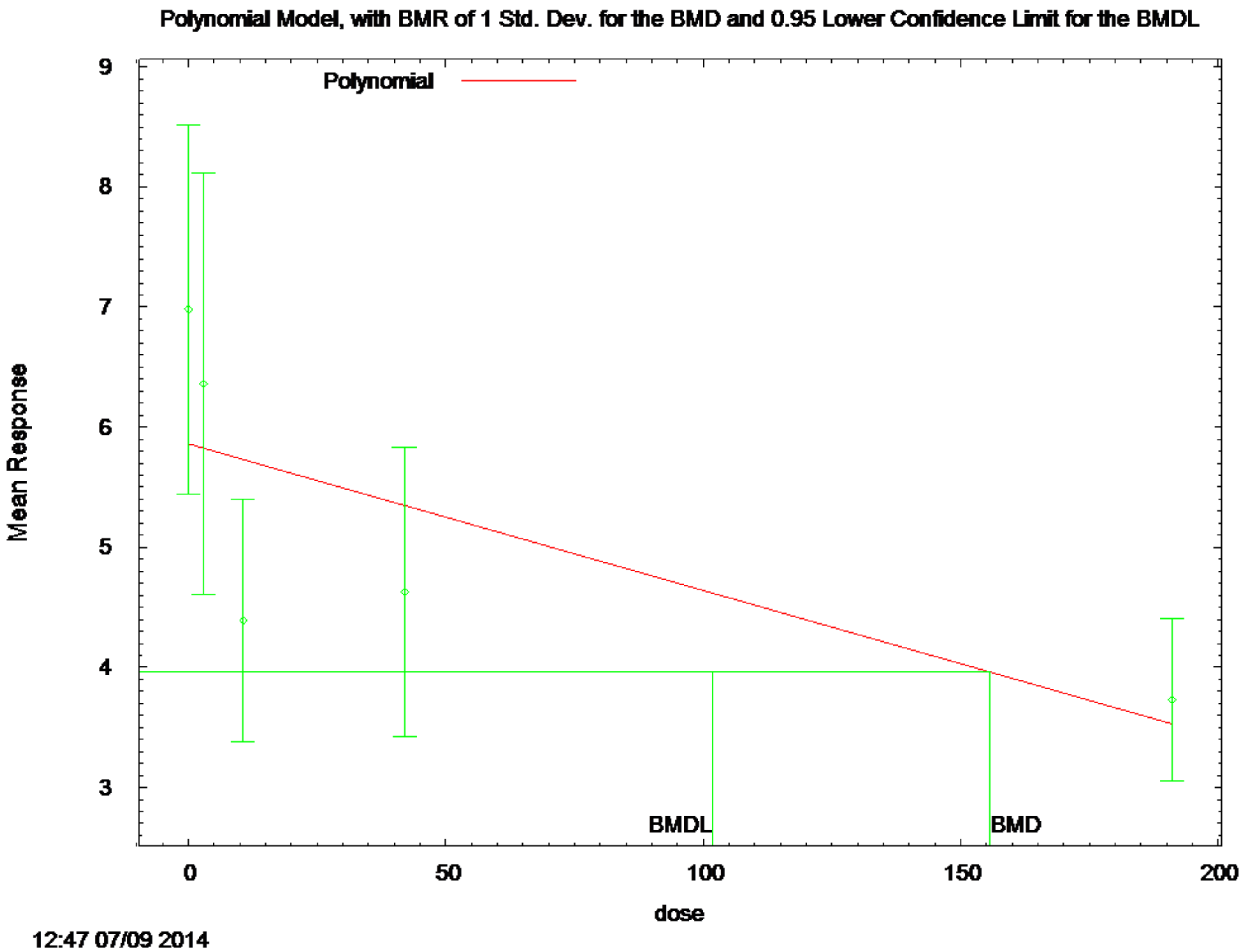
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 73.5309

BMDL = 2.76278



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:47 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.plt
                                       Wed Jul 09 12:47:23 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =      6.28333
                         beta_1 =   -0.0582096
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	3.9e-007	-1.1e-006
beta_0	3.9e-007	1	-0.56
beta_1	-1.1e-006	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.61272	0.737443	2.16736	5.05808
beta_0	5.86108	0.332086	5.2102	6.51196
beta_1	-0.0122035	0.00372175	-0.019498	-0.00490898
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.15	1.9	1.86
2.9	10	6.36	5.83	2.45	1.9	0.889
10.6	9	4.39	5.73	1.31	1.9	-2.12
42	9	4.63	5.35	1.56	1.9	-1.13
191.1	10	3.73	3.53	0.941	1.9	0.334

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-54.827112	3	115.654225
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	11.3887	3	0.0098

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

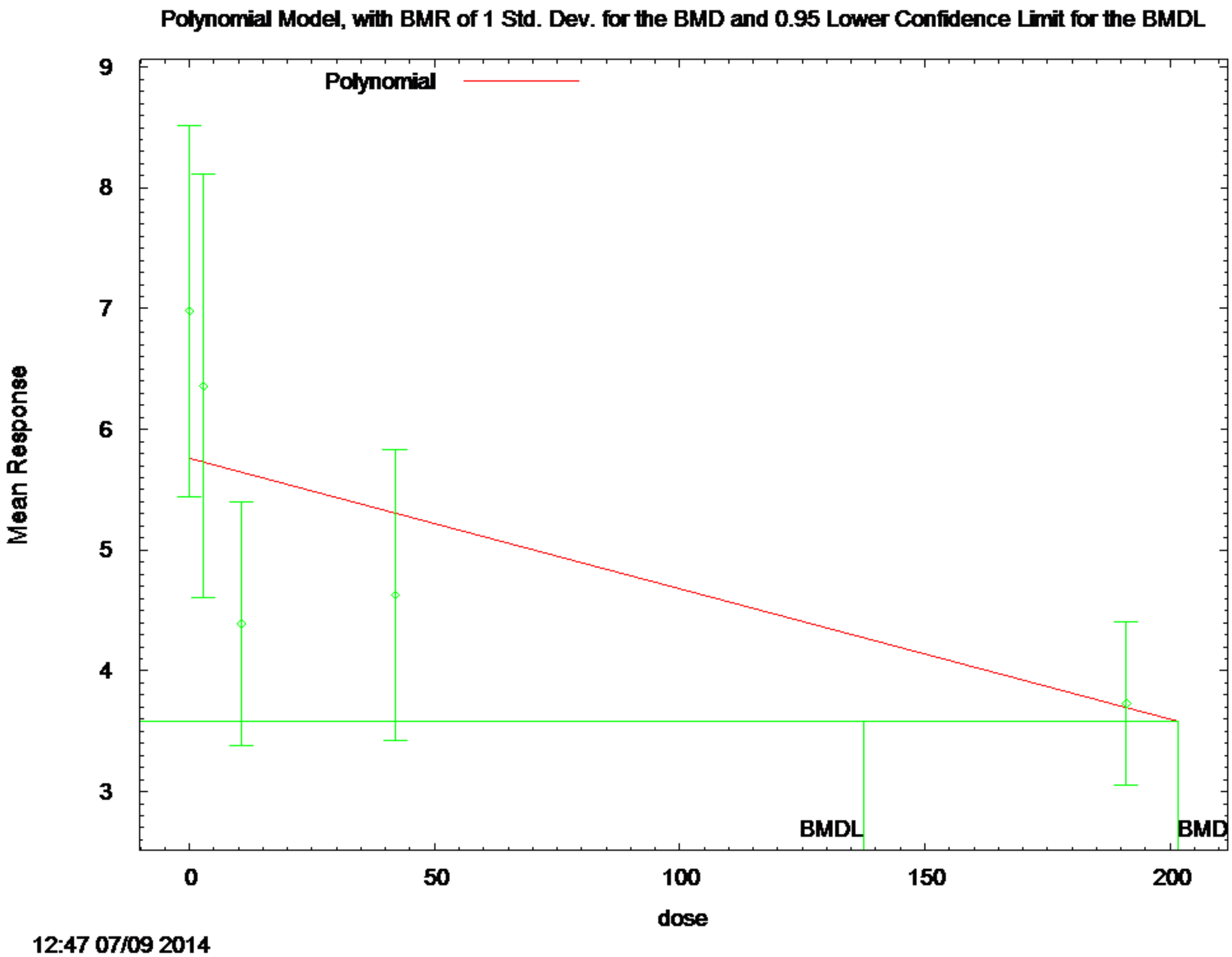
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 155.752

BMDL = 101.835



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:47 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:47:25 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      6.28333
                         beta_1 =   -0.0582096
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.046	-0.055
rho	-0.99	1	-0.047	0.056
beta_0	0.046	-0.047	1	-0.81
beta_1	-0.055	0.056	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.65714	1.90045	-9.38195	-1.93233
rho	4.12209	1.15308	1.86209	6.3821
beta_0	5.76447	0.365011	5.04907	6.47988
beta_1	-0.0108344	0.00248095	-0.015697	-0.00597186
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.15	2.19	1.76
2.9	10	6.36	5.73	2.45	2.16	0.917
10.6	9	4.39	5.65	1.31	2.1	-1.8
42	9	4.63	5.31	1.56	1.84	-1.1

191.1 10 3.73 3.69 0.941 0.873
0.13

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-50.343208	4	108.686416
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	12.3314	3	0.00633

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

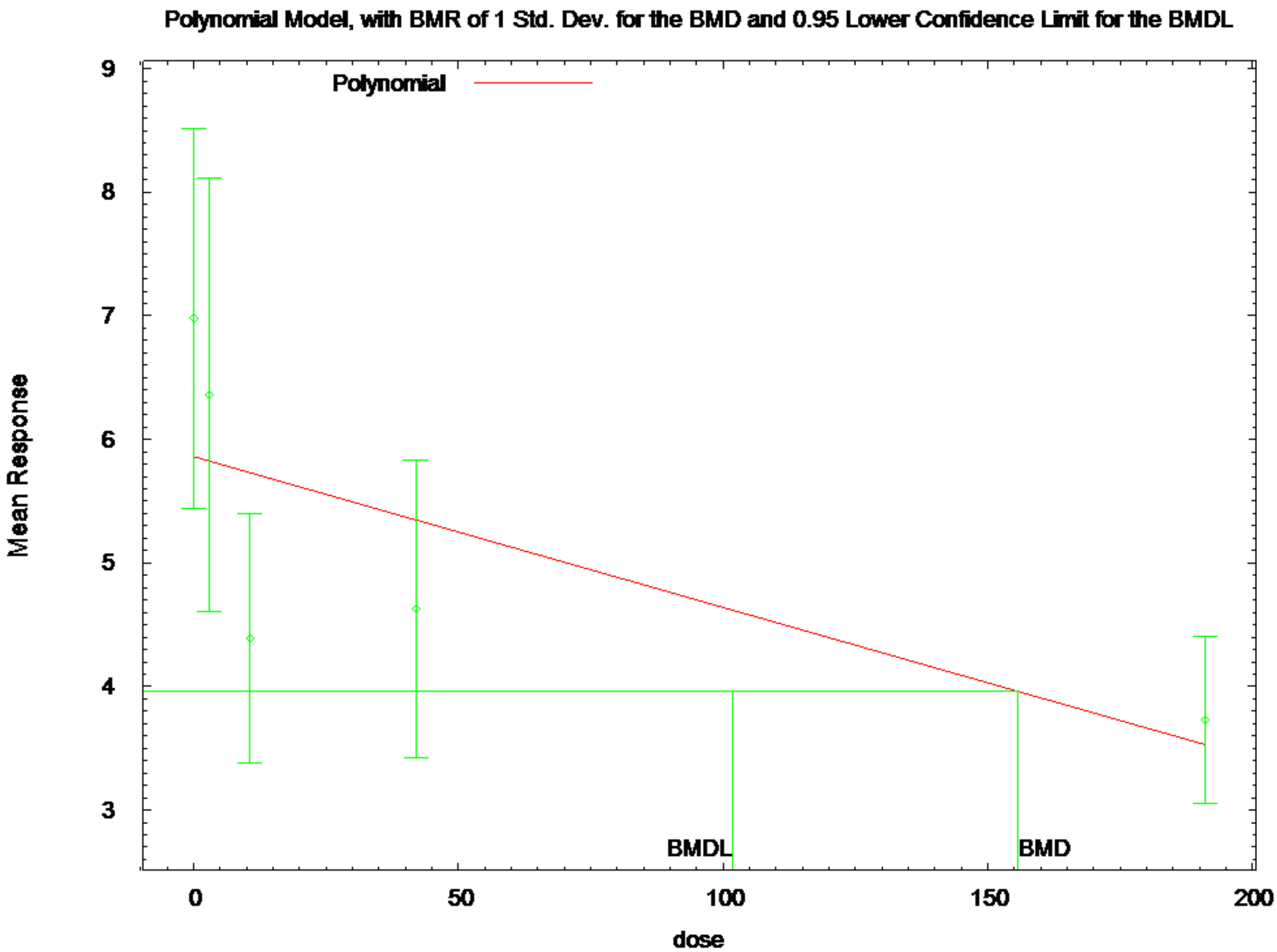
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 201.708

BMDL = 137.467



12:47 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.plt
                                       Wed Jul 09 12:47:23 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =      7.08617
                         beta_1 =    -0.327588
                         beta_2 =            0
                         beta_3 = -3.20797e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-2.3e-007	1.4e-006
beta_0	-2.3e-007	1	-0.56
beta_1	1.4e-006	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.61273	0.737445	2.16736	5.0581
beta_0	5.86108	0.332087	5.2102	6.51196
beta_1	-0.0122034	0.00372175	-0.0194979	-0.00490893
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.15	1.9	1.86
2.9	10	6.36	5.83	2.45	1.9	0.889
10.6	9	4.39	5.73	1.31	1.9	-2.12
42	9	4.63	5.35	1.56	1.9	-1.13
191.1	10	3.73	3.53	0.941	1.9	

0.334

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-54.827112	3	115.654225
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	11.3887	3	0.0098

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

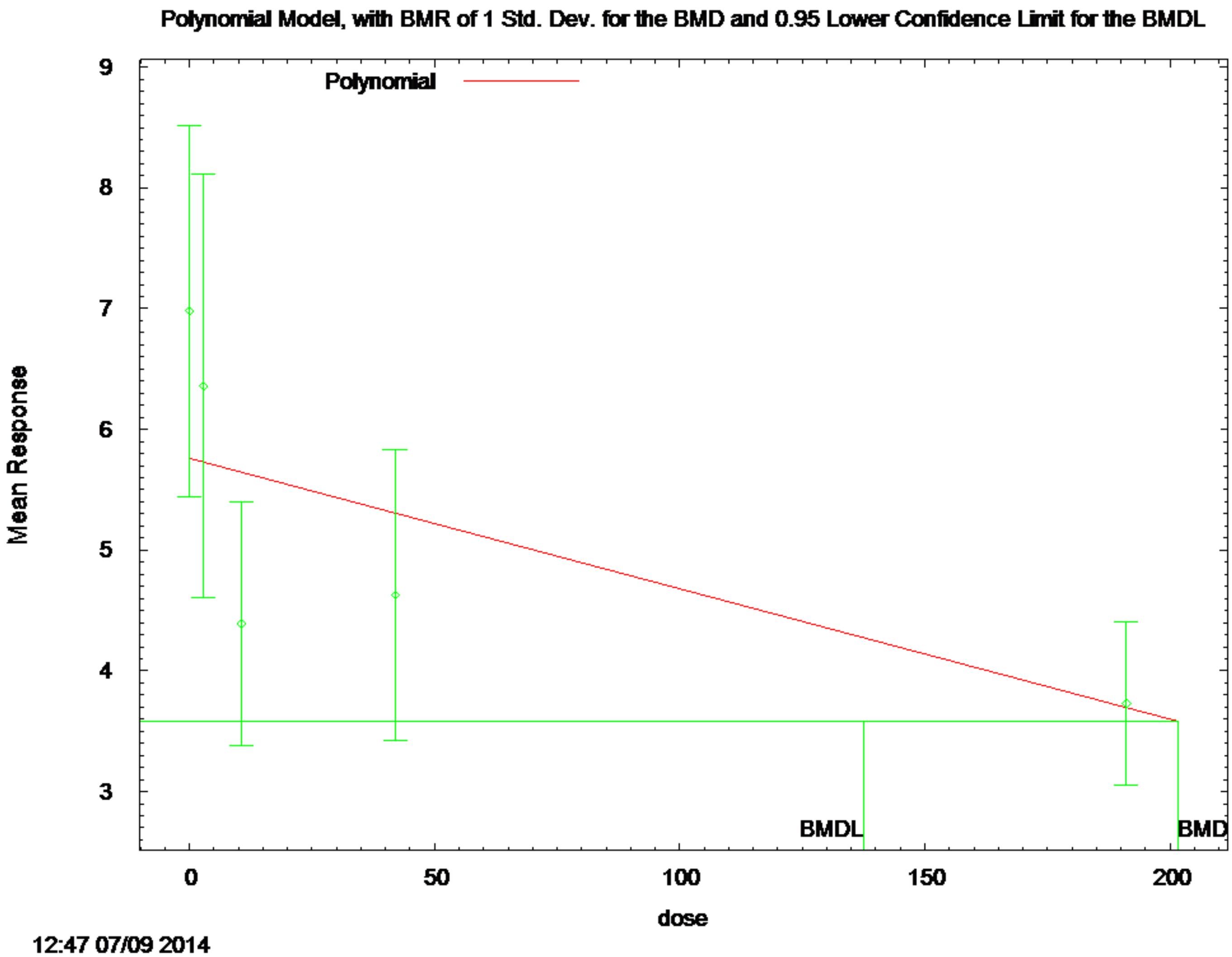
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 155.753

BMDL = 101.835



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:47 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:47:24 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      7.08617
                         beta_1 =    -0.327588
                         beta_2 =            0
                         beta_3 = -3.20797e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.046	-0.055
rho	-0.99	1	-0.047	0.056
beta_0	0.046	-0.047	1	-0.81
beta_1	-0.055	0.056	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.65713	1.90045	-9.38194	-1.93232
rho	4.12209	1.15308	1.86209	6.38209
beta_0	5.76447	0.365011	5.04907	6.47988
beta_1	-0.0108344	0.00248095	-0.015697	-0.00597186
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.15	2.19	1.76
2.9	10	6.36	5.73	2.45	2.16	0.917
10.6	9	4.39	5.65	1.31	2.1	-1.8

42	9	4.63	5.31	1.56	1.84
-1.1					
191.1	10	3.73	3.69	0.941	0.873
0.13					

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-50.343208	4	108.686416
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593

Test 4	12.3314	3	0.00633

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

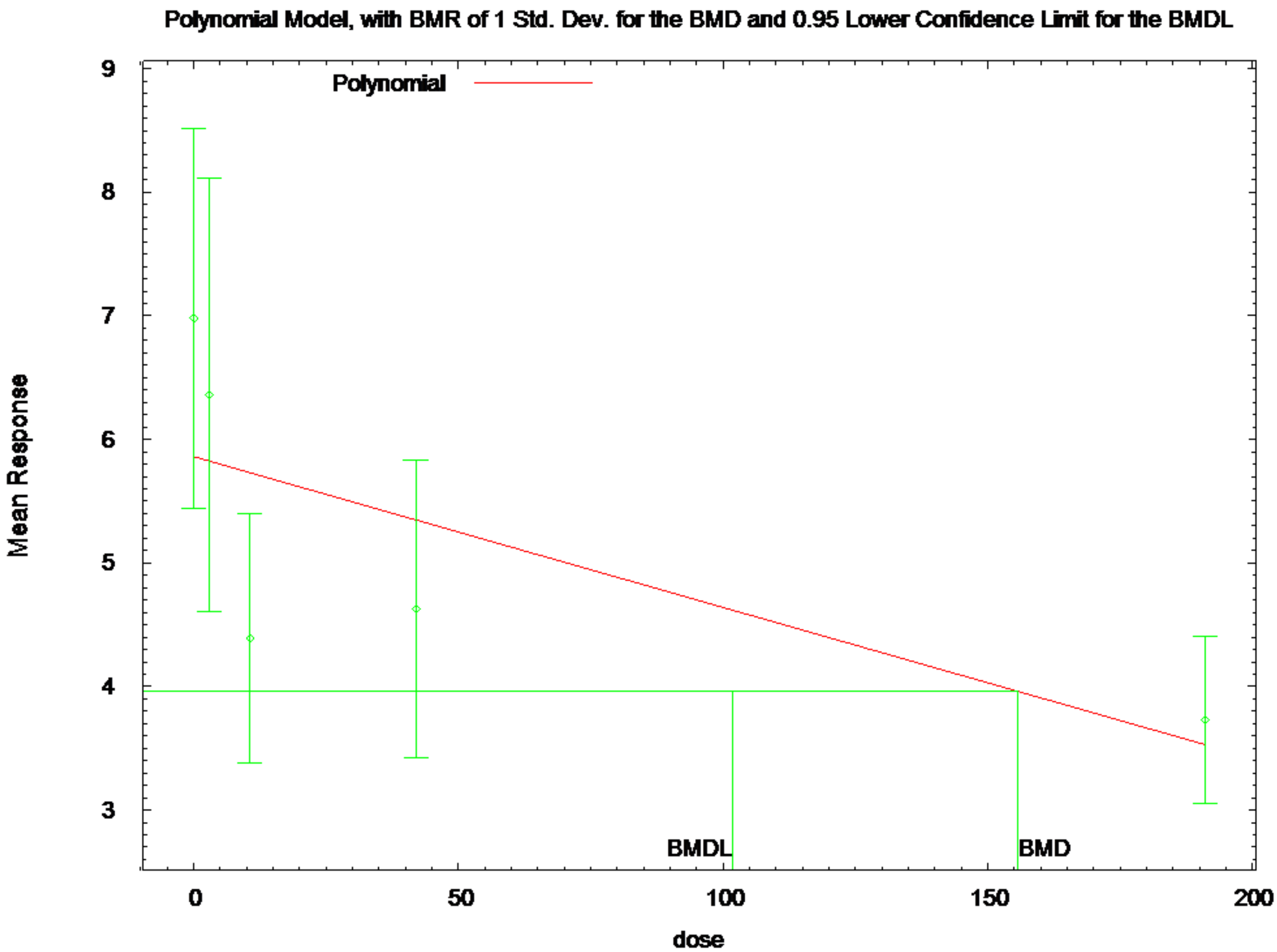
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 201.708

BMDL = 137.467



12:47 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:47:23 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =         6.98
                         beta_1 =    -0.192486
                         beta_2 =  -0.00831882
                         beta_3 =            0
                         beta_4 = -1.52335e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	4.5e-008	-9.4e-009
beta_0	4.5e-008	1	-0.56
beta_1	-9.4e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.61273	0.737445	2.16736	5.05809
beta_0	5.86108	0.332087	5.2102	6.51196
beta_1	-0.0122035	0.00372175	-0.019498	-0.00490895
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.15	1.9	1.86
2.9	10	6.36	5.83	2.45	1.9	0.889
10.6	9	4.39	5.73	1.31	1.9	-2.12
42	9	4.63	5.35	1.56	1.9	

-1.13
191.1   10   3.73   3.53   0.941   1.9
0.334

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-54.827112	3	115.654225
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	11.3887	3	0.0098

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

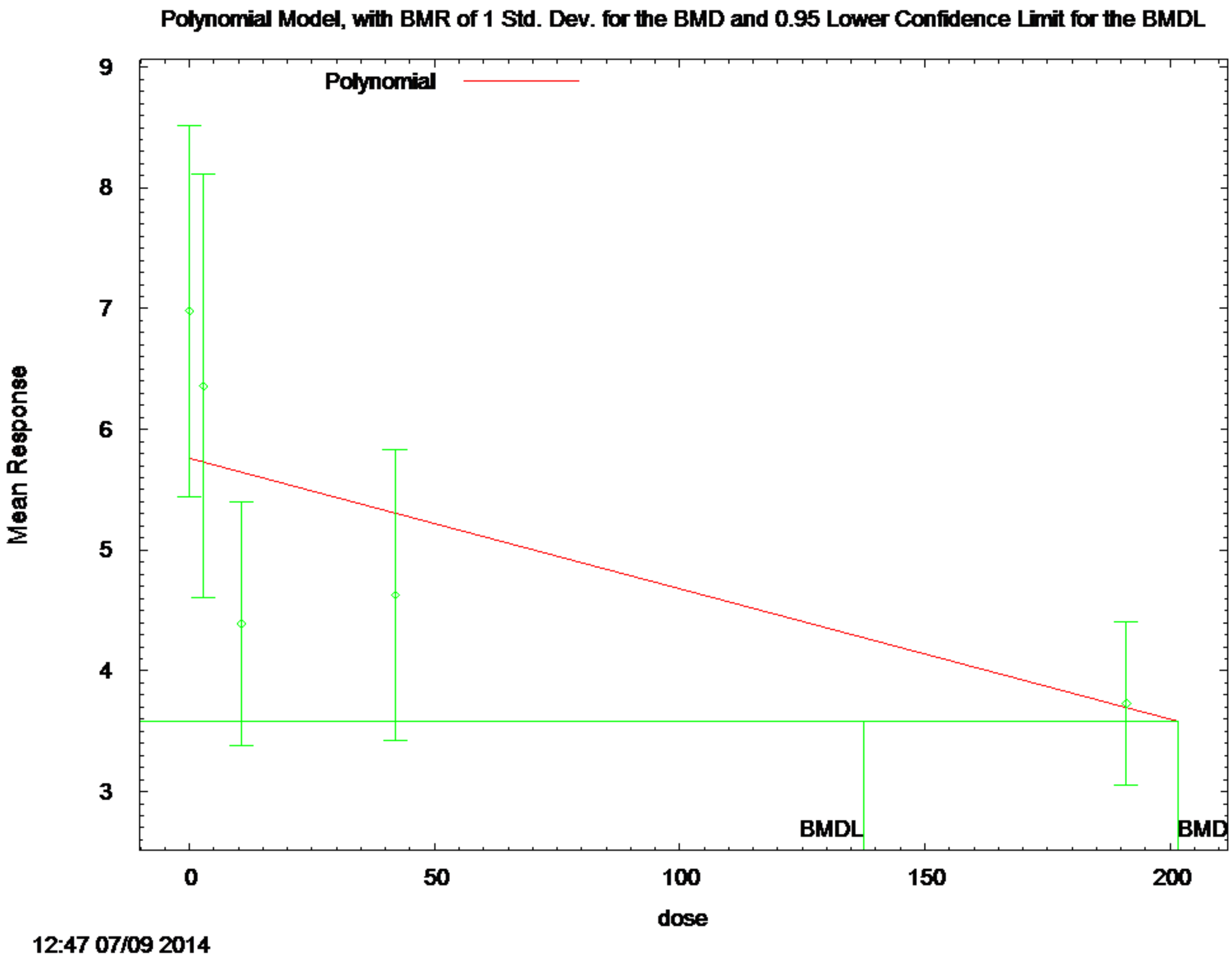
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 155.752

BMDL = 101.835


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:47 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent/Lymphocyte_C
oncurrent_Normal-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:47:24 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =         6.98
                         beta_1 =    -0.192486
                         beta_2 =  -0.00831882
                         beta_3 =            0
                         beta_4 = -1.52335e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.046	-0.055
rho	-0.99	1	-0.047	0.056
beta_0	0.046	-0.047	1	-0.81
beta_1	-0.055	0.056	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.65714	1.90045	-9.38195	-1.93233
rho	4.12209	1.15308	1.86209	6.3821
beta_0	5.76447	0.365011	5.04907	6.47988
beta_1	-0.0108344	0.00248095	-0.015697	-0.00597186
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.15	2.19	1.76
2.9	10	6.36	5.73	2.45	2.16	

						0.917
10.6	9	4.39	5.65	1.31	2.1	-1.8
42	9	4.63	5.31	1.56	1.84	-1.1
191.1	10	3.73	3.69	0.941	0.873	0.13

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-50.343208	4	108.686416
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	12.3314	3	0.00633

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

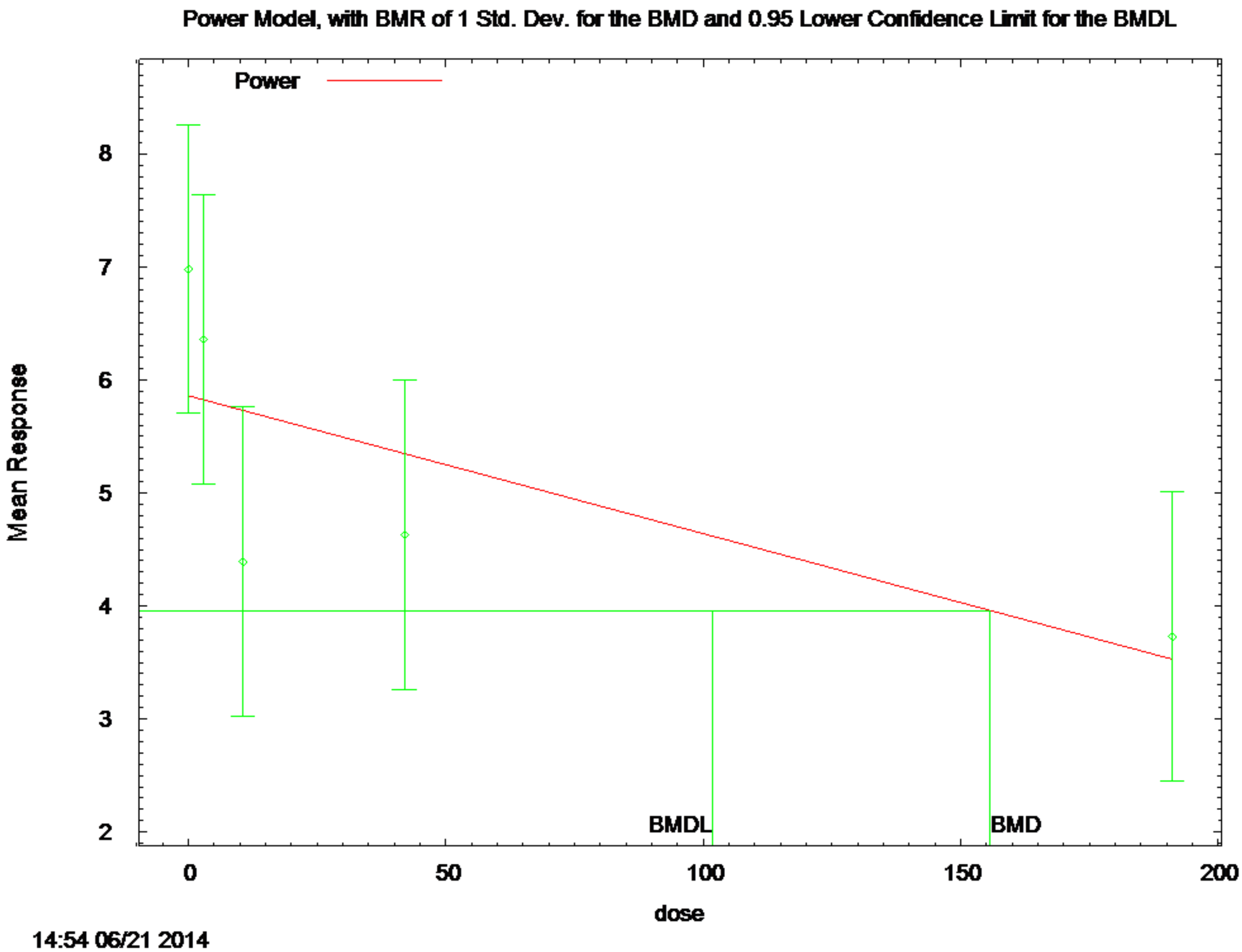
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 201.708

BMDL = 137.467


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
8
7
6
5
4
3
2
BMDL
BMD
0
50
100
150
200
dose
14:54 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.plt
                                       Sat Jun 21 14:54:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                        control =         3.73
                          slope =      2.97763
                          power =    -0.394692


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-8.8e-009	2e-008
control	-8.8e-009	1	-0.56
slope	2e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.61273	0.737445	2.16736	5.05809
control	5.86108	0.332087	5.2102	6.51196
slope	-0.0122035	0.00372175	-0.019498	-0.00490895
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.15	1.9	1.86
2.9	10	6.36	5.83	2.45	1.9	0.889
10.6	9	4.39	5.73	1.31	1.9	-2.12
42	9	4.63	5.35	1.56	1.9	-1.13
191.1	10	3.73	3.53	0.941	1.9	0.334

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-54.827112	3	115.654225
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	11.3887	3	0.0098

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

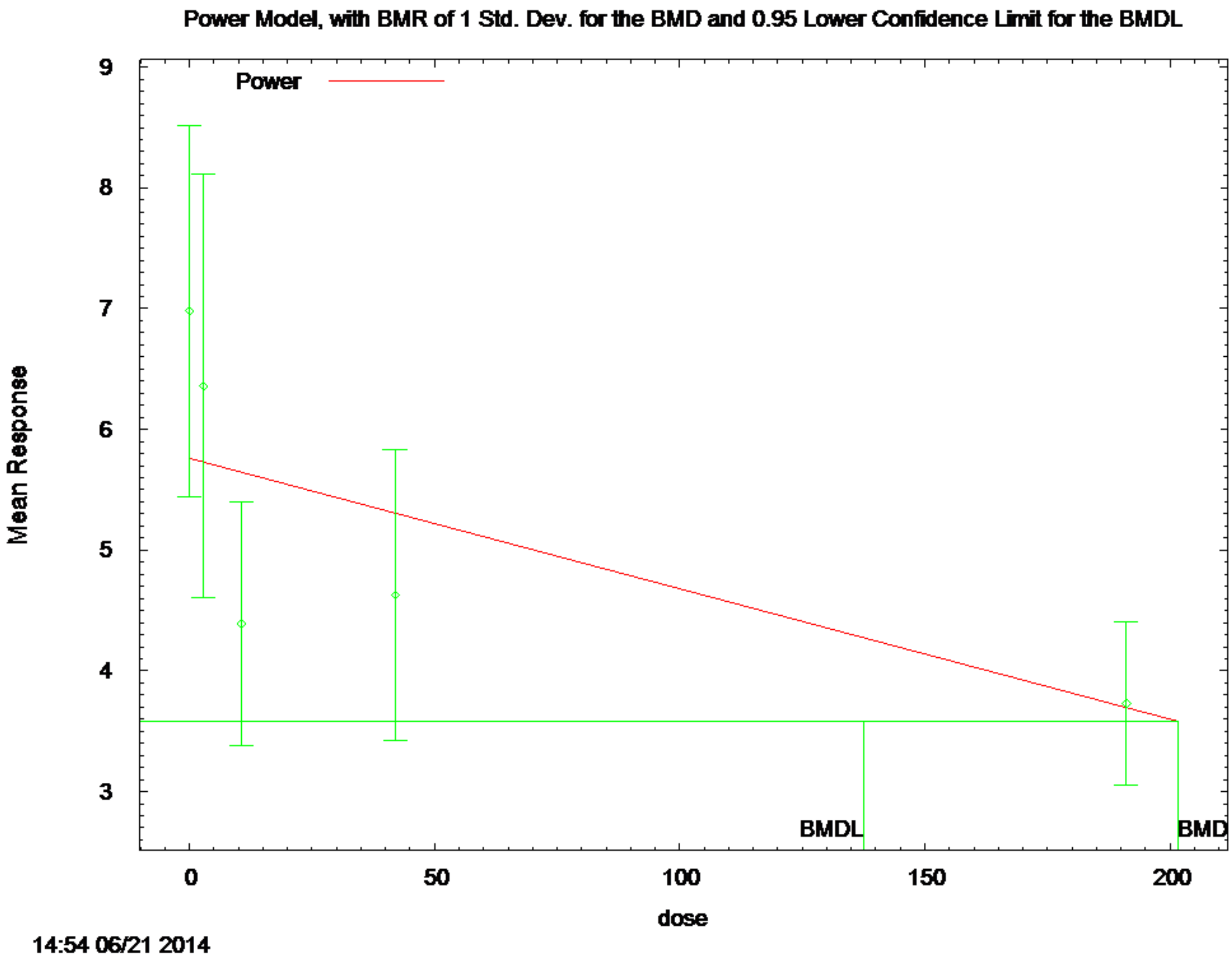
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 155.752

BMDL = 101.835


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
50
100
150
200
14:54 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.plt
                                      Sat Jun 21 14:54:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                        control =         3.73
                          slope =      2.97763
                          power =    -0.394692


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-0.99	0.4	-0.63
rho	-0.99	1	-0.47	0.66
control	0.4	-0.47	1	-0.81
slope	-0.63	0.66	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.65714	2.52061	-10.5974	-0.716839
rho	4.12209	1.56056	1.06346	7.18072
control	5.76447	0.366767	5.04562	6.48332
slope	-0.0108344	0.00248067	-0.0156965	-0.0059724
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.15	2.19	1.76
2.9	10	6.36	5.73	2.45	2.16	0.917
10.6	9	4.39	5.65	1.31	2.1	-1.8
42	9	4.63	5.31	1.56	1.84	-1.1

191.1 10 3.73 3.69 0.941 0.873
0.13

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-50.343208	4	108.686416
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	12.3314	3	0.00633

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

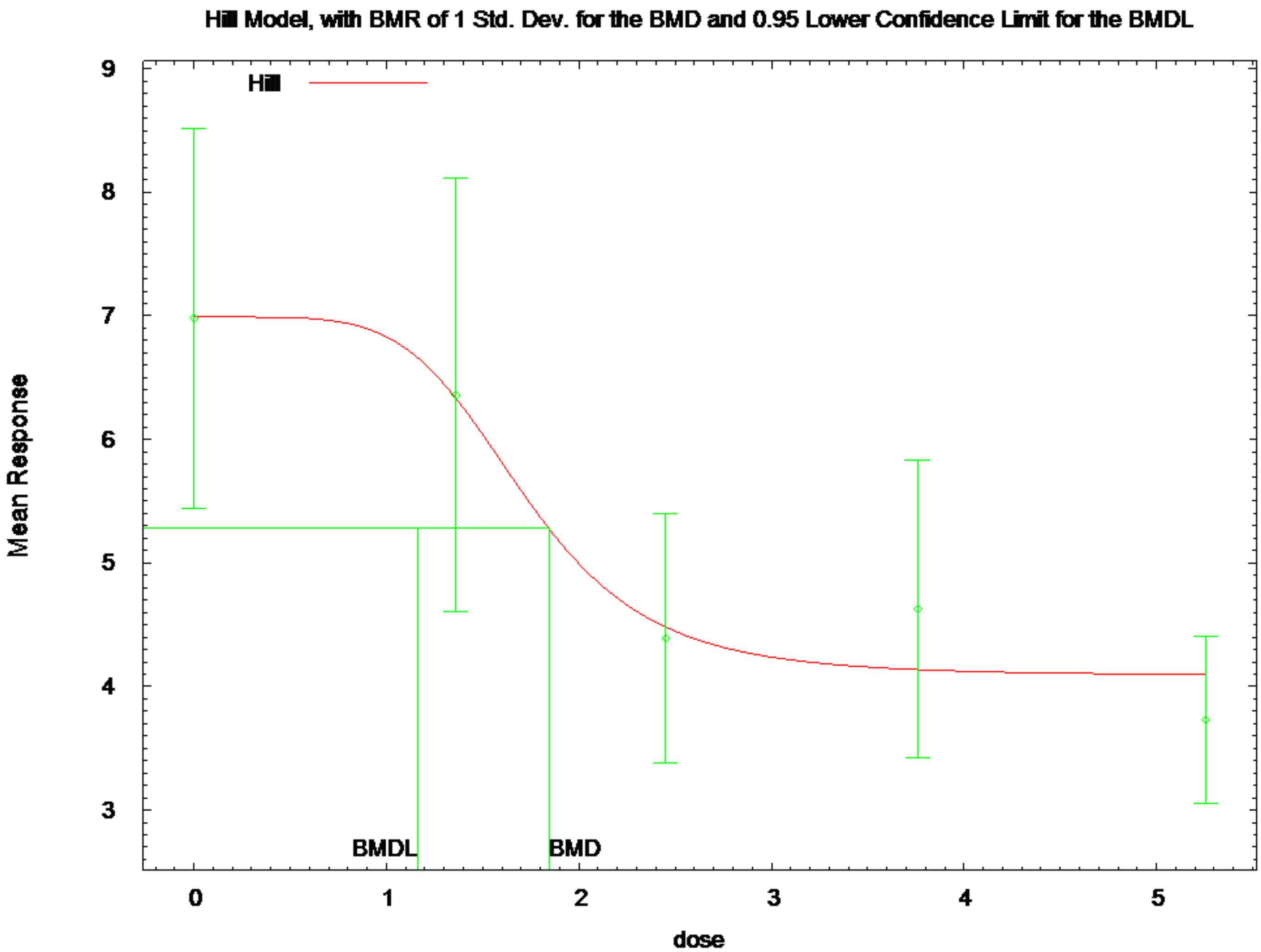
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 201.708

BMDL = 137.467

BMDS Model Results for Lymphocyte Count (Log-transformed Doses, Concurrent Controls)



15:00 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.plt
                                      Sat Jun 21 15:00:53 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                      intercept =         6.98
                              v =        -3.25
                              n =      3.73558
                              k =      1.91707


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-5.5e-009	2.3e-010	-3e-009	-5.7e-009
intercept	-5.5e-009	1	-0.76	-0.27	-0.35
v	2.3e-010	-0.76	1	0.63	-0.15
n	-3e-009	-0.27	0.63	1	-0.46
k	-5.7e-009	-0.35	-0.15	-0.46	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	2.92519	0.597102	1.75489	4.09549
intercept	6.99164	0.538504	5.93619	8.04709
v	-2.90088	0.770715	-4.41146	-1.39031
n	5.25235	5.26679	-5.07036	15.5751
k	1.72188	0.43844	0.862555	2.58121

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.99	2.15	1.71	-0.0215

1.361	10	6.36	6.34	2.45	1.71
0.0403					
2.451	9	4.39	4.48	1.31	1.71
-0.164					
3.761	9	4.63	4.14	1.56	1.71
0.863					
5.258	10	3.73	4.1	0.941	1.71
-0.682					

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-49.760637	5	109.521275
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test   -2*log(Likelihood Ratio) Test df   p-value

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	1.25572	1	0.2625

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

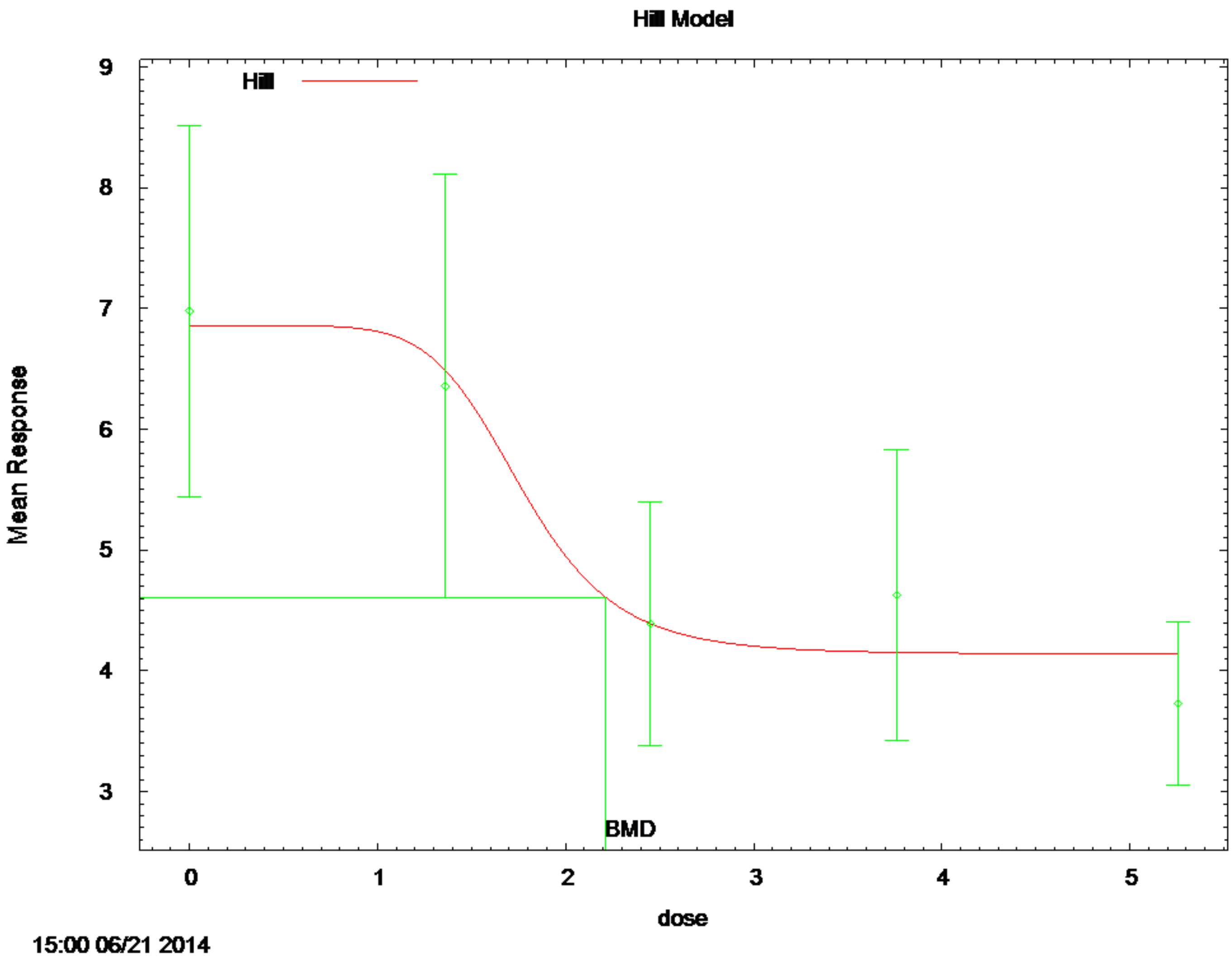
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 1.84483

BMDL = 1.16494



Hill Model
Hill
9
8
7
6
5
4
3
Mean Response
BMD
0
1
2
3
4
5
dose
15:00 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.plt
                                      Sat Jun 21 15:00:54 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                      intercept =         6.98
                              v =        -3.25
                              n =      3.73558
                              k =      1.91707


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

	lalpha	rho	intercept	v	n	k
lalpha	1	-0.99	0.33	-0.4	-0.11	-0.05
rho	-0.99	1	-0.36	0.42	0.11	0.05
intercept	0.33	-0.36	1	-0.92	-0.47	-0.46
v	-0.4	0.42	-0.92	1	0.64	0.27
n	-0.11	0.11	-0.47	0.64	1	0.037
k	-0.05	0.05	-0.46	0.27	0.037	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-2.88611	1.69349	-6.20529	0.433065
rho	2.34243	1.03058	0.322528	4.36233
intercept	6.86104	0.687328	5.5139	8.20818
v	-2.71896	0.819674	-4.32549	-1.11243
n	7.0209	7.30818	-7.30287	21.3447
k	1.76898	0.407522	0.970252	2.56771

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.86	2.15	2.25	0.167

```
1.361    10       6.36          6.49          2.45          2.11
-0.193
2.451     9       4.39          4.39          1.31          1.34
-0.00499
3.761     9       4.63          4.16          1.56          1.25
1.14
5.258    10       3.73          4.14         0.941          1.25
-1.05



 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -49.132777          6     110.265553
             A2          -43.798233         10     107.596466
             A3          -44.177523          7     102.355046
         fitted          -46.454509          6     104.909018
              R          -59.677903          2     123.355807


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	4.55397	1	0.03284

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

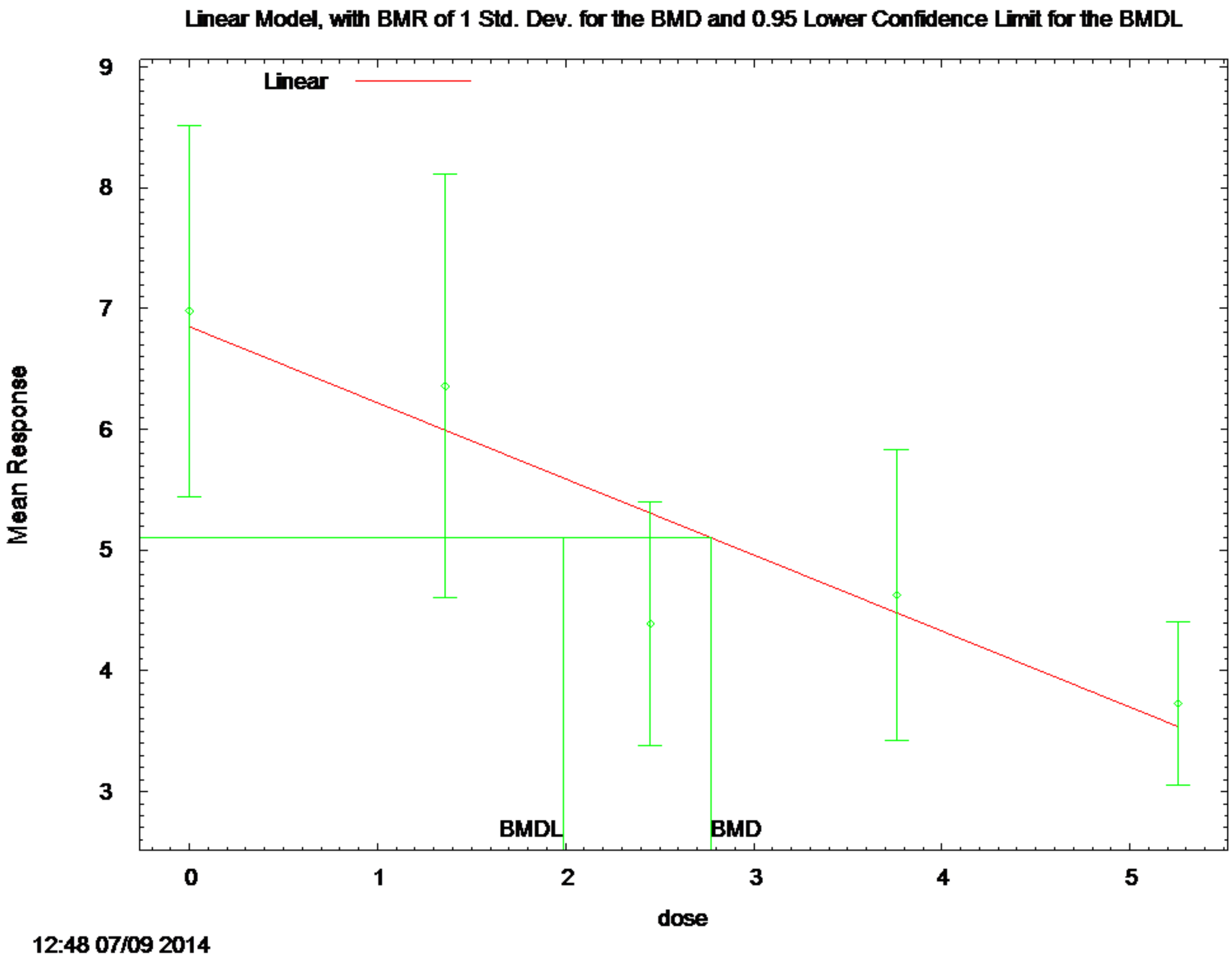
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.21464

BMDL computation failed.



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:48:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =      6.83073
                         beta_1 =    -0.628452


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.2e-008	1.2e-010
beta_0	1.2e-008	1	-0.81
beta_1	1.2e-010	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.05049	0.622679	1.83006	4.27092
beta_0	6.85042	0.427333	6.01286	7.68798
beta_1	-0.630151	0.13565	-0.89602	-0.364283

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.15	1.75	0.235
1.361	10	6.36	5.99	2.45	1.75	0.665
2.451	9	4.39	5.31	1.31	1.75	-1.57
3.761	9	4.63	4.48	1.56	1.75	0.257
5.258	10	3.73	3.54	0.941	1.75	0.349

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-50.767279	3	107.534558
R	-59.677903	2	123.355807

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	3.269	3	0.352

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a

different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

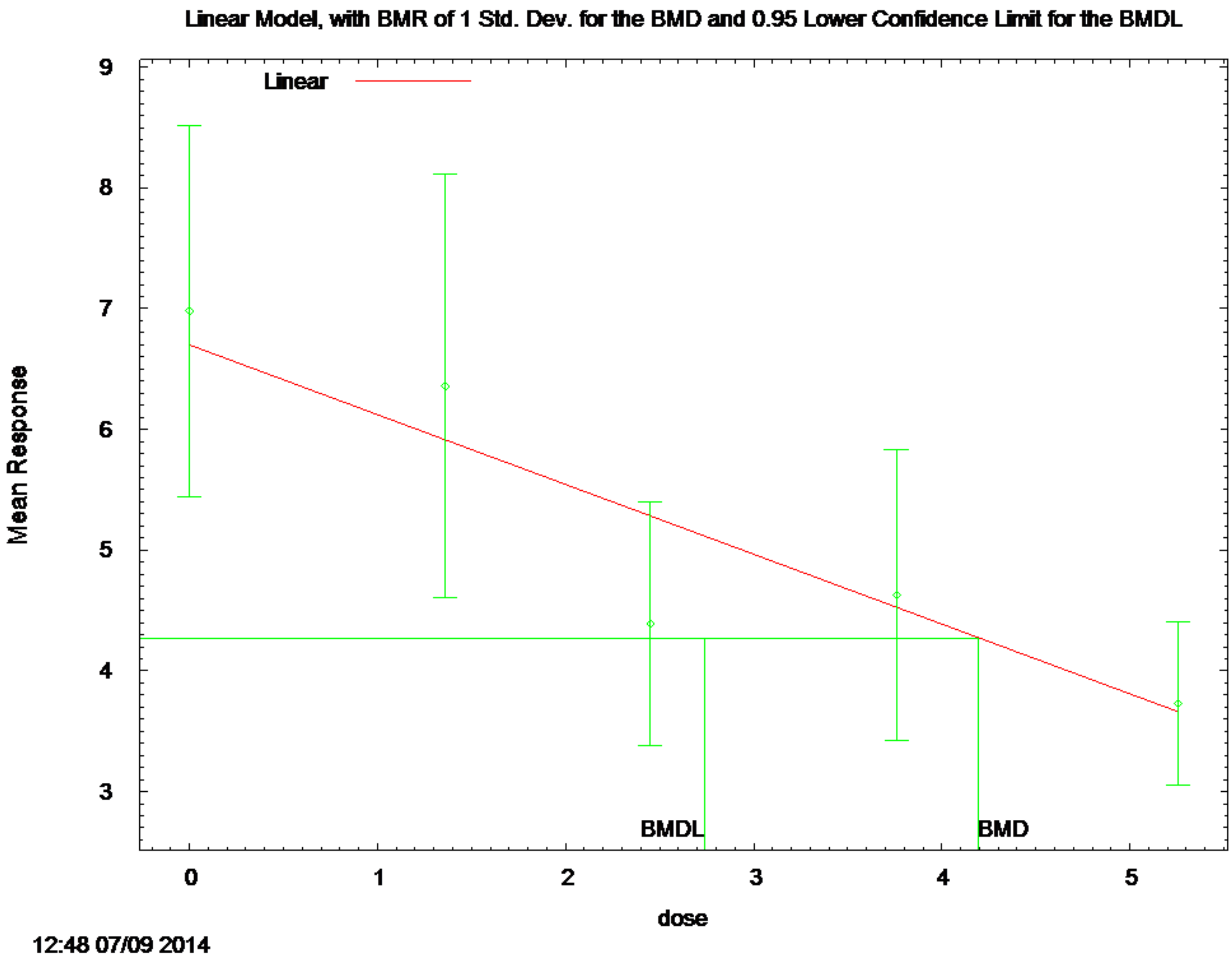
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.77166

BMDL = 1.99011


Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
12:48 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File: 
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File: 
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:48:53 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is: 

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values  
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      6.83073
                         beta_1 =    -0.628452


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99         0.17         -0.2
```

rho	-0.99	1	-0.17	0.2
beta_0	0.17	-0.17	1	-0.91
beta_1	-0.2	0.2	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.00629	1.70369	-7.34546	-0.667114
rho	3.03769	1.03603	1.0071	5.06828
beta_0	6.69816	0.5031	5.7121	7.68422
beta_1	-0.577576	0.122436	-0.817545	-0.337606

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.7	2.15	2.42	0.368
1.361	10	6.36	5.91	2.45	2.01	0.706
2.451	9	4.39	5.28	1.31	1.69	-1.58
3.761	9	4.63	4.53	1.56	1.34	0.234
5.258	10	3.73	3.66	0.941	0.969	0.224

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-46.826872	4	101.653745
R	-59.677903	2	123.355807

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	5.2987	3	0.1512

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance
appears

to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

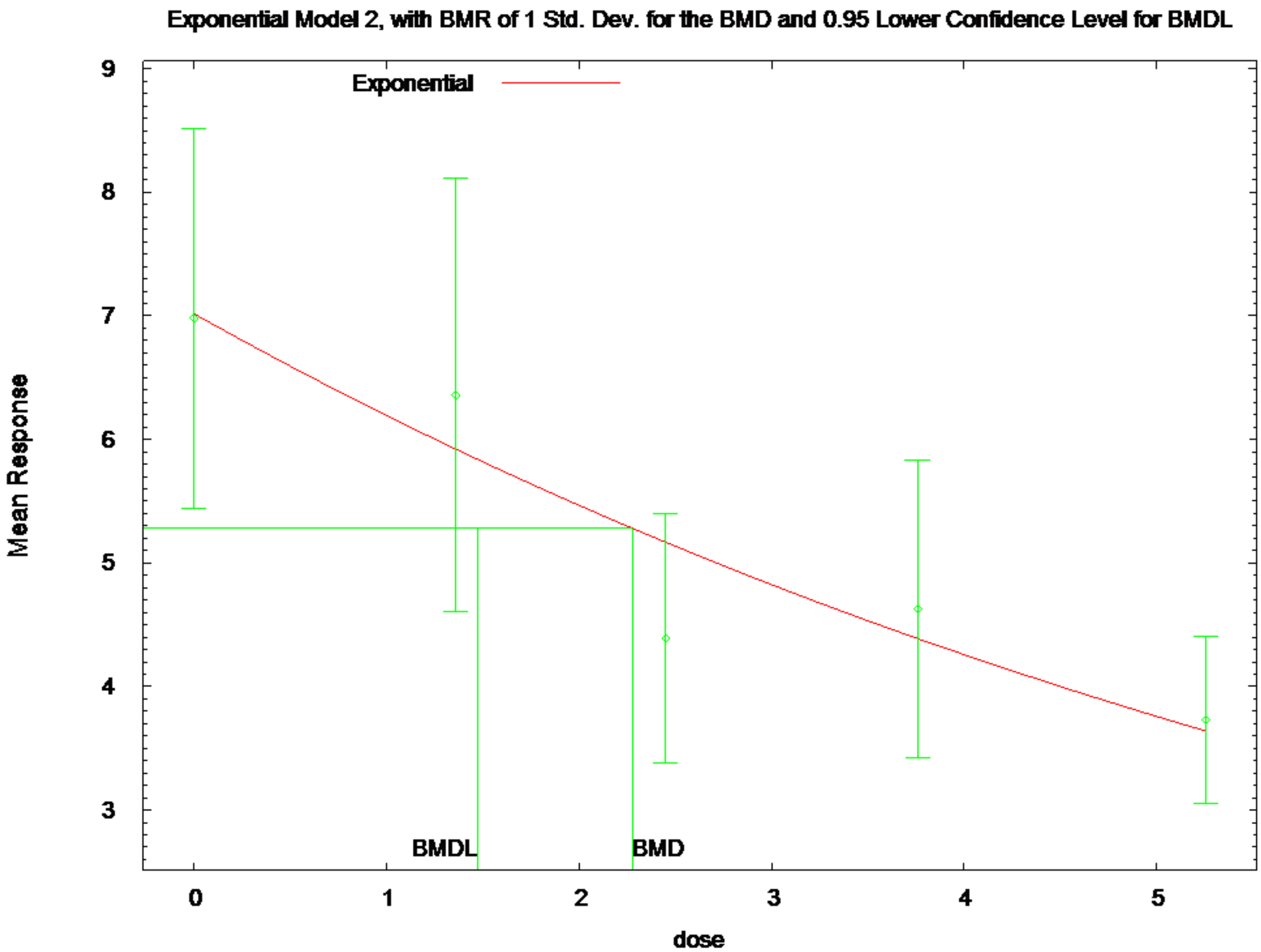
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.19696

BMDL = 2.73754



15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.0472
rho(S)	0
a	3.75105
b	0.120756
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.10399
rho	0
a	7.01811
b	0.12488
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.018	1.737	-0.0694
1.361	5.921	1.737	0.7991
2.451	5.168	1.737	-1.343
3.761	4.388	1.737	0.4184
5.258	3.64	1.737	0.1646

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
2	-50.49569	3	106.9914

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

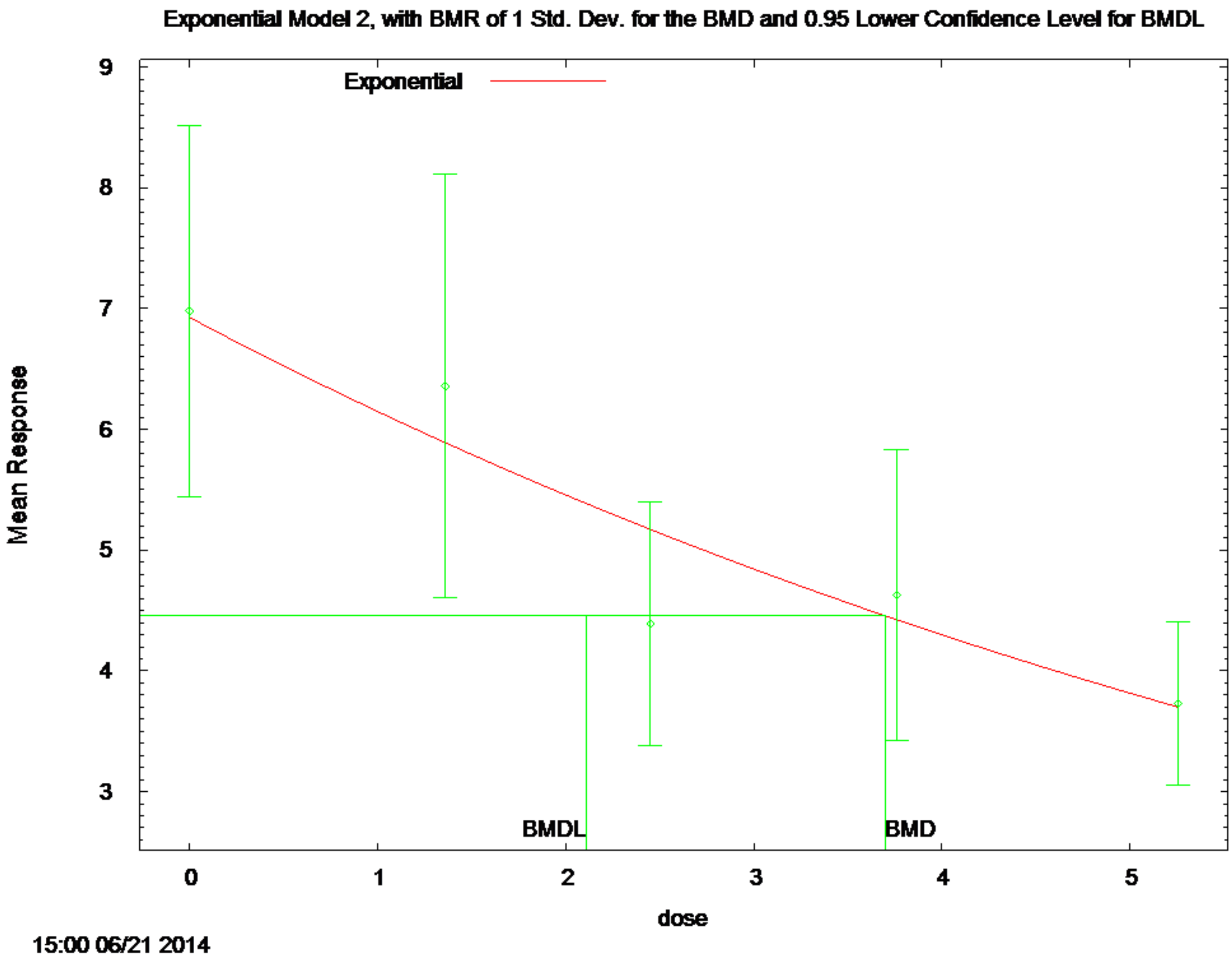
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	

```
0.0001029
     Test 2                              10.67          4
0.03055
     Test 3                              10.67          4
0.03055
     Test 4                              2.726          3
0.4359


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  Consider running
     a non-homogeneous variance model.

     The p-value for Test 3 is less than .1.  You may want to
     consider a different variance model.

     The p-value for Test 4 is greater than .1.  Model 2 seems
     to adequately describe the data.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =       2.2766

                 BMDL =      1.47441
```



Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:54 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-3.58873
rho	2.77965
a	3.75105
b	0.120756
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-3.68376
rho	2.83845
a	6.92765
b	0.119268
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.928	2.472	0.06697
1.361	5.89	1.963	0.7575
2.451	5.172	1.633	-1.436
3.761	4.424	1.308	0.4734
5.258	3.7	1.015	0.09256

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
             Var{e(ij)} = Sigma(i)^2

   Model A3:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

   Model  R:        Yij = Mu + e(i)
             Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
2	-46.77567	4	101.5513

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

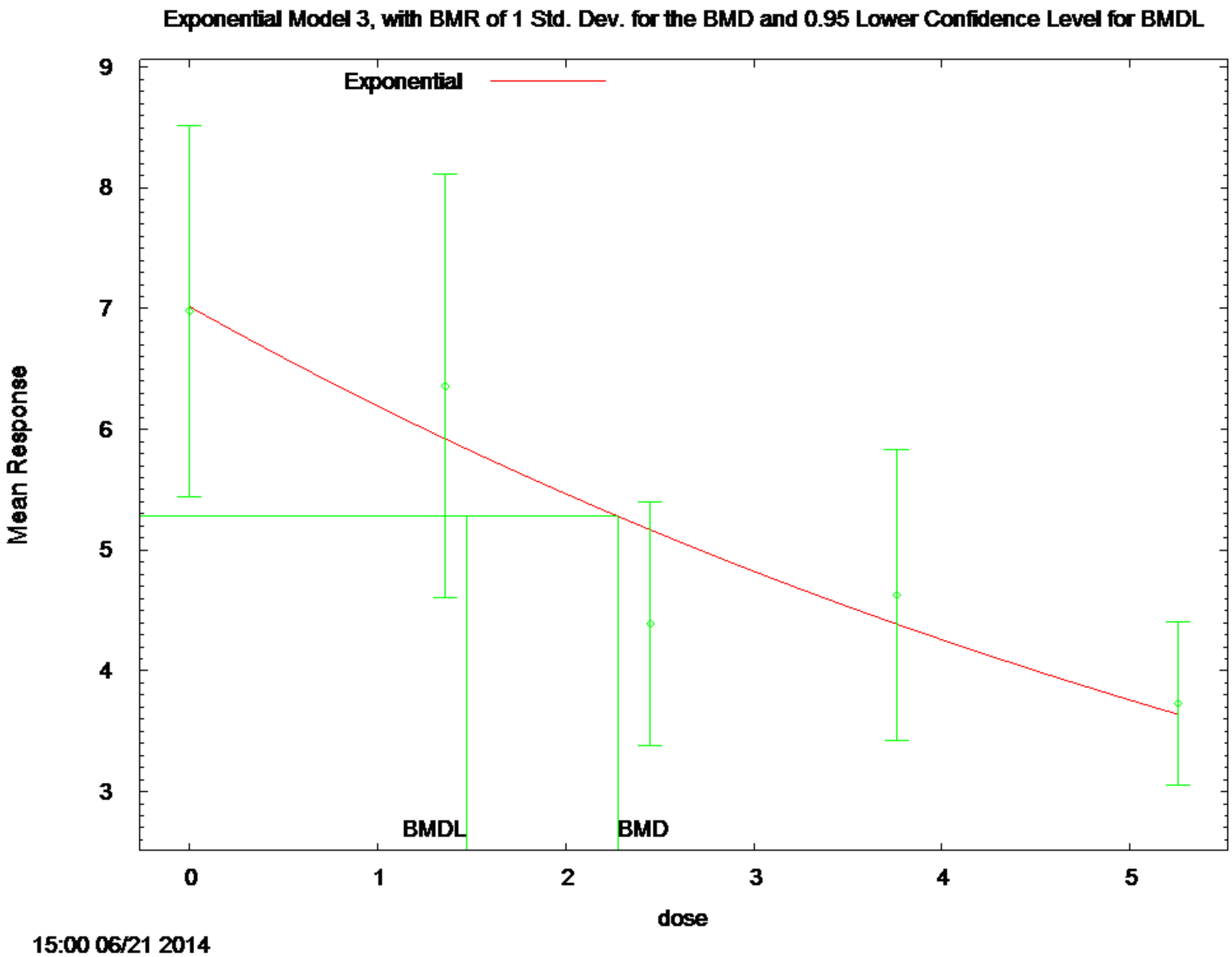
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029
Test 2	10.67	4	

```
0.03055
     Test 3                         0.7586          3
0.8593
     Test 4                          5.196          3
0.158


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 4 is greater than .1.  Model 2 seems
     to adequately describe the data.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      3.70064

                 BMDL =      2.11166
```



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.0472
rho(S)	0
a	3.75105
b	0.120756
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.10399
rho	0
a	7.01811
b	0.12488
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.018	1.737	-0.0694
1.361	5.921	1.737	0.7991
2.451	5.168	1.737	-1.343
3.761	4.388	1.737	0.4184
5.258	3.64	1.737	0.1646

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
3	-50.49569	3	106.9914

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 5a	2.726	3	0.4359

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

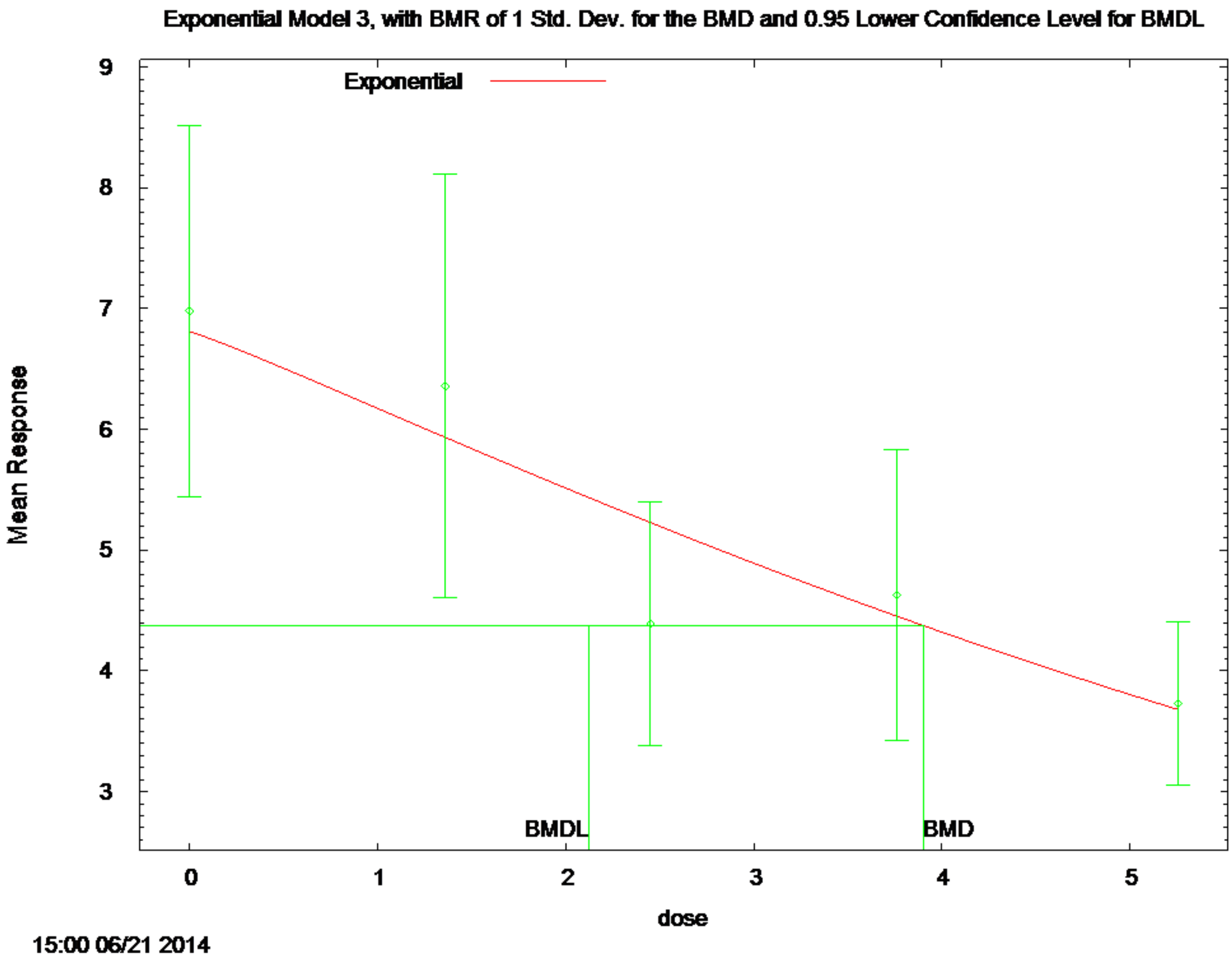
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.2766

BMDL = 1.47441



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
15:00 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sat Jun 21 15:00:54 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-3.58873
rho	2.77965
a	3.75105
b	0.120756
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-3.804
rho	2.9112
a	6.80909
b	0.122743
c	0
d	1.10799

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.809	2.436	0.2219
1.361	5.933	1.993	0.6771
2.451	5.228	1.658	-1.516
3.761	4.453	1.313	0.4044
5.258	3.679	0.9942	0.1617

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
3	-46.74085	5	103.4817

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029

Test 2	10.67	4	0.03055
Test 3	0.7586	3	0.8593
Test 5a	5.127	2	0.07705

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

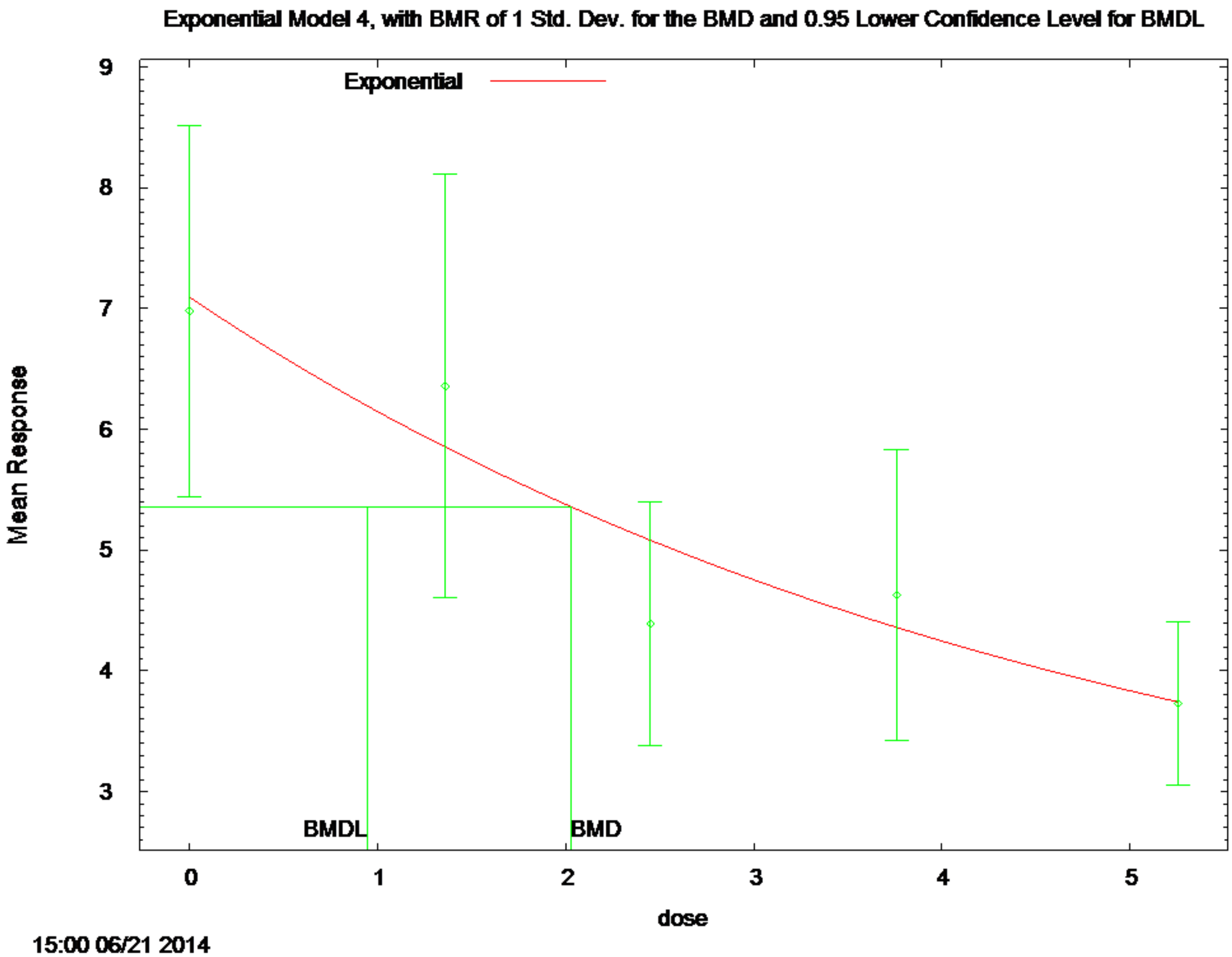
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.90494

BMDL = 2.12529



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.0472
rho(S)	0
a	7.329
b	0.208885
c	0.254469
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.10181
rho	0
a	7.09555
b	0.208122
c	0.289709
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.096	1.735	-0.2106
1.361	5.852	1.735	0.9254
2.451	5.082	1.735	-1.196
3.761	4.36	1.735	0.4676
5.258	3.743	1.735	-0.02344

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
4	-50.44333	4	108.8867

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 6a	2.621	2	0.2697

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

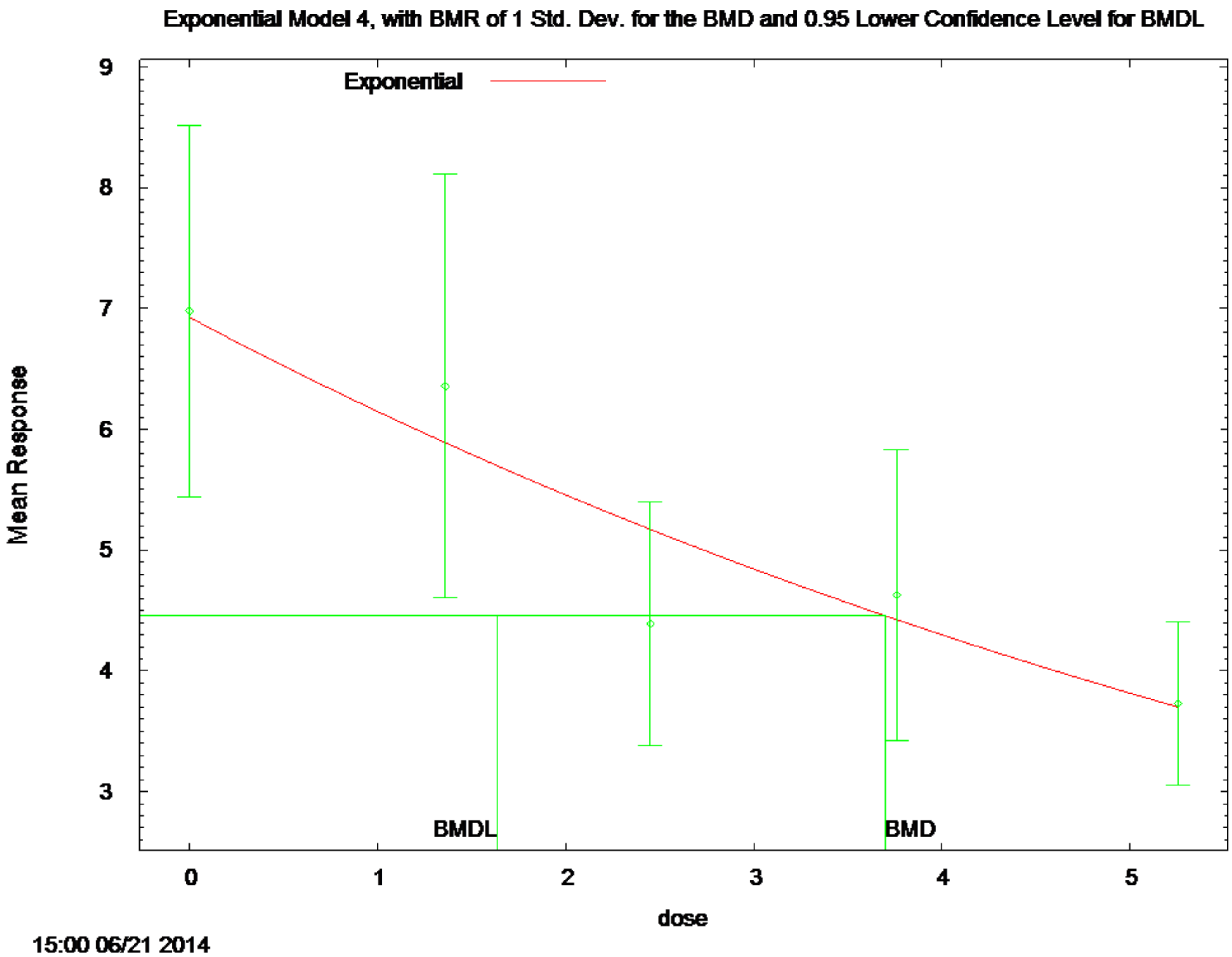
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.02729

BMDL = 0.94493


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:54 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-3.58873
rho	2.77965
a	7.329
b	0.208885
c	0.254469
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-3.68376
rho	2.83845
a	6.92765
b	0.119268
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.928	2.472	0.06697
1.361	5.89	1.963	0.7575
2.451	5.172	1.633	-1.436
3.761	4.424	1.308	0.4734
5.258	3.7	1.015	0.09256

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
4	-46.77567	4	101.5513

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029

Test 2	10.67	4	0.03055
Test 3	0.7586	3	0.8593
Test 6a	5.196	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

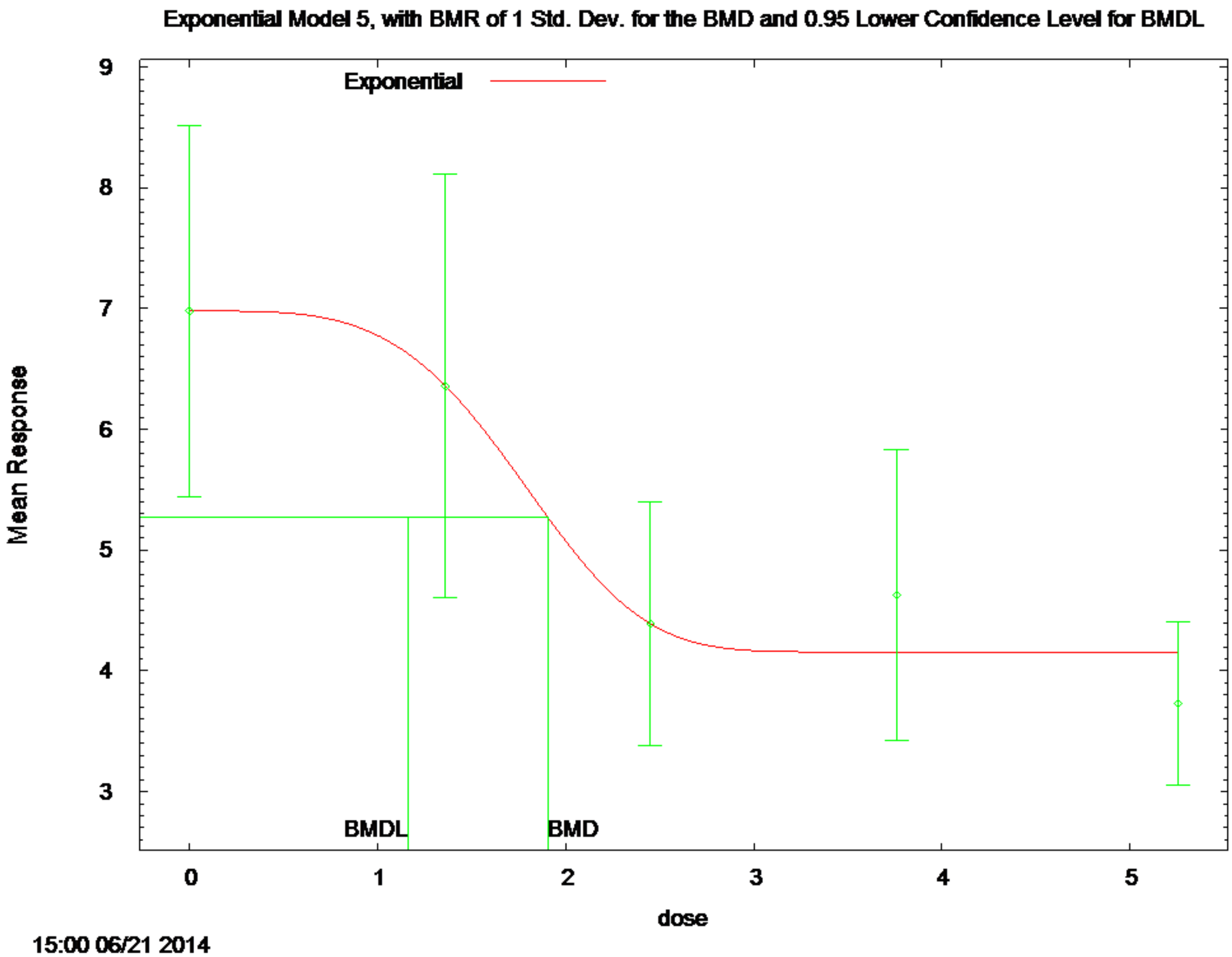
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.70064

BMDL = 1.6333


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
15:00 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:52 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.0472
rho(S)	0
a	7.329
b	0.208885
c	0.254469
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.07486
rho	0
a	6.98002
b	0.514905
c	0.595454
d	3.92235

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.98	1.712	-3.861e-005
1.361	6.36	1.712	6.283e-005
2.451	4.39	1.712	-0.0001466
3.761	4.156	1.712	0.8303
5.258	4.156	1.712	-0.7876

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-49.13278	6	110.2656
R	-59.6779	2	123.3558
5	-49.79671	5	109.5934

```
   Additive constant for all log-likelihoods =     -44.11.  This
constant added to the
   above values gives the log-likelihood including the term that
does not
   depend on the model parameters.
```

Explanation of Tests

```
   Test 1:  Does response and/or variances differ among Dose
levels? (A2 vs. R)
   Test 2:  Are Variances Homogeneous? (A2 vs. A1)
   Test 3:  Are variances adequately modeled? (A2 vs. A3)

   Test 7a: Does Model 5 fit the data? (A3 vs 5)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.76	8	0.0001029
Test 2	10.67	4	0.03055
Test 3	10.67	4	0.03055
Test 7a	1.328	1	0.2492

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

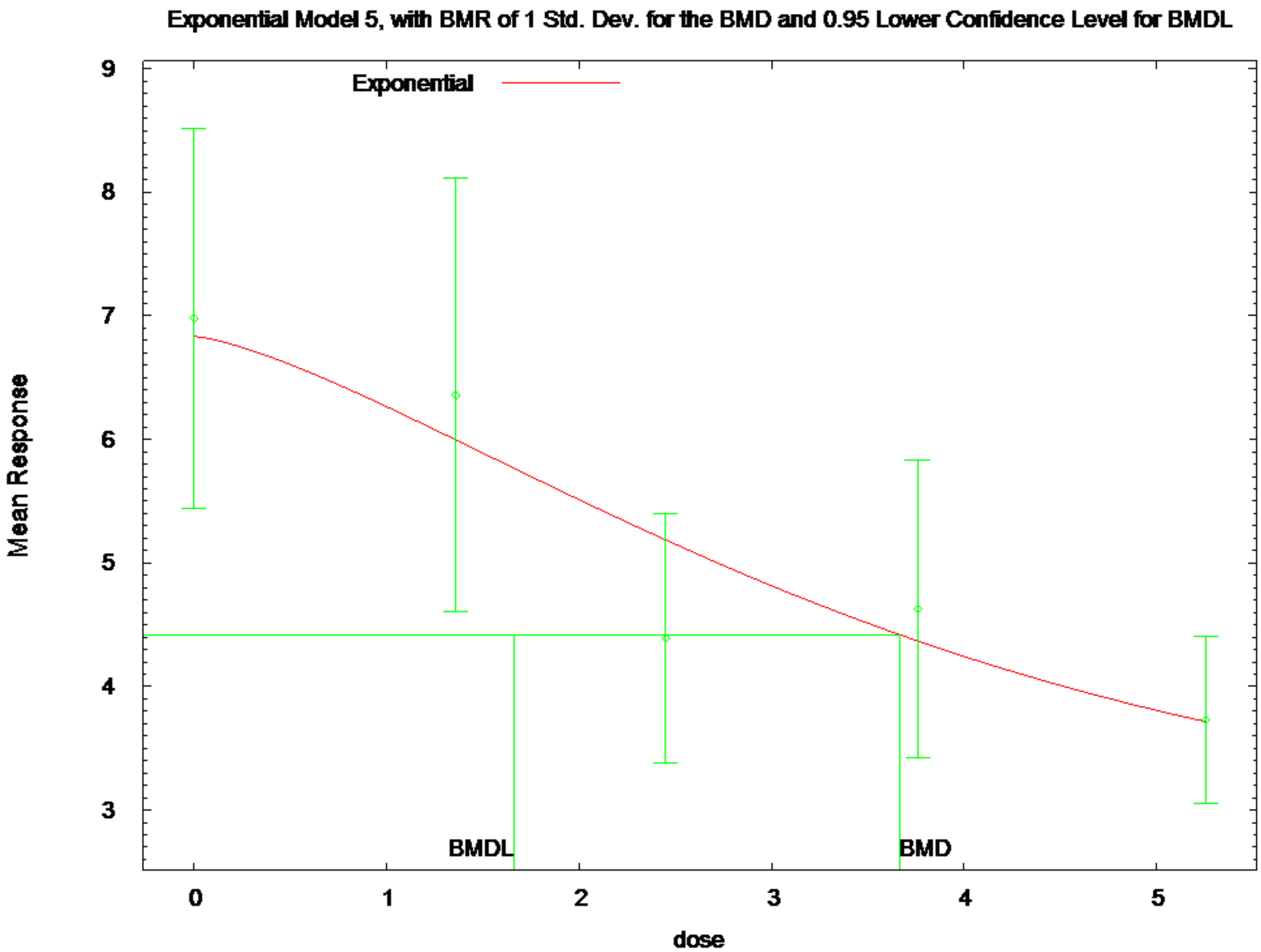
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 1.90743

BMDL = 1.16077



15:00 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:00:54 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-3.58873
rho	2.77965
a	7.329
b	0.208885
c	0.254469
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-3.65305
rho	2.81765
a	6.83365
b	0.262032
c	0.422483
d	1.38992

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.146
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.834	2.413	0.1918
1.361	5.996	2.007	0.5734
2.451	5.186	1.636	-1.46
3.761	4.368	1.285	0.6107
5.258	3.715	1.023	0.04492

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-49.13278	6	110.2656
A2	-43.79823	10	107.5965
A3	-44.17752	7	102.355
R	-59.6779	2	123.3558
5	-46.69115	6	105.3823

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.76	8	0.0001029

Test 2 10.67 4
0.03055
Test 3 0.7586 3
0.8593
Test 7a 5.027 1
0.02495

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous
variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled
variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

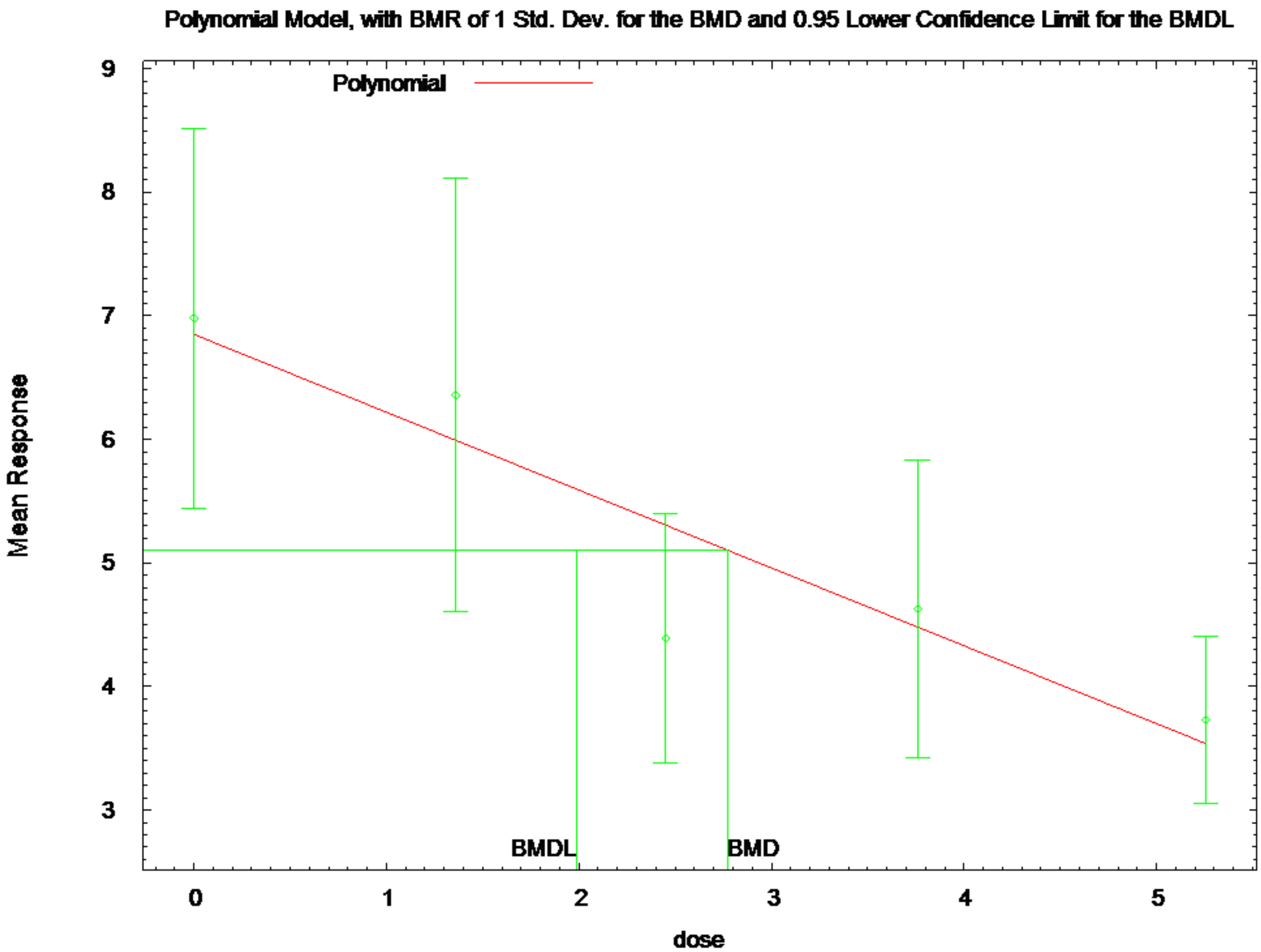
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.66557

BMDL = 1.66159



12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:48:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =      7.10002
                         beta_1 =     -1.02021
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1e-007	-1.1e-007
beta_0	1e-007	1	-0.81
beta_1	-1.1e-007	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.05049	0.622679	1.83006	4.27092
beta_0	6.85042	0.427333	6.01286	7.68798
beta_1	-0.630151	0.13565	-0.89602	-0.364283
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.15	1.75	0.235
1.361	10	6.36	5.99	2.45	1.75	0.665
2.451	9	4.39	5.31	1.31	1.75	-1.57
3.761	9	4.63	4.48	1.56	1.75	0.257
5.258	10	3.73	3.54	0.941	1.75	0.349

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-50.767279	3	107.534558
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	3.269	3	0.352

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

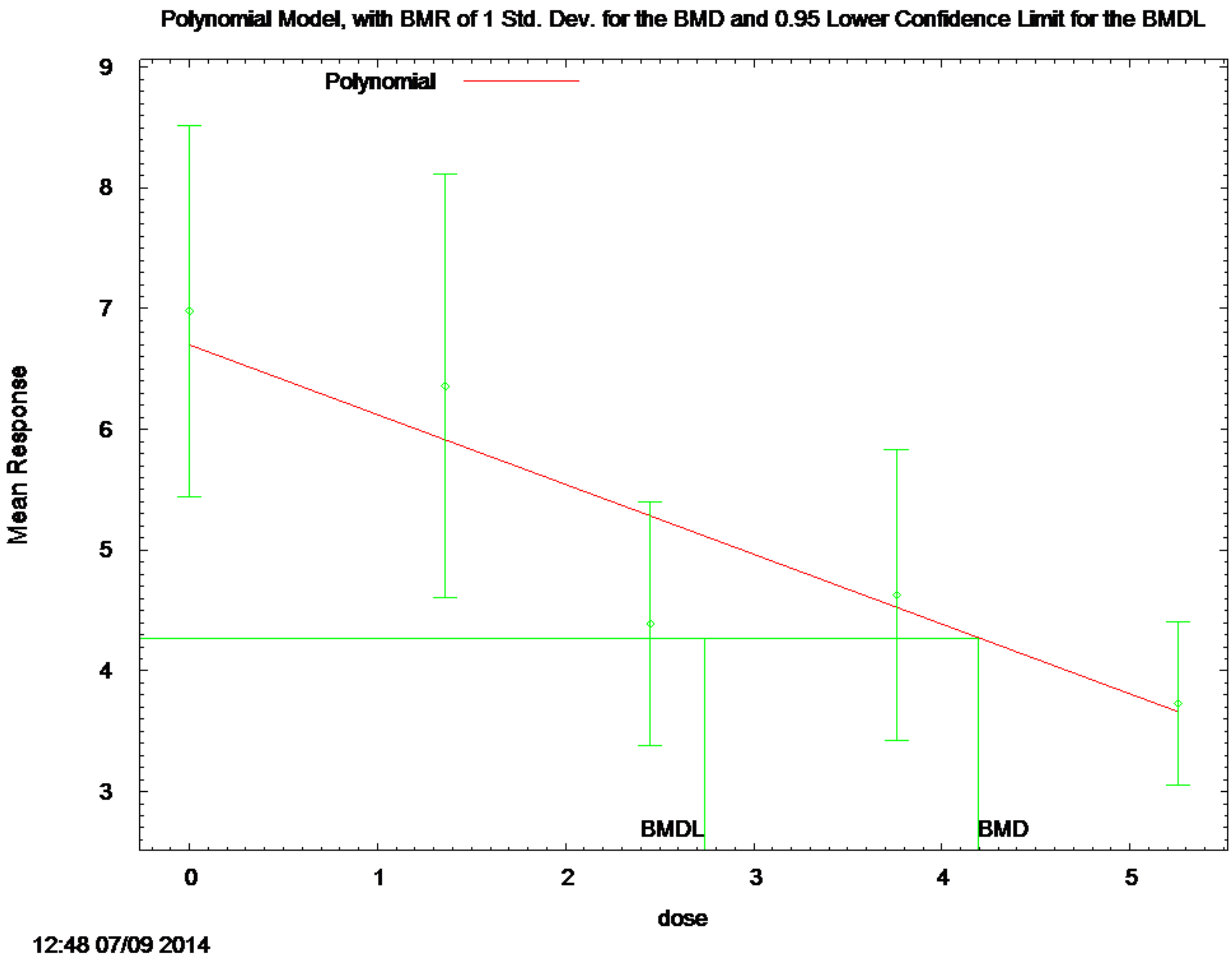
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.77166

BMDL = 1.99011


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.plt
                                    Wed Jul 09 12:48:53 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      7.10002
                         beta_1 =     -1.02021
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.17	-0.2
rho	-0.99	1	-0.17	0.2
beta_0	0.17	-0.17	1	-0.91
beta_1	-0.2	0.2	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.00629	1.70369	-7.34546	-0.667115
rho	3.03769	1.03603	1.0071	5.06828
beta_0	6.69816	0.5031	5.7121	7.68422
beta_1	-0.577576	0.122436	-0.817545	-0.337606
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.7	2.15	2.42	0.368
1.361	10	6.36	5.91	2.45	2.01	0.706
2.451	9	4.39	5.28	1.31	1.69	-1.58
3.761	9	4.63	4.53	1.56	1.34	0.234

5.258 10 3.73 3.66 0.941 0.969
0.224

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-46.826872	4	101.653745
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	5.2987	3	0.1512

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

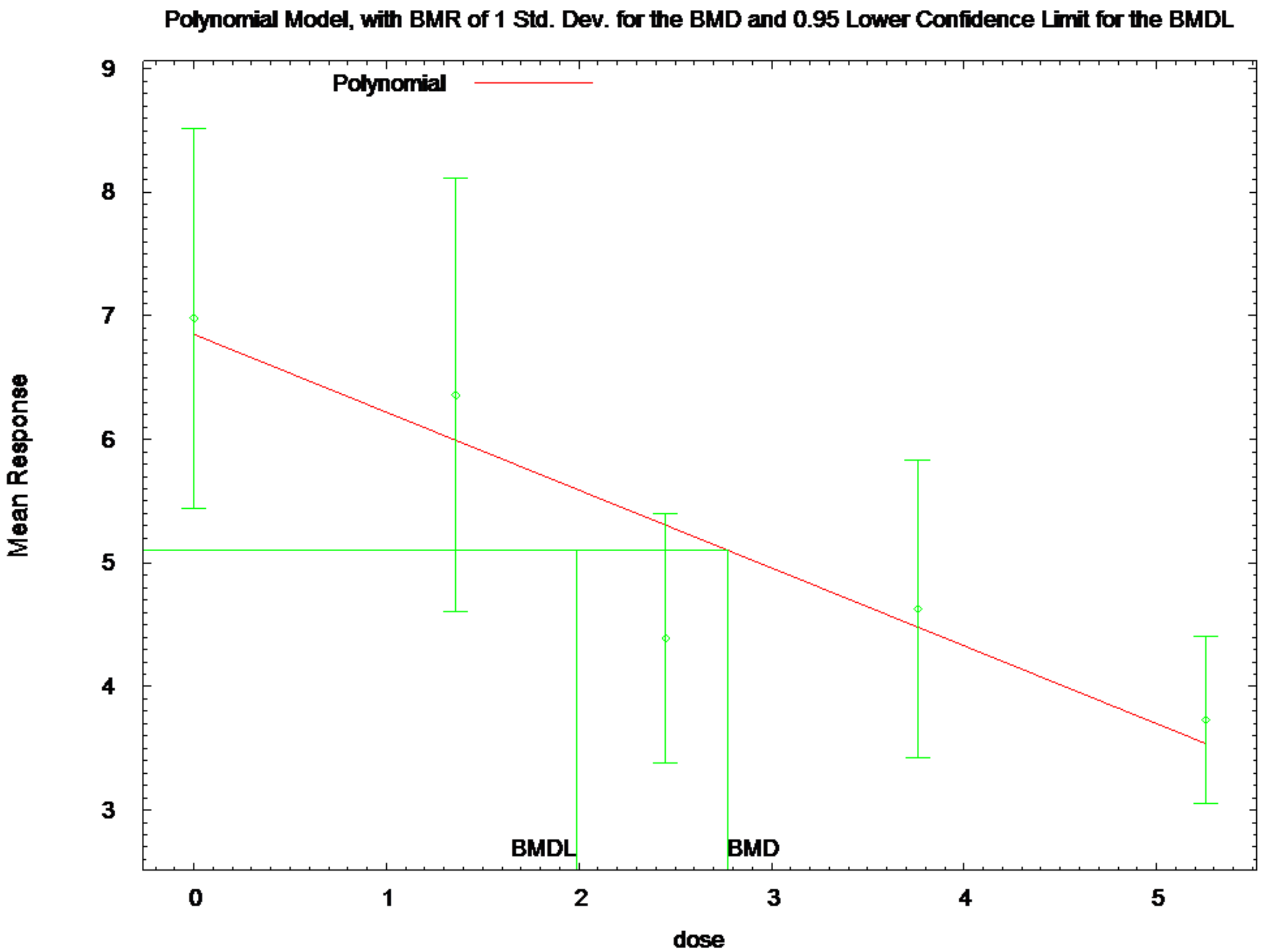
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.19696

BMDL = 2.73754



12:48 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.plt
                                    Wed Jul 09 12:48:52 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =      7.07831
                         beta_1 =    -0.897602
                         beta_2 =            0
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-3e-008	-1.3e-008
beta_0	-3e-008	1	-0.81
beta_1	-1.3e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.05049	0.622679	1.83006	4.27092
beta_0	6.85042	0.427333	6.01286	7.68798
beta_1	-0.630151	0.13565	-0.89602	-0.364283
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.15	1.75	0.235
1.361	10	6.36	5.99	2.45	1.75	0.665
2.451	9	4.39	5.31	1.31	1.75	-1.57
3.761	9	4.63	4.48	1.56	1.75	0.257
5.258	10	3.73	3.54	0.941	1.75	

0.349

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-50.767279	3	107.534558
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	3.269	3	0.352

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

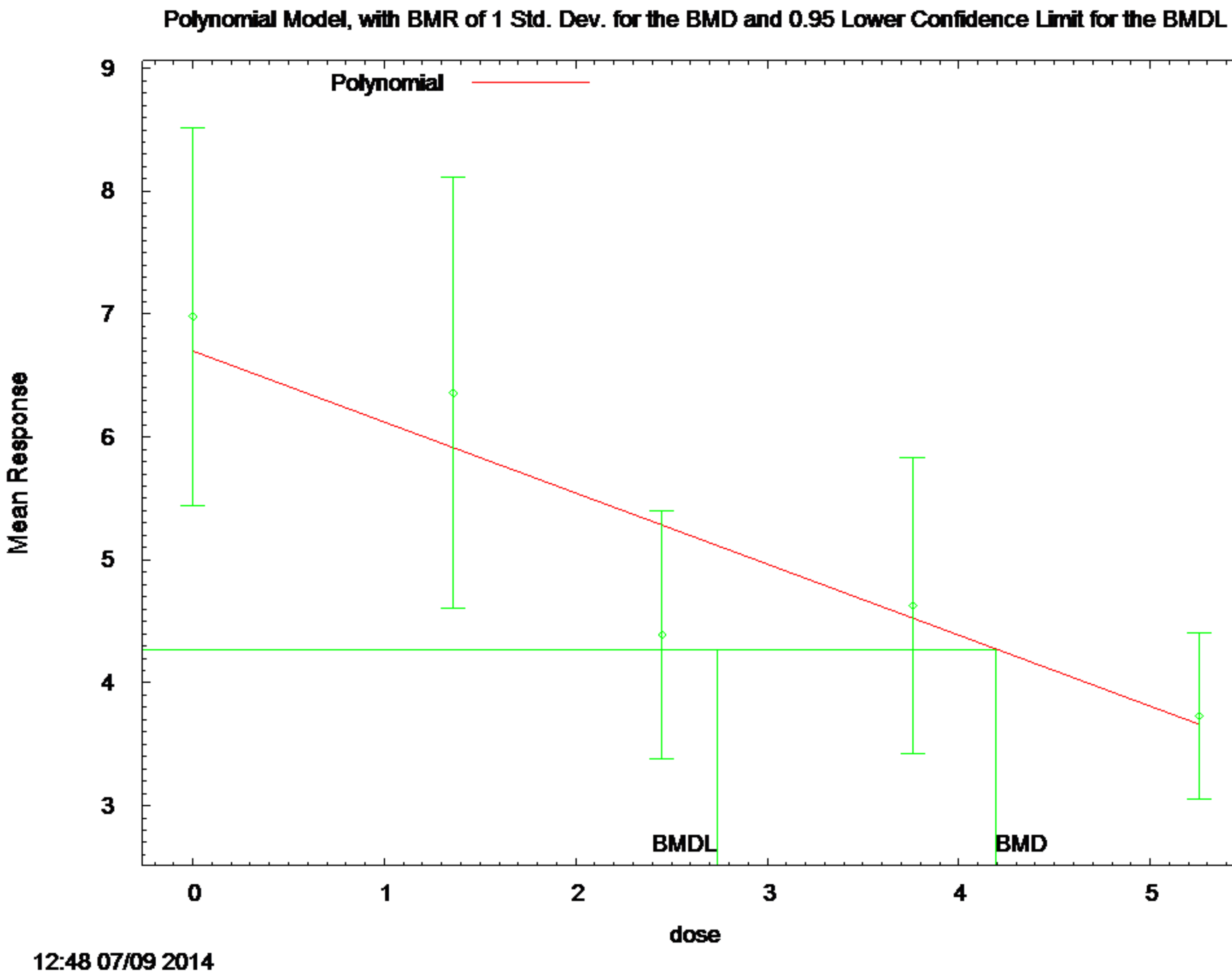
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.77166

BMDL = 1.99011


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.plt
                                    Wed Jul 09 12:48:53 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =      7.07831
                         beta_1 =    -0.897602
                         beta_2 =            0
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.17	-0.2
rho	-0.99	1	-0.17	0.2
beta_0	0.17	-0.17	1	-0.91
beta_1	-0.2	0.2	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.00629	1.70369	-7.34547	-0.667116
rho	3.03769	1.03603	1.0071	5.06828
beta_0	6.69816	0.5031	5.7121	7.68422
beta_1	-0.577575	0.122436	-0.817545	-0.337606
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.7	2.15	2.42	0.368
1.361	10	6.36	5.91	2.45	2.01	0.706
2.451	9	4.39	5.28	1.31	1.69	-1.58

3.761 0.234	9	4.63	4.53	1.56	1.34
5.258 0.224	10	3.73	3.66	0.941	0.969

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-46.826872	4	101.653745
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593

Test 4 5.2987 3 0.1512

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

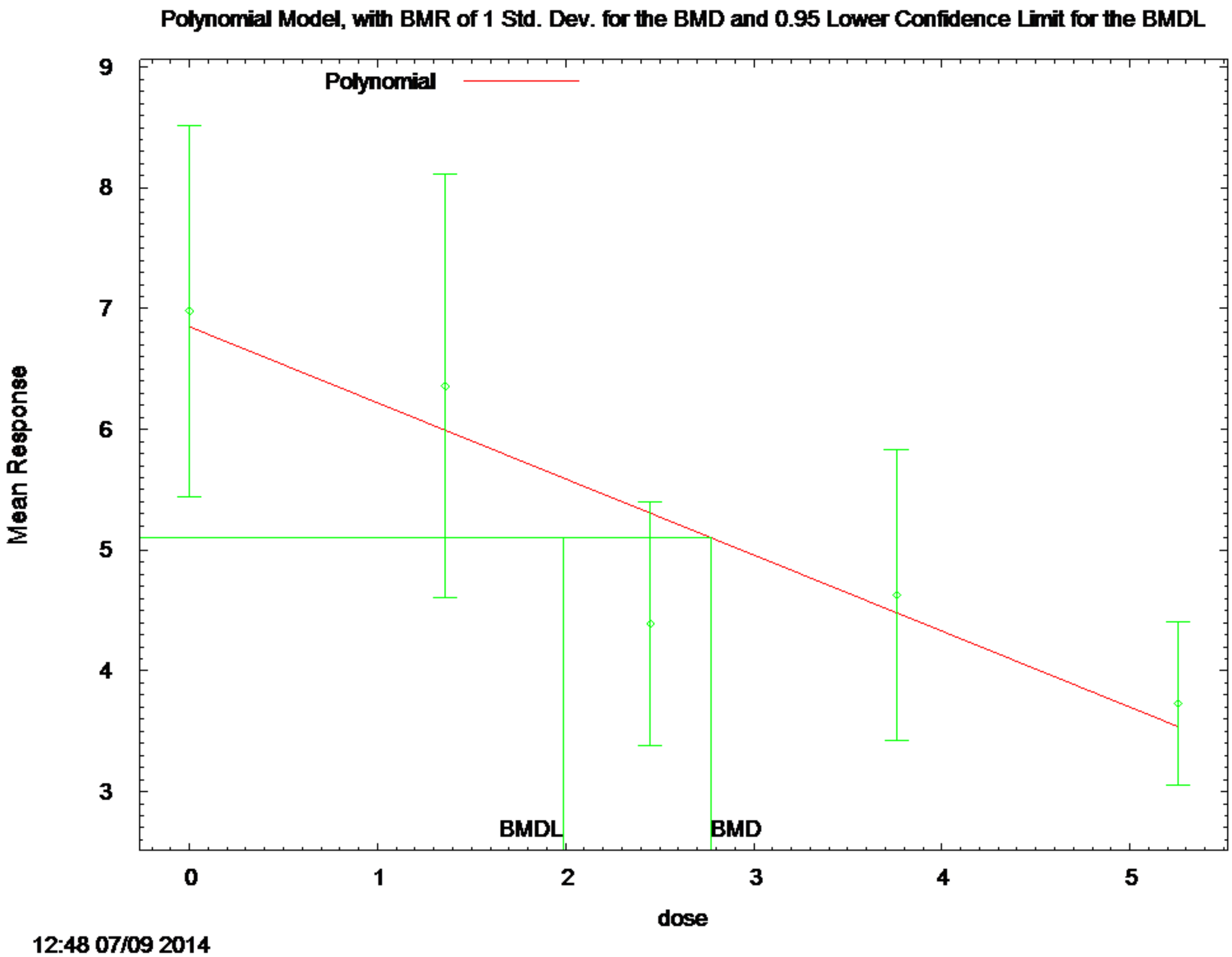
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.19697

BMDL = 2.73754


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.plt
                                    Wed Jul 09 12:48:52 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                         beta_0 =         6.98
                         beta_1 =            0
                         beta_2 =     -4.14163
                         beta_3 =            0
                         beta_4 =    -0.123946


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-3.4e-008	4.2e-008
beta_0	-3.4e-008	1	-0.81
beta_1	4.2e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.05049	0.622679	1.83006	4.27092
beta_0	6.85042	0.427333	6.01286	7.68798
beta_1	-0.630151	0.13565	-0.89602	-0.364282
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.15	1.75	0.235
1.361	10	6.36	5.99	2.45	1.75	0.665
2.451	9	4.39	5.31	1.31	1.75	-1.57
3.761	9	4.63	4.48	1.56	1.75	

0.257
5.258 10 3.73 3.54 0.941 1.75
0.349

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-50.767279	3	107.534558
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	3.269	3	0.352

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

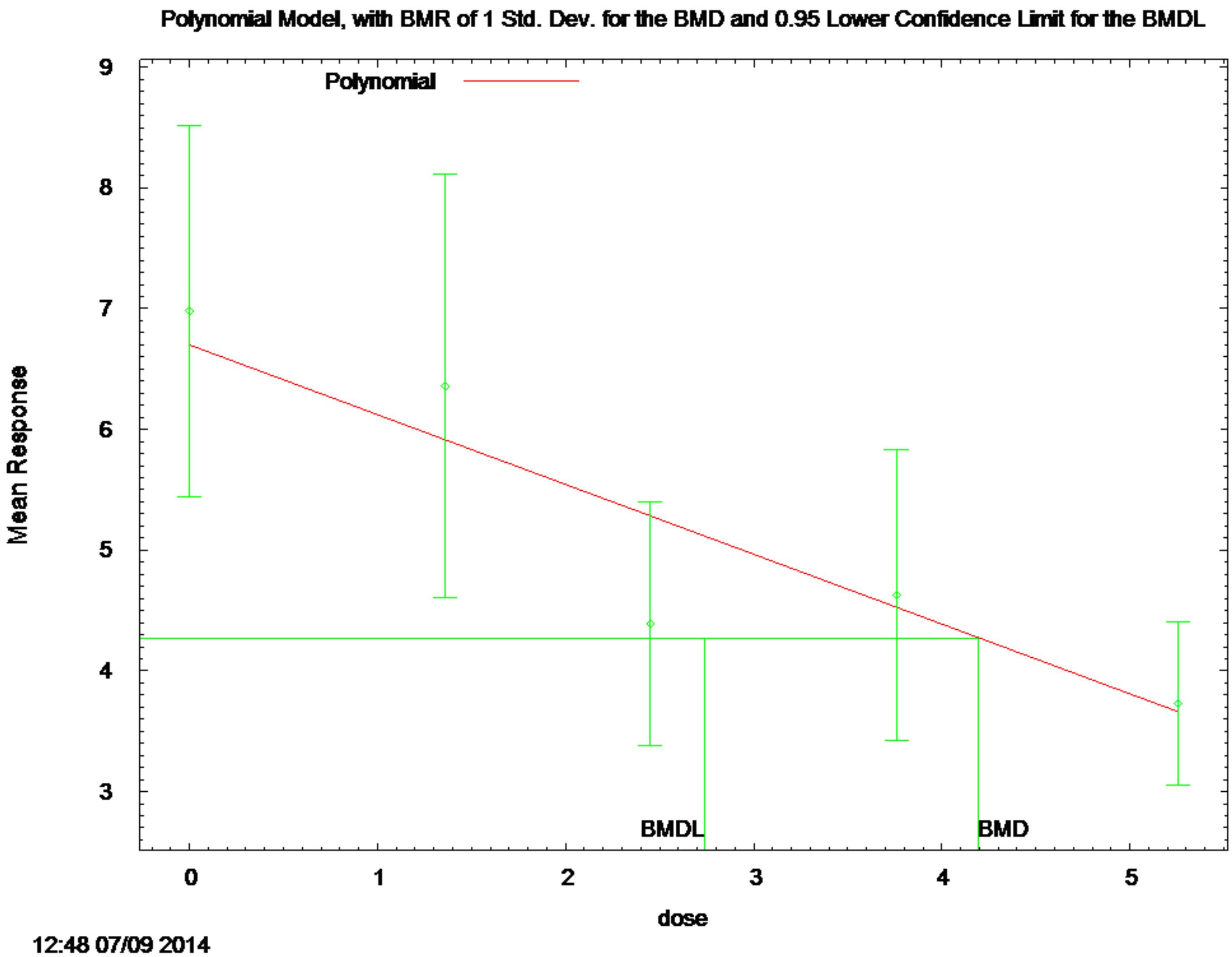
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.77166

BMDL = 1.99011


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
12:48 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Concurrent_Ln/Lymphocyt
e_Concurrent_LN-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.plt
                                          Wed Jul 09 12:48:53 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                         beta_0 =         6.98
                         beta_1 =            0
                         beta_2 =     -4.14163
                         beta_3 =            0
                         beta_4 =    -0.123946


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.17	-0.2
rho	-0.99	1	-0.17	0.2
beta_0	0.17	-0.17	1	-0.91
beta_1	-0.2	0.2	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.00629	1.70369	-7.34547	-0.667111
rho	3.03769	1.03604	1.0071	5.06828
beta_0	6.69816	0.503101	5.7121	7.68422
beta_1	-0.577575	0.122436	-0.817545	-0.337606
beta_2	-0	NA		
beta_3	-2.72589e-104	NA		
beta_4	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.7	2.15	2.42	0.368
1.361	10	6.36	5.91	2.45	2.01	

```
0.706
2.451     9       4.39         5.28         1.31         1.69
-1.58
3.761     9       4.63         4.53         1.56         1.34
0.234
5.258    10       3.73         3.66        0.941        0.969
0.224
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -49.132777           6     110.265553
             A2          -43.798233          10     107.596466
             A3          -44.177523           7     102.355046
         fitted          -46.826872           4     101.653745
              R          -59.677903           2     123.355807


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	5.2987	3	0.1512

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

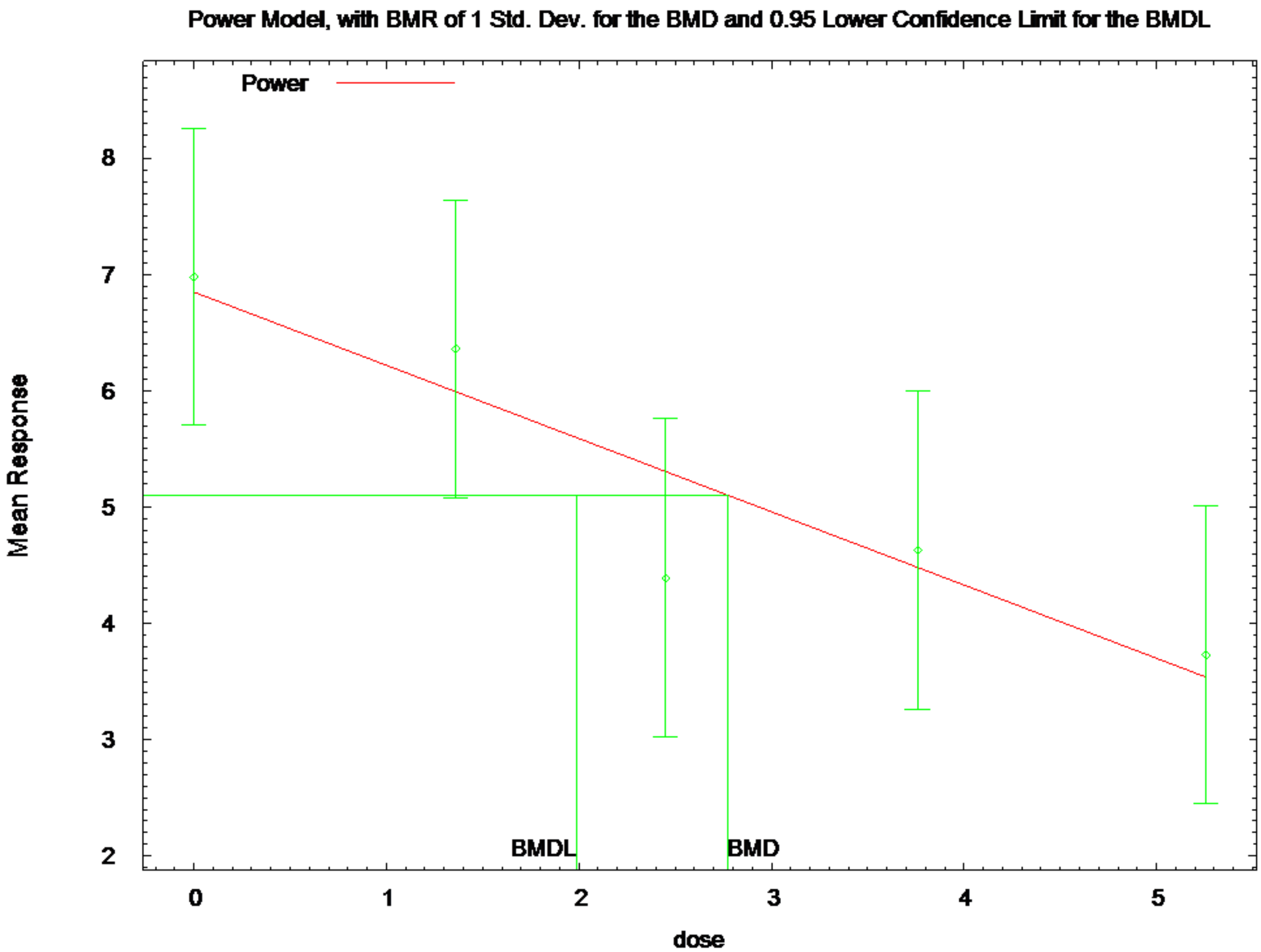
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.19697

BMDL = 2.73754



15:00 06/21 2014

```
=================================================================
===
        Power Model. (Version: 2.18;  Date: 05/19/2014)
        Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.(d)
        Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.plt
                                        Sat Jun 21 15:00:53 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.18101
                            rho =            0   Specified
                        control =         3.73
                          slope =       3.0162
                          power =     -1.13303


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	3.7e-011	-3.5e-011
control	3.7e-011	1	-0.81
slope	-3.5e-011	-0.81	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.05049	0.622679	1.83006	4.27092
control	6.85042	0.427333	6.01286	7.68798
slope	-0.630151	0.13565	-0.89602	-0.364283
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.15	1.75	0.235
1.361	10	6.36	5.99	2.45	1.75	0.665
2.451	9	4.39	5.31	1.31	1.75	-1.57
3.761	9	4.63	4.48	1.56	1.75	0.257
5.258	10	3.73	3.54	0.941	1.75	0.349

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-49.132777	6	110.265553
fitted	-50.767279	3	107.534558
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	10.6691	4	0.03055
Test 4	3.269	3	0.352

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

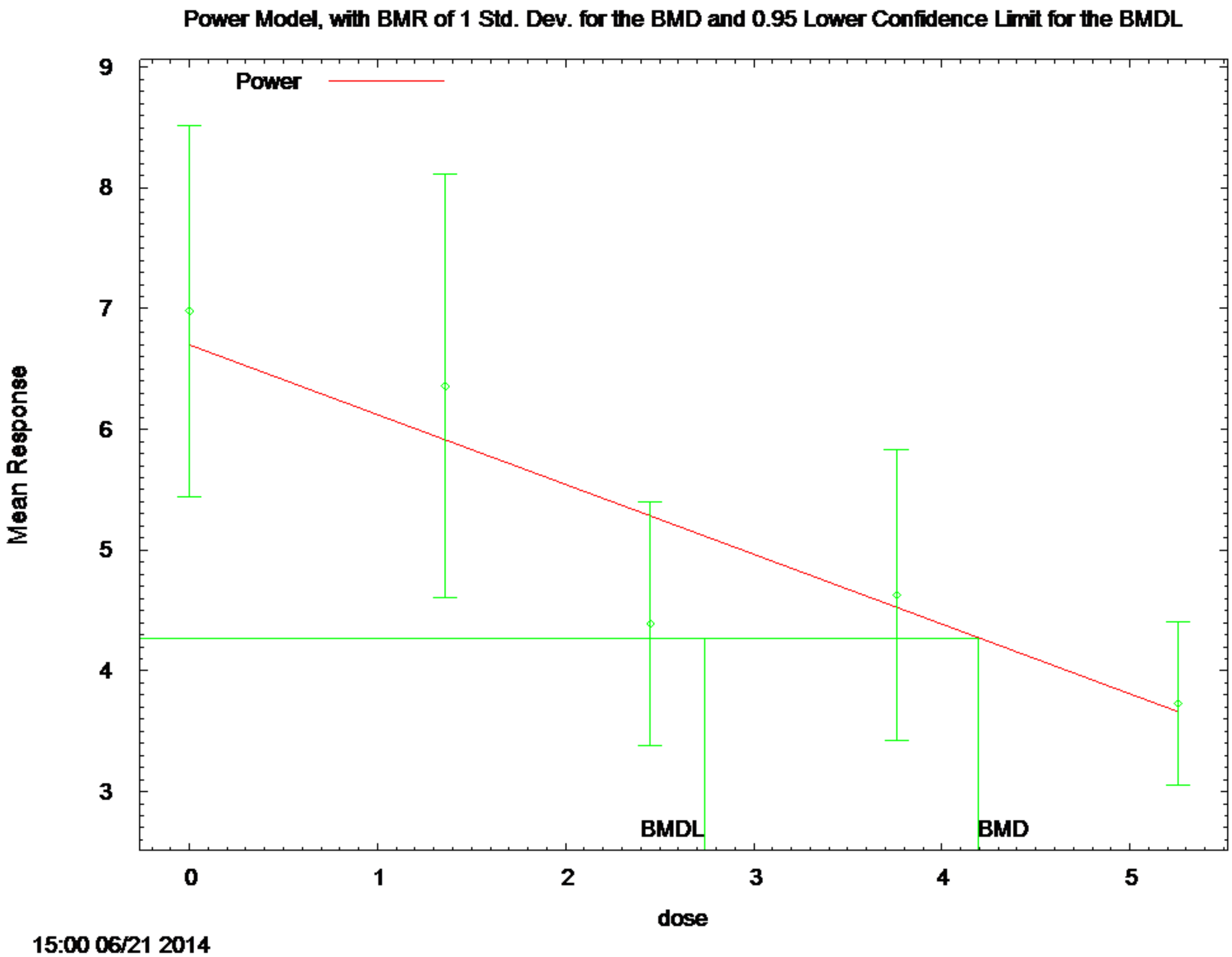
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.77166

BMDL = 1.99011


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
dose
BMDL
BMD
0
1
2
3
4
5
3
4
5
6
7
8
9
15:00 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Concurrent_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.plt
                                      Sat Jun 21 15:00:54 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.1572
                            rho =            0
                        control =         3.73
                          slope =       3.0162
                          power =     -1.13303


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-0.99	0.43	-0.55
rho	-0.99	1	-0.48	0.58
control	0.43	-0.48	1	-0.91
slope	-0.55	0.58	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.00629	2.05361	-8.03128	0.0187019
rho	3.03769	1.26122	0.565751	5.50963
control	6.69816	0.505256	5.70788	7.68845
slope	-0.577575	0.122984	-0.81862	-0.33653
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.7	2.15	2.42	0.368
1.361	10	6.36	5.91	2.45	2.01	0.706
2.451	9	4.39	5.28	1.31	1.69	-1.58
3.761	9	4.63	4.53	1.56	1.34	0.234

5.258   10   3.73   3.66   0.941   0.969
0.224

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-49.132777	6	110.265553
A2	-43.798233	10	107.596466
A3	-44.177523	7	102.355046
fitted	-46.826872	4	101.653745
R	-59.677903	2	123.355807

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7593	8	0.0001029
Test 2	10.6691	4	0.03055
Test 3	0.75858	3	0.8593
Test 4	5.2987	3	0.1512

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

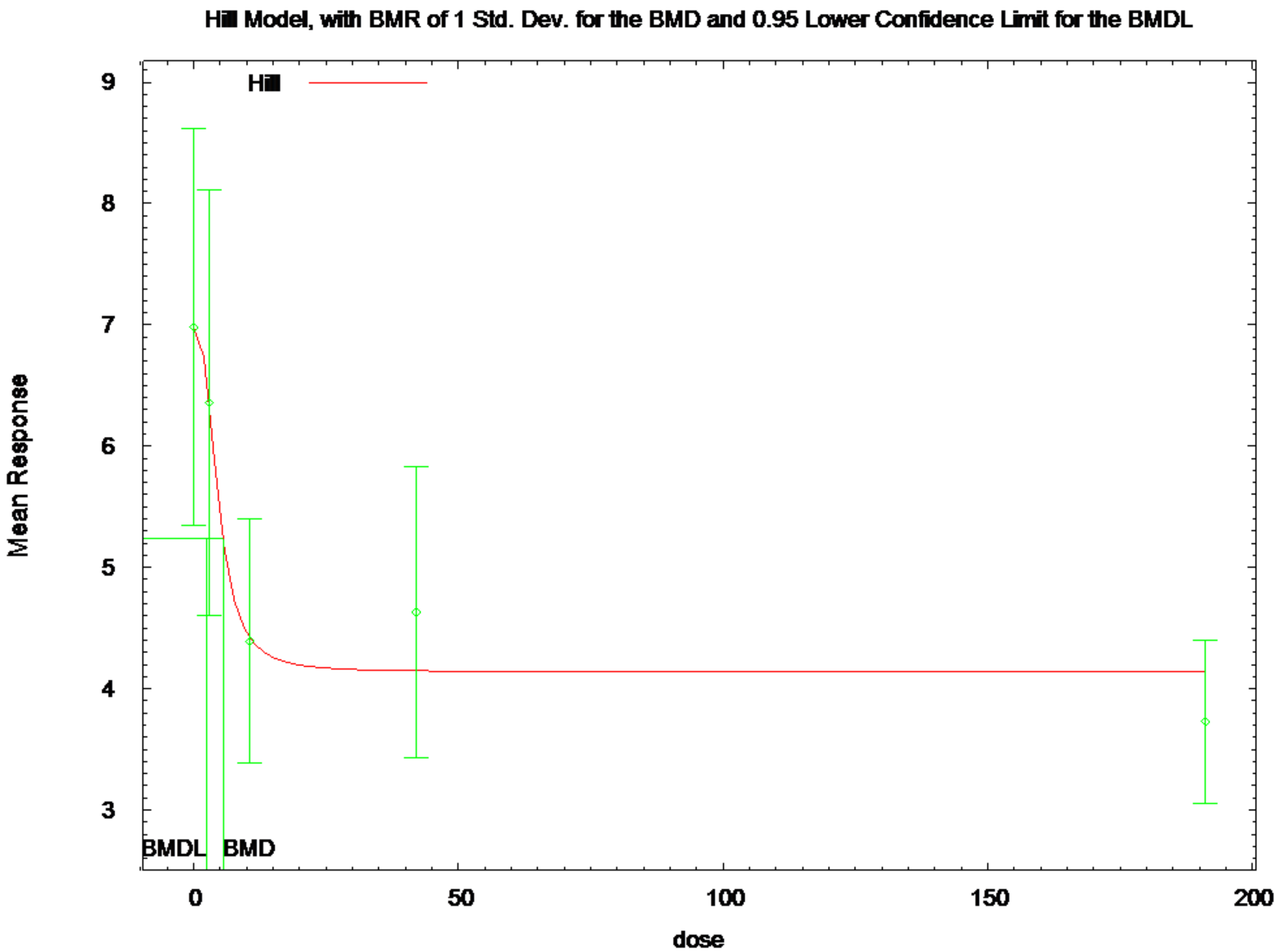
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.19697

BMDL = 2.73754

BMDS Model Results for Lymphocyte Count
(Untransformed Doses, Historical Controls)



10:03 06/22 2014

```
==================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-HillCV-1SD-5d.plt
                                       Sun Jun 22 10:03:59 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                      intercept =         6.98
                              v =        -3.25
                              n =       1.7748
                              k =      6.82817


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-1.4e-007	-2.7e-007	2e-007	1.5e-007
intercept	-1.4e-007	1	-0.8	-0.24	-0.39
v	-2.7e-007	-0.8	1	0.5	0.0043
n	2e-007	-0.24	0.5	1	-0.45
k	1.5e-007	-0.39	0.0043	-0.45	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.04783	0.622135	1.82847	4.26719
intercept	6.98398	0.551753	5.90257	8.0654
v	-2.84388	0.708322	-4.23217	-1.45559
n	2.67791	2.62413	-2.4653	7.82111
k	4.63334	2.54804	-0.360729	9.6274

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.98	2.29	1.75	-0.00722

2.9	10	6.36	6.35	2.45	1.75	0.0127
10.6	9	4.39	4.42	1.31	1.75	-0.051
42	9	4.63	4.15	1.56	1.75	0.829
191.1	10	3.73	4.14	0.941	1.75	-0.743

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-50.746309	5	111.492618
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	1.2578	1	0.2621

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

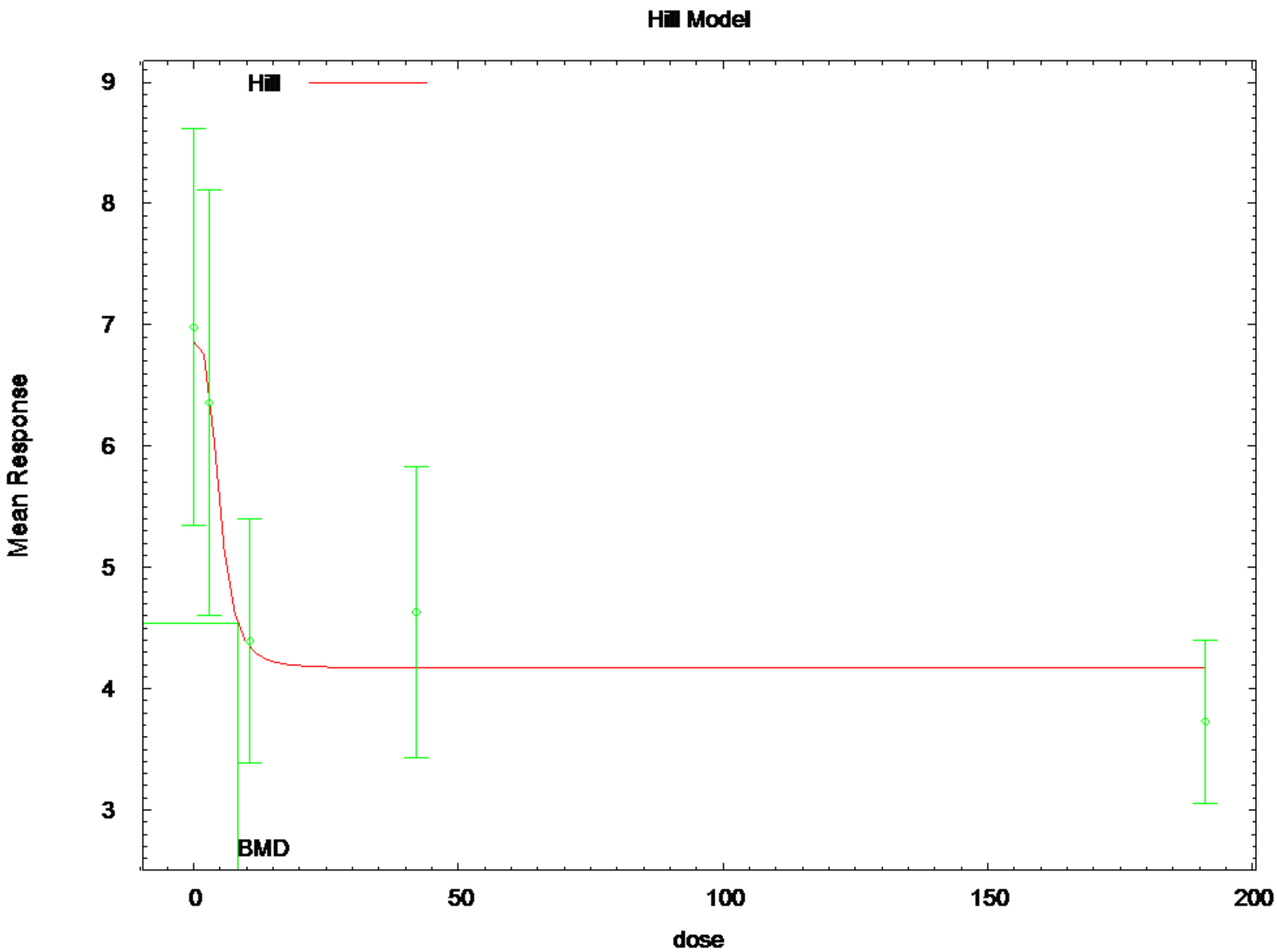
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 5.50919

BMDL = 2.35382



10:04 06/22 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-HillNCV-1SD-5d.plt
                                       Sun Jun 22 10:04:00 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                      intercept =         6.98
                              v =        -3.25
                              n =       1.7748
                              k =      6.82817


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	-0.99	0.34	-0.43	-0.1	-0.045
rho	-0.99	1	-0.37	0.45	0.1	0.045
intercept	0.34	-0.37	1	-0.93	-0.39	-0.5
v	-0.43	0.45	-0.93	1	0.52	0.33
n	-0.1	0.1	-0.39	0.52	1	-0.0023
k	-0.045	0.045	-0.5	0.33	-0.0023	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.08024	1.71715	-6.4458	0.285316
rho	2.47594	1.04624	0.425339	4.52653
intercept	6.86429	0.699318	5.49365	8.23493
v	-2.69337	0.77583	-4.21397	-1.17277
n	3.47624	3.09597	-2.59174	9.54423
k	4.89095	2.7048	-0.410352	10.1923

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.86	2.29	2.33	0.157

2.9	10	6.36	6.49	2.45	2.17
-0.186					
10.6	9	4.39	4.34	1.31	1.32
0.108					
42	9	4.63	4.17	1.56	1.26
1.09					
191.1	10	3.73	4.17	0.941	1.26
-1.11					

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-47.027008	6	106.054017
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	4.64874	1	0.03108

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

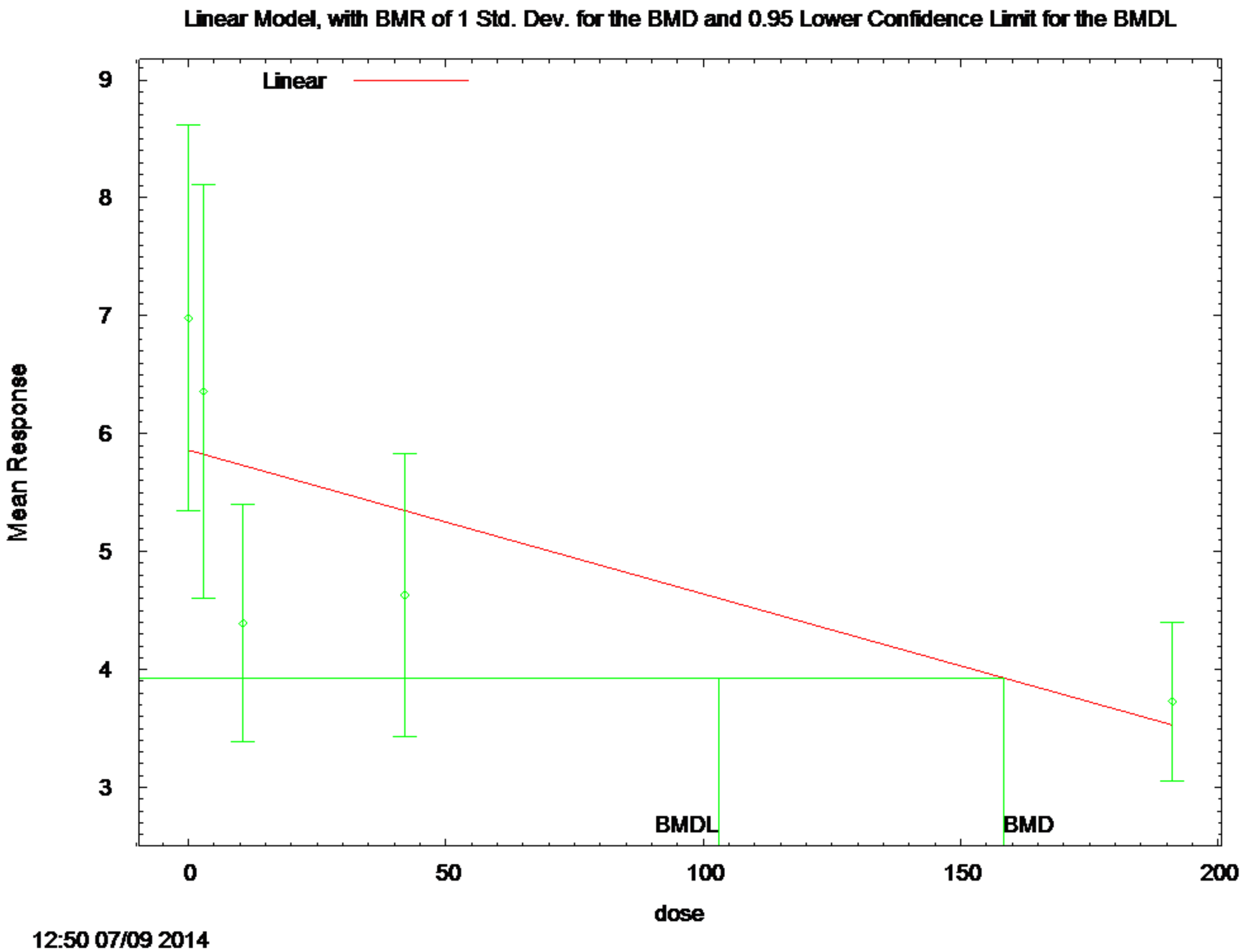
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 8.32507

BMDL computation failed.


Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:50 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:50:23 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      5.80912
                         beta_1 =   -0.0119854


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-2.7e-007	-6.9e-009
beta_0	-2.7e-007	1	-0.56
beta_1	-6.9e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.73207	0.761805	2.23896	5.22518
beta_0	5.86108	0.337527	5.19954	6.52262
beta_1	-0.0122035	0.00378272	-0.0196175	-0.00478945

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.29	1.93	1.83
2.9	10	6.36	5.83	2.45	1.93	0.875
10.6	9	4.39	5.73	1.31	1.93	-2.08
42	9	4.63	5.35	1.56	1.93	-1.12
191.1	10	3.73	3.53	0.941	1.93	0.329

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-55.607114	3	117.214227
R	-60.317047	2	124.634093

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	10.9794	3	0.01184

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

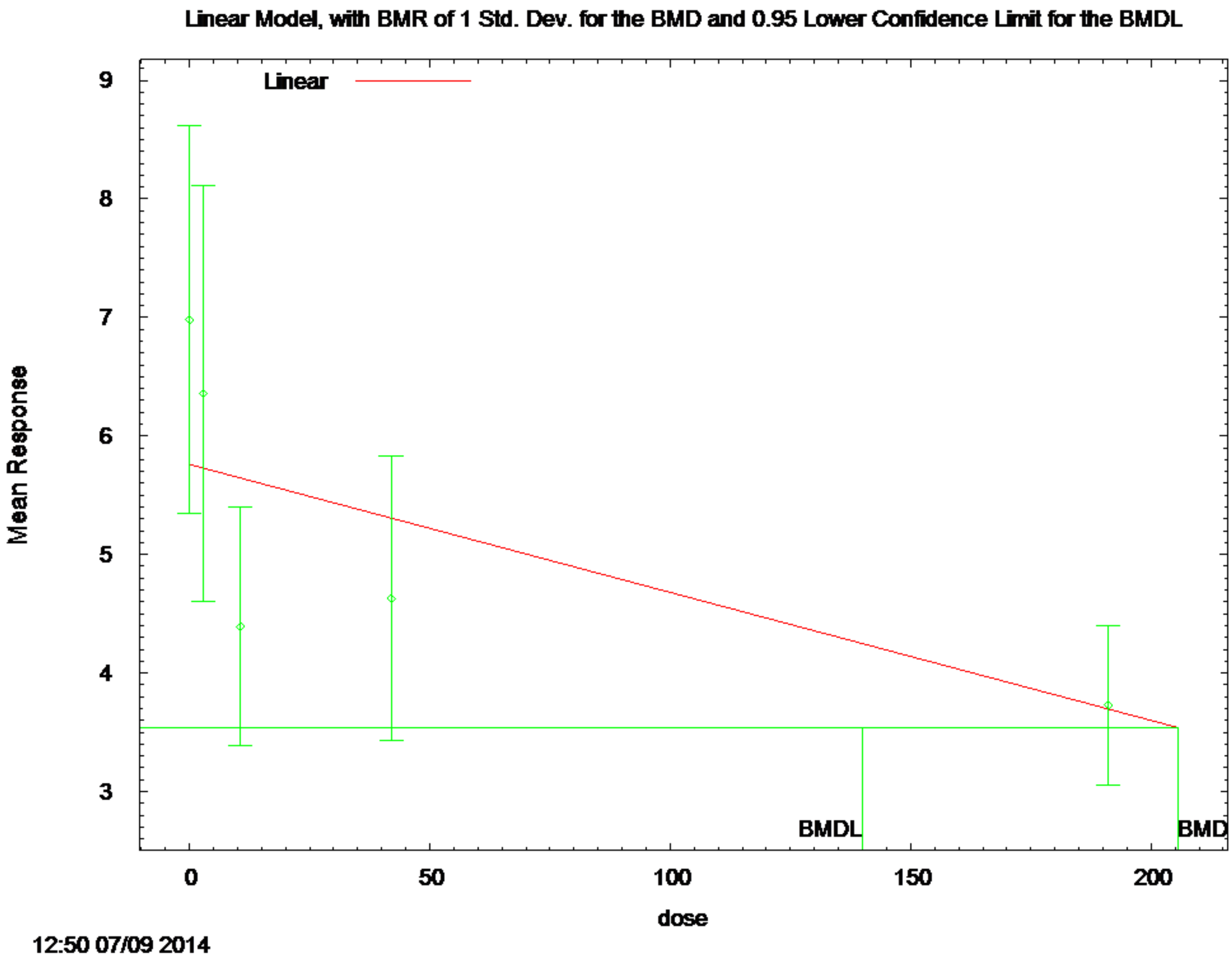
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 158.304

BMDL = 102.979



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
50
100
150
200
12:50 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:50:25 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =      5.80912
                         beta_1 =   -0.0119854


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99        0.041       -0.047
```

rho	-0.99	1	-0.042	0.048
beta_0	0.041	-0.042	1	-0.82
beta_1	-0.047	0.048	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.79277	1.89821	-9.51319	-2.07234
rho	4.22044	1.15187	1.96281	6.47806
beta_0	5.76177	0.371198	5.03424	6.48931
beta_1	-0.0108106	0.00250705	-0.0157243	-0.00589687

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.29	2.22	1.73
2.9	10	6.36	5.73	2.45	2.2	0.906
10.6	9	4.39	5.65	1.31	2.13	-1.77
42	9	4.63	5.31	1.56	1.87	-1.09
191.1	10	3.73	3.7	0.941	0.871	0.124

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -50.117411            6     112.234822
             A2          -44.445511           10     108.891023
             A3          -44.702636            7     103.405272
         fitted          -50.932591            4     109.865181
              R          -60.317047            2     124.634093


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              31.7431          8       0.0001035
   Test 2              11.3438          4         0.02296
   Test 3             0.514249          3          0.9157
   Test 4              12.4599          3        0.005963

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance
appears
```

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

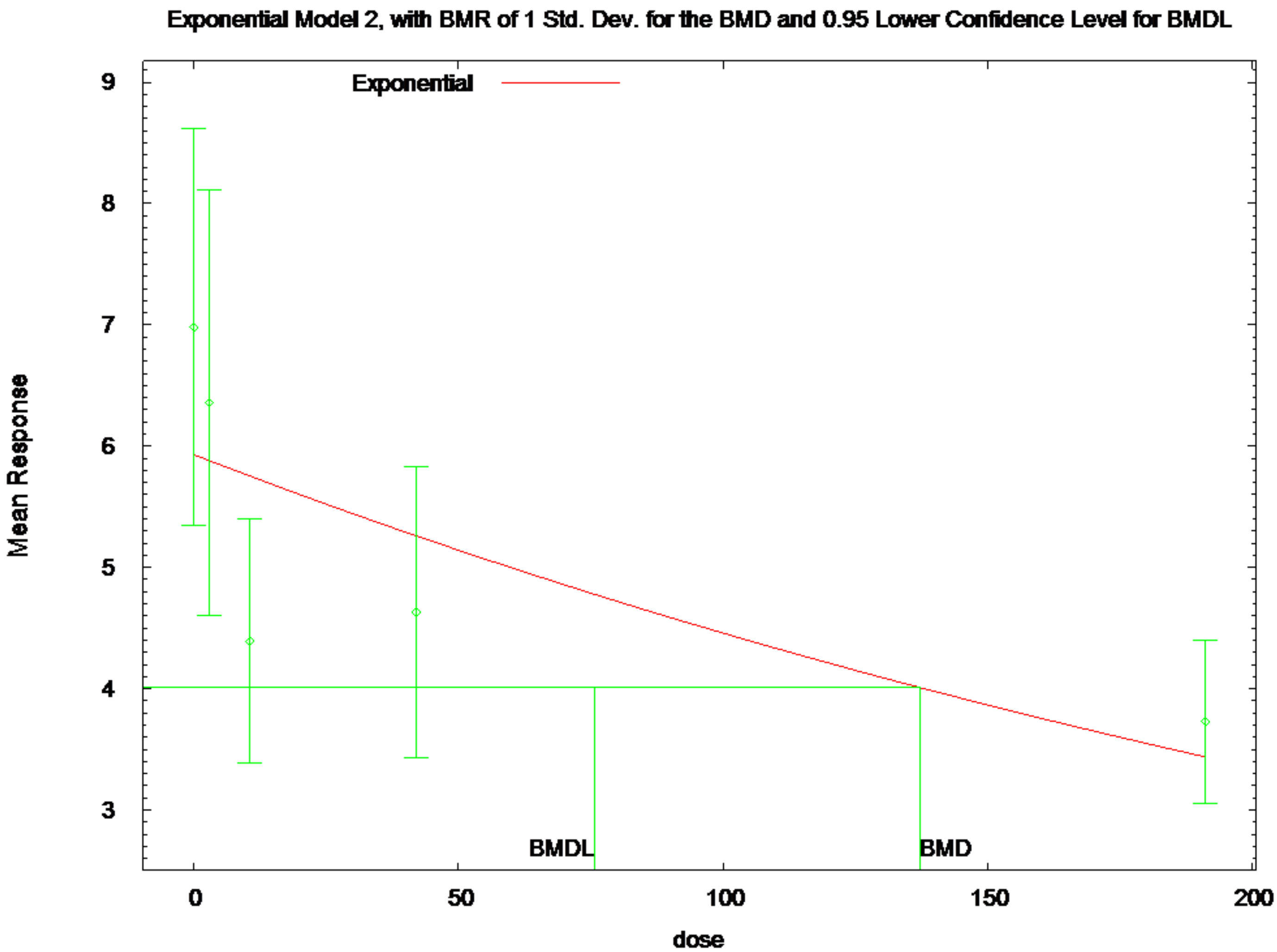
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 205.687

BMDL = 139.91



10:03 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:58 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.08823
rho(S)	0
a	4.506
b	0.00246217
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.30489
rho	0
a	5.93021
b	0.00285331
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.93	1.92	1.729
2.9	5.881	1.92	0.7883
10.6	5.754	1.92	-2.13
42	5.26	1.92	-0.985
191.1	3.438	1.92	0.4814

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
2	-55.31726	3	116.6345

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	

```
0.0001035
     Test 2                              11.34           4
0.02296
     Test 3                              11.34           4
0.02296
     Test 4                               10.4           3
0.01546
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

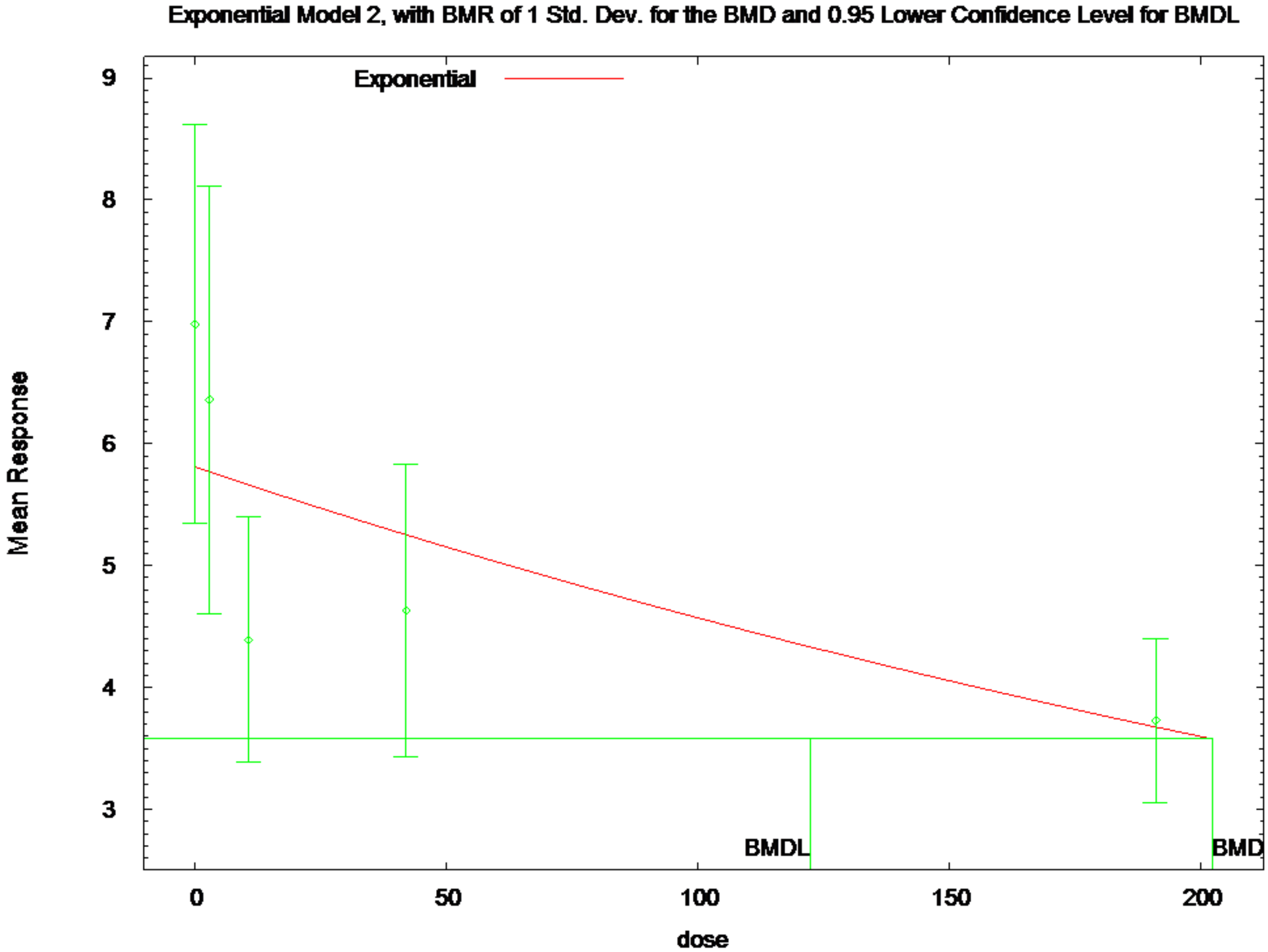
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 137.129

BMDL = 75.742



10:04 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:59 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-3.80501
rho	2.92874
a	4.506
b	0.00246217
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-5.63395
rho	4.11509
a	5.80788
b	0.00239458
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.808	2.232	1.661
2.9	5.768	2.2	0.8514
10.6	5.662	2.118	-1.802
42	5.252	1.814	-1.029
191.1	3.675	0.8704	0.1991

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
2	-50.63837	4	109.2767

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

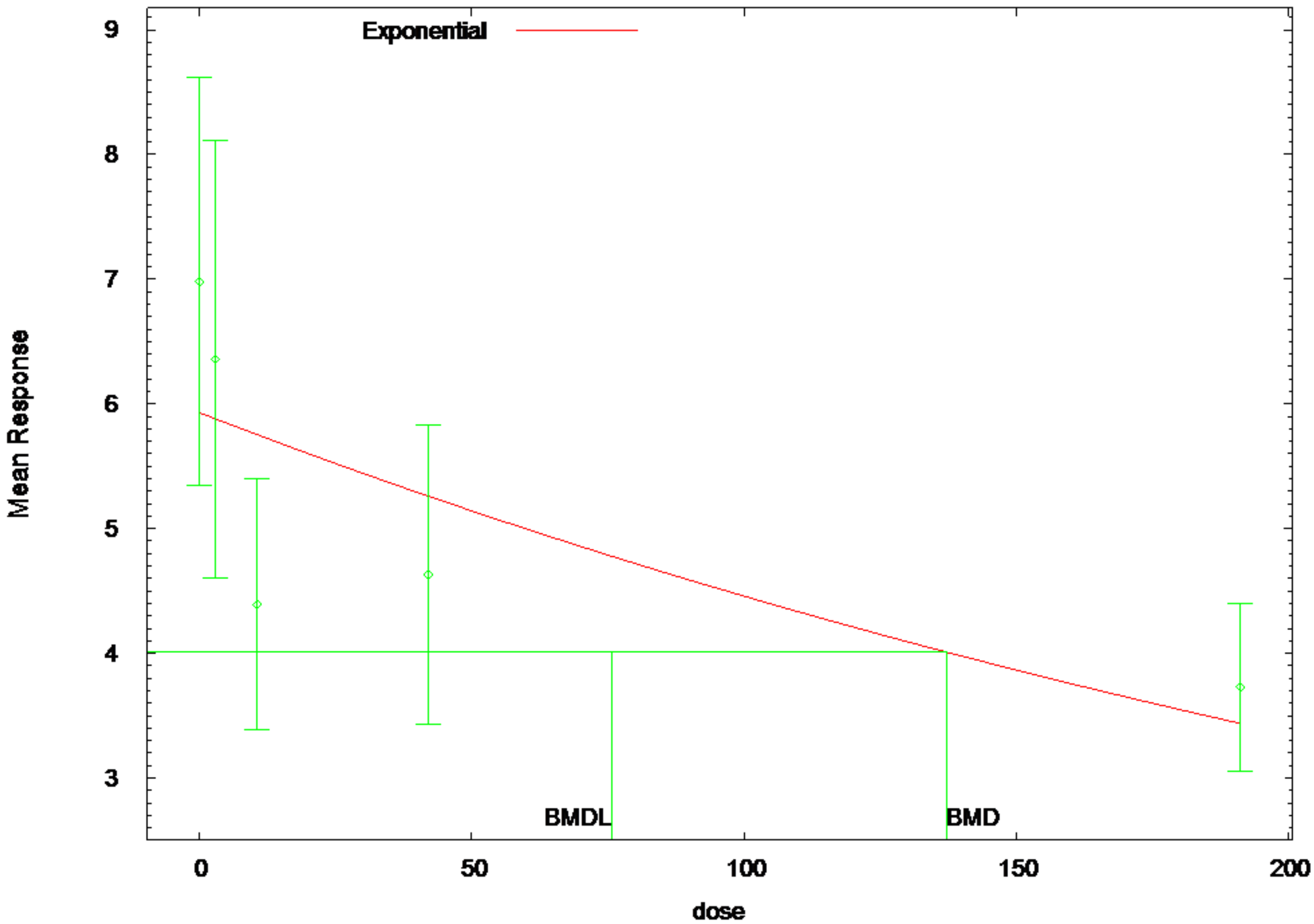
Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035
Test 2	11.34	4	

```
0.02296
     Test 3                          0.5142          3
0.9157
     Test 4                           11.87          3
0.007837


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 4 is less than .1.  Model 2 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      202.488

                 BMDL =      122.382
```

Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:03 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:58 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.08823
rho(S)	0
a	4.506
b	0.00246217
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.30489
rho	0
a	5.93021
b	0.00285331
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.93	1.92	1.729
2.9	5.881	1.92	0.7883
10.6	5.754	1.92	-2.13
42	5.26	1.92	-0.985
191.1	3.438	1.92	0.4814

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
3	-55.31726	3	116.6345

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

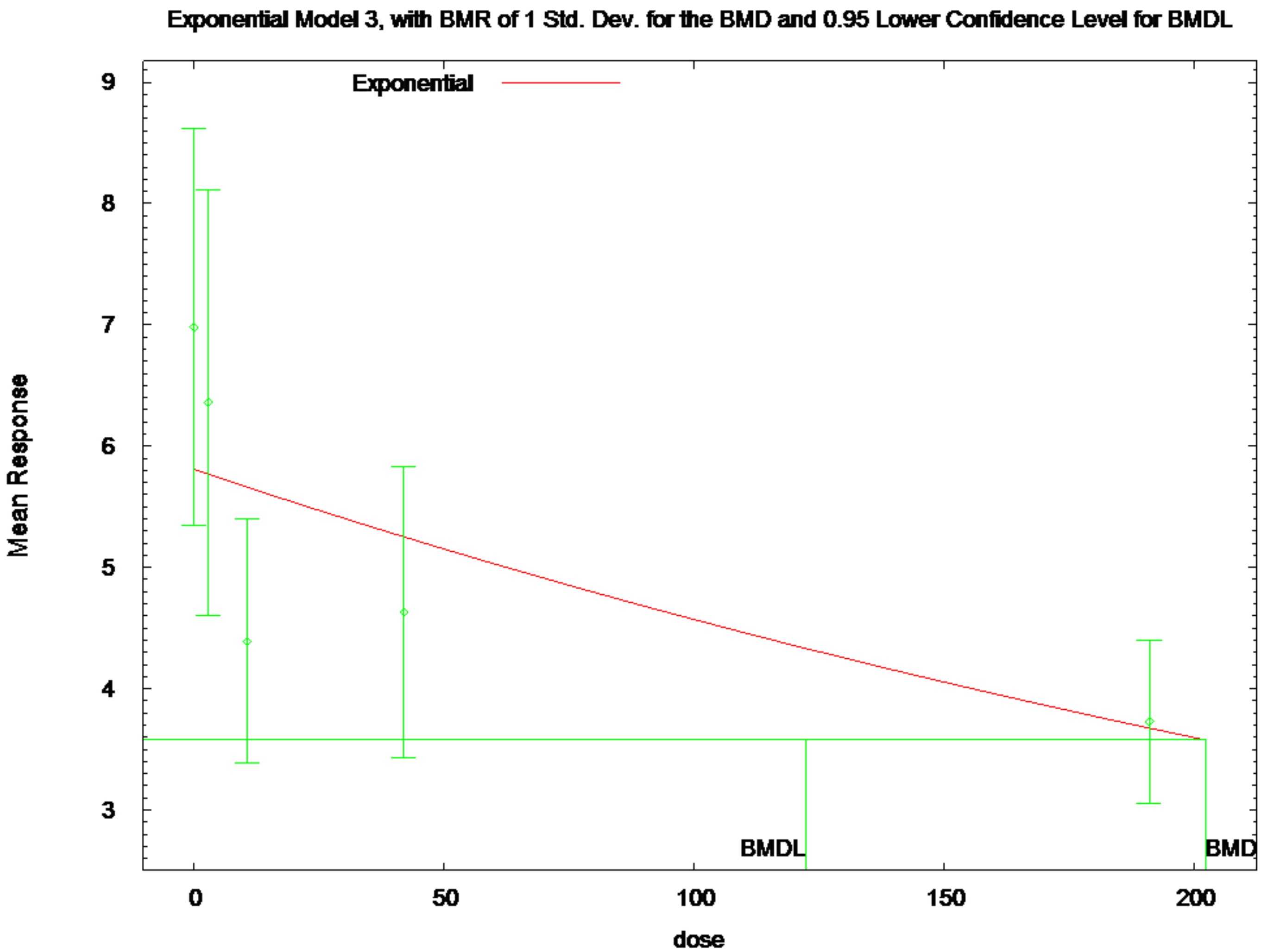
Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

```
     Test 1                              31.74          8
0.0001035
     Test 2                              11.34          4
0.02296
     Test 3                              11.34          4
0.02296
    Test 5a                               10.4          3
0.01546


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  Consider running
     a non-homogeneous variance model.

     The p-value for Test 3 is less than .1.  You may want to
     consider a different variance model.

     The p-value for Test 5a is less than .1.  Model 3 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      137.129

                 BMDL =       75.742
```



10:04 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:59 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-3.80501
rho	2.92874
a	4.506
b	0.00246217
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-5.63395
rho	4.11509
a	5.80788
b	0.00239458
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	5.808	2.232	1.661
2.9	5.768	2.2	0.8514
10.6	5.662	2.118	-1.802
42	5.252	1.814	-1.029
191.1	3.675	0.8704	0.1991

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
3	-50.63837	4	109.2767

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

Test 2	11.34	4	0.02296
Test 3	0.5142	3	0.9157
Test 5a	11.87	3	0.007837

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

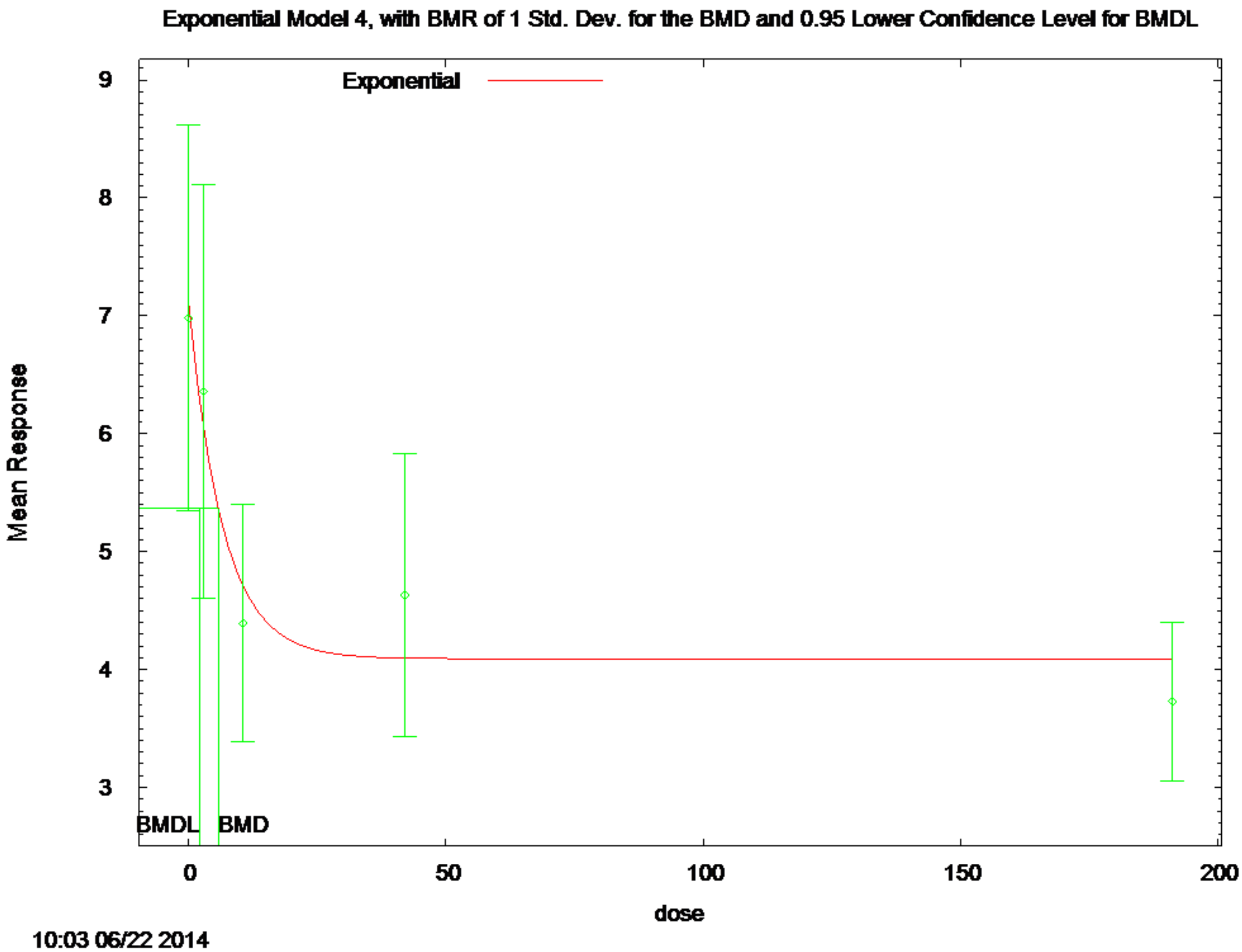
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 202.488

BMDL = 122.382



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
10:03 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:58 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.08823
rho(S)	0
a	7.329
b	0.0170211
c	0.484702
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.12896
rho	0
a	7.12238
b	0.150285
c	0.574374
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.122	1.759	-0.256
2.9	6.051	1.759	0.5549
10.6	4.707	1.759	-0.5412
42	4.096	1.759	0.9103
191.1	4.091	1.759	-0.649

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
4	-51.09512	4	110.1902

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.74	8	0.0001035
Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 6a	1.955	2	0.3762

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

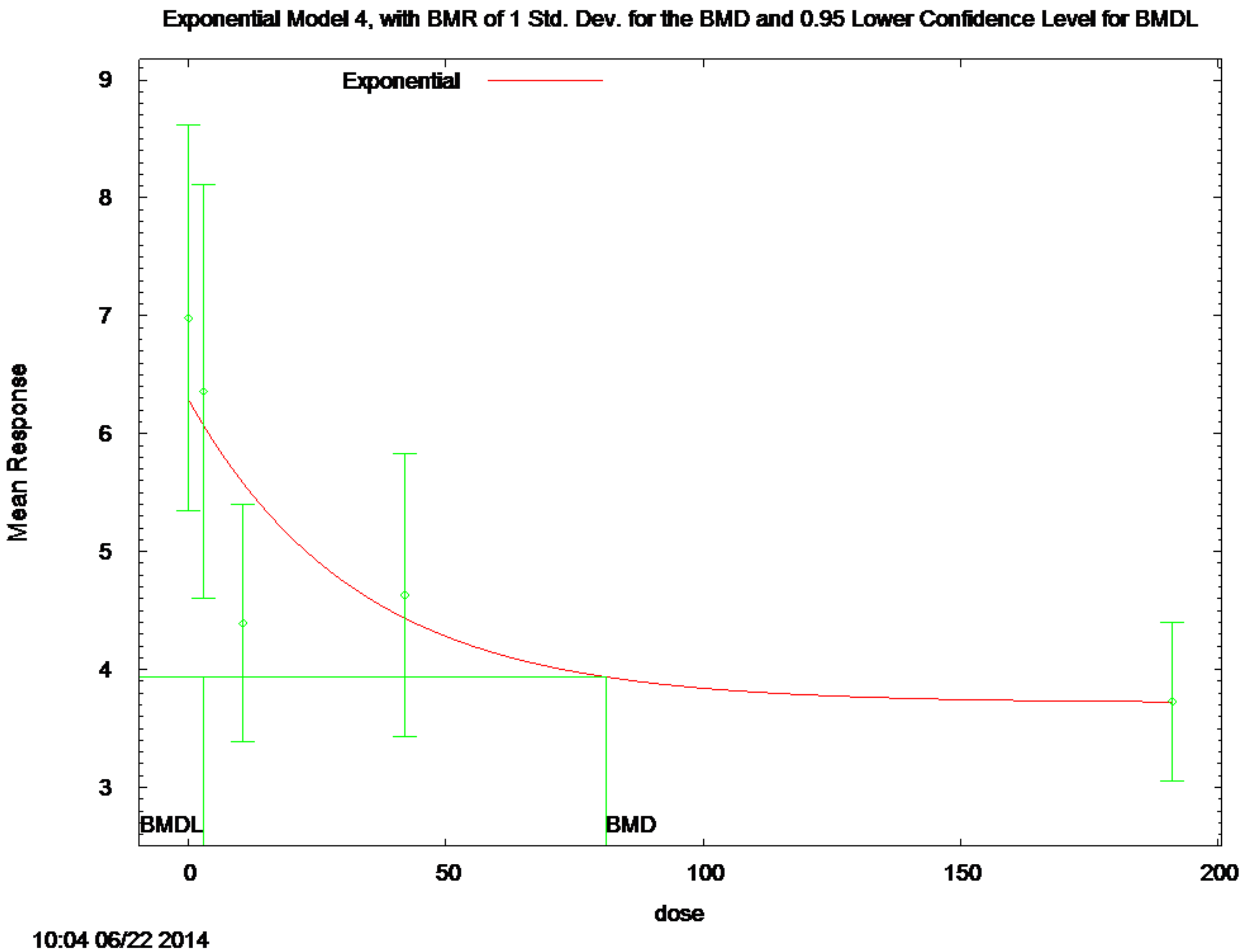
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 5.77383

BMDL = 2.26317



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
50
100
150
200
10:04 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:59 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-3.80501
rho	2.92874
a	7.329
b	0.0170211
c	0.484702
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-4.52284
rho	3.39008
a	6.28865
b	0.0303979
c	0.591176
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.289	2.352	0.9295
2.9	6.072	2.216	0.4113
10.6	5.58	1.921	-1.859
42	4.435	1.301	0.4498
191.1	3.725	0.9684	0.01497

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
4	-48.43541	5	106.8708

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

Test 2	11.34	4	0.02296
Test 3	0.5142	3	0.9157
Test 6a	7.466	2	0.02393

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

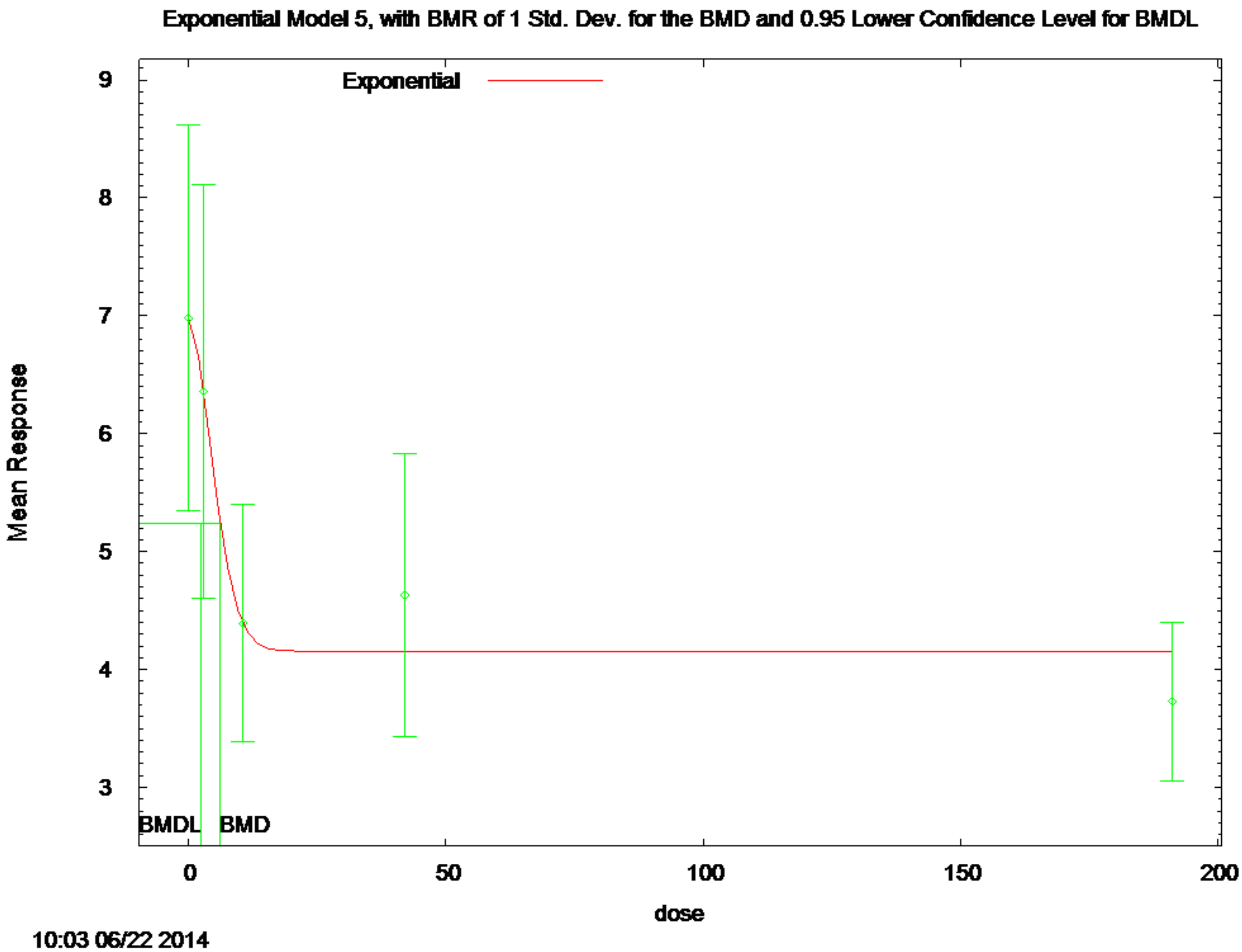
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 81.0526

BMDL = 2.80644



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
10:03 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:03:58 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.08823
rho(S)	0
a	7.329
b	0.0170211
c	0.484702
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.11479
rho	0
a	6.98
b	0.157544
c	0.595461
d	1.78044

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.98	1.746	6.523e-007
2.9	6.36	1.746	-6.948e-007
10.6	4.39	1.746	-2.243e-007
42	4.156	1.746	0.8138
191.1	4.156	1.746	-0.7721

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
5	-50.75502	5	111.51

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.74	8	0.0001035
Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 7a	1.275	1	0.2588

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

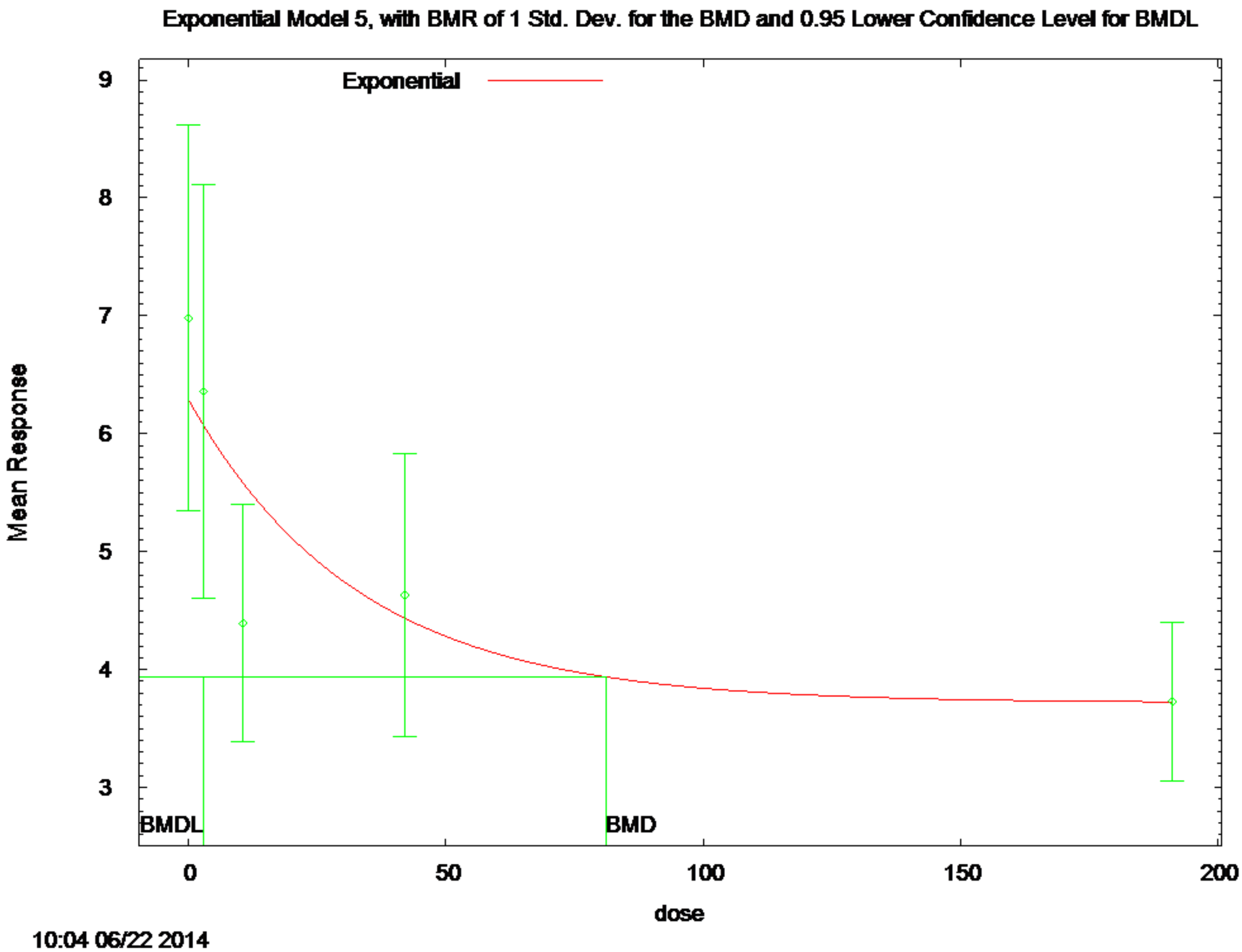
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 6.21566

BMDL = 2.54297


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
50
100
150
200
10:04 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 10:03:59 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-3.80501
rho	2.92874
a	7.329
b	0.0170211
c	0.484702
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-4.52284
rho	3.39008
a	6.28866
b	0.0303979
c	0.591176
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
2.9	10	6.36	2.452
10.6	9	4.39	1.308
42	9	4.63	1.564
191.1	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.289	2.352	0.9295
2.9	6.072	2.216	0.4113
10.6	5.58	1.921	-1.859
42	4.435	1.301	0.4498
191.1	3.725	0.9684	0.01497

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
5	-48.43541	5	106.8708

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

Test 2	11.34	4	0.02296
Test 3	0.5142	3	0.9157
Test 7a	7.466	2	0.02393

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

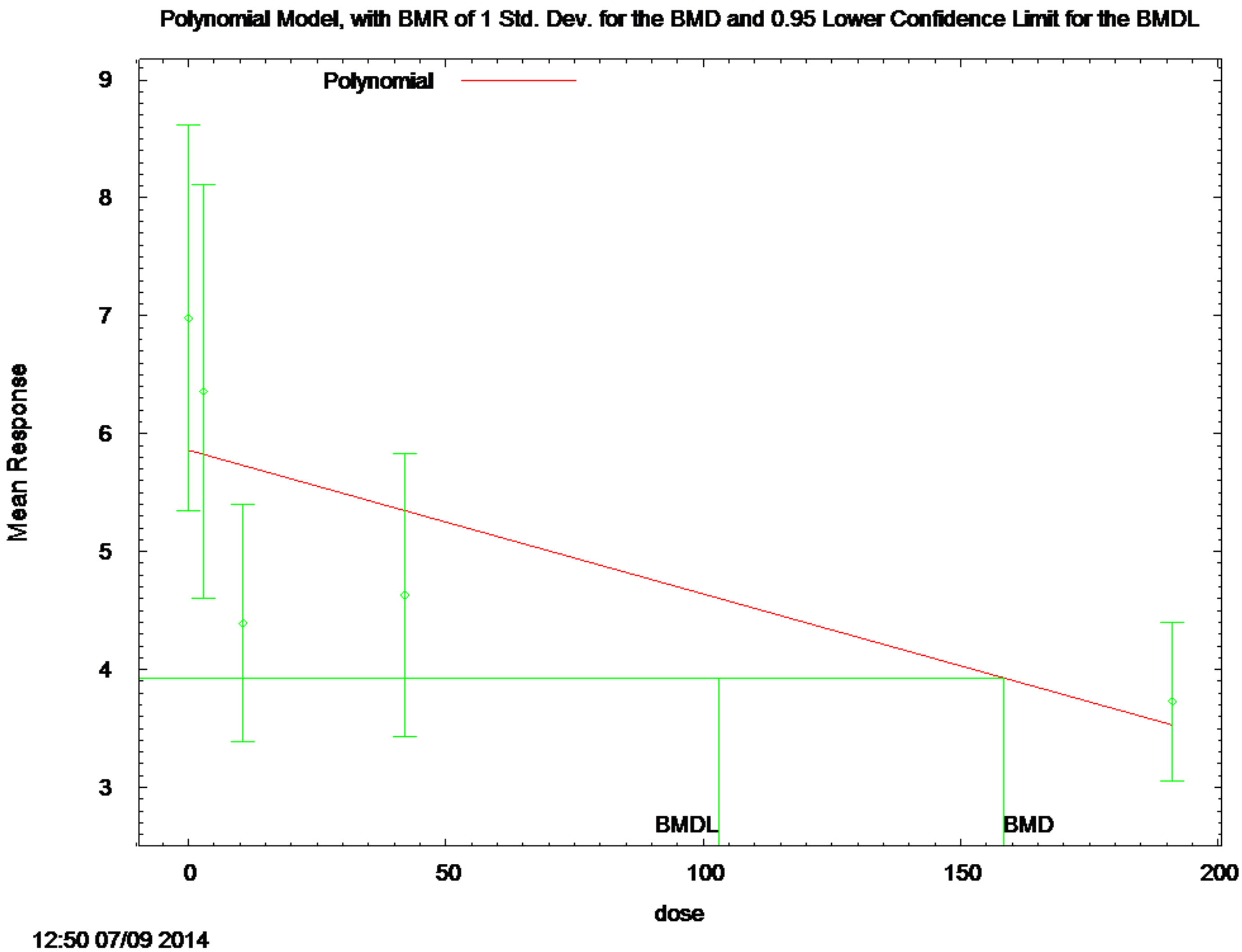
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 81.0527

BMDL = 2.80644



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:50 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.plt
                                        Wed Jul 09 12:50:23 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      6.28333
                         beta_1 =   -0.0582096
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	8.6e-008	-1.1e-007
beta_0	8.6e-008	1	-0.56
beta_1	-1.1e-007	-0.56	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.73207	0.761805	2.23896	5.22518
beta_0	5.86108	0.337527	5.19954	6.52262
beta_1	-0.0122035	0.00378272	-0.0196175	-0.00478945
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.29	1.93	1.83
2.9	10	6.36	5.83	2.45	1.93	0.875
10.6	9	4.39	5.73	1.31	1.93	-2.08
42	9	4.63	5.35	1.56	1.93	-1.12
191.1	10	3.73	3.53	0.941	1.93	0.329

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-55.607114	3	117.214227
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	10.9794	3	0.01184

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

Specified effect = 1

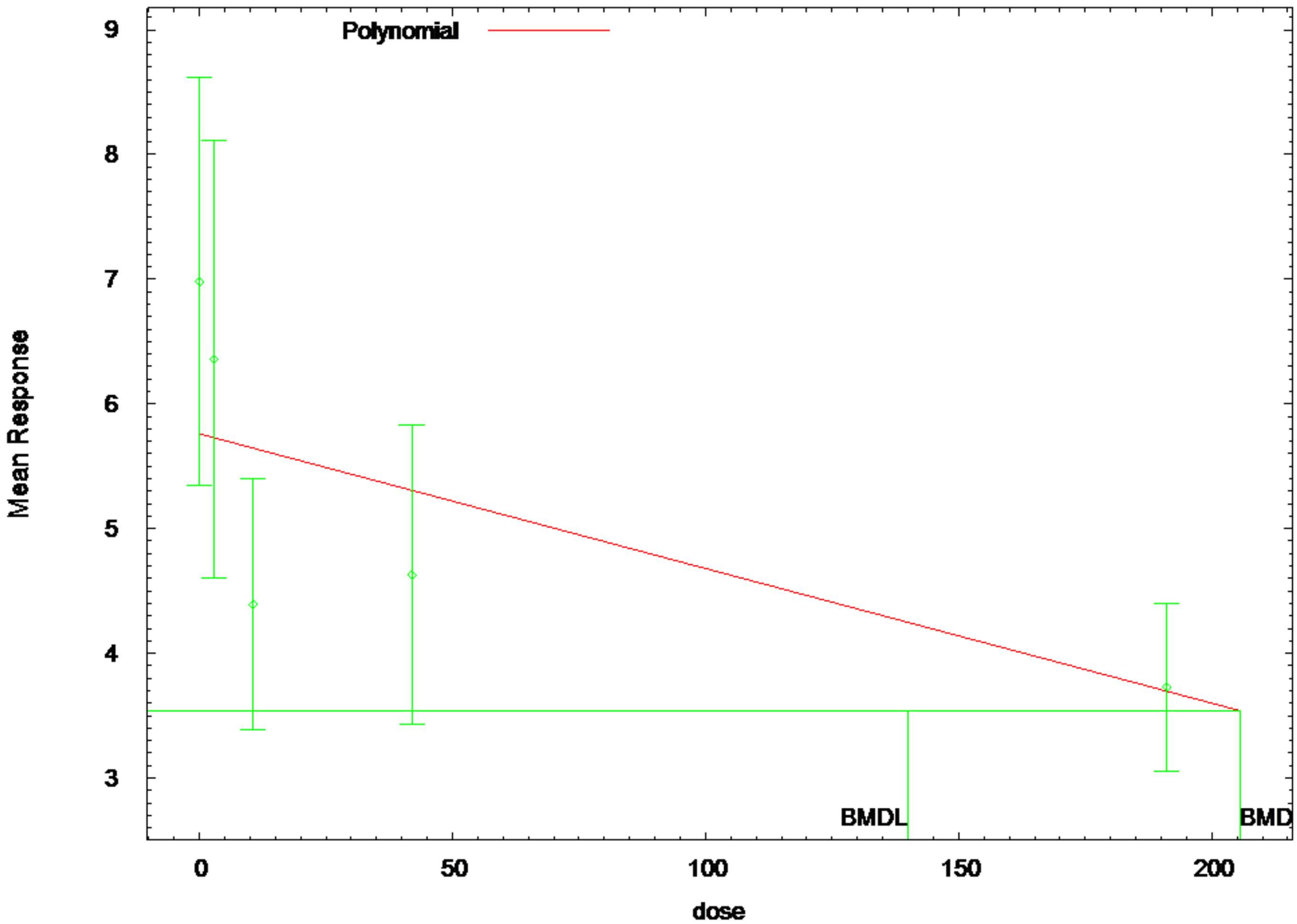
Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 158.304

BMDL = 102.979

Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:50 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.plt
                                       Wed Jul 09 12:50:25 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.19823
                            rho =             0
                         beta_0 =       6.28333
                         beta_1 =    -0.0582096
                         beta_2 =             0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.041	-0.047
rho	-0.99	1	-0.042	0.048
beta_0	0.041	-0.042	1	-0.82
beta_1	-0.047	0.048	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.79277	1.89821	-9.51319	-2.07234
rho	4.22044	1.15187	1.96281	6.47807
beta_0	5.76177	0.371198	5.03424	6.48931
beta_1	-0.0108106	0.00250705	-0.0157243	-0.00589687
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.29	2.22	1.73
2.9	10	6.36	5.73	2.45	2.2	0.906
10.6	9	4.39	5.65	1.31	2.13	-1.77
42	9	4.63	5.31	1.56	1.87	-1.09

191.1 10 3.73 3.7 0.941 0.871
0.124

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-50.932591	4	109.865181
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	12.4599	3	0.005963

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

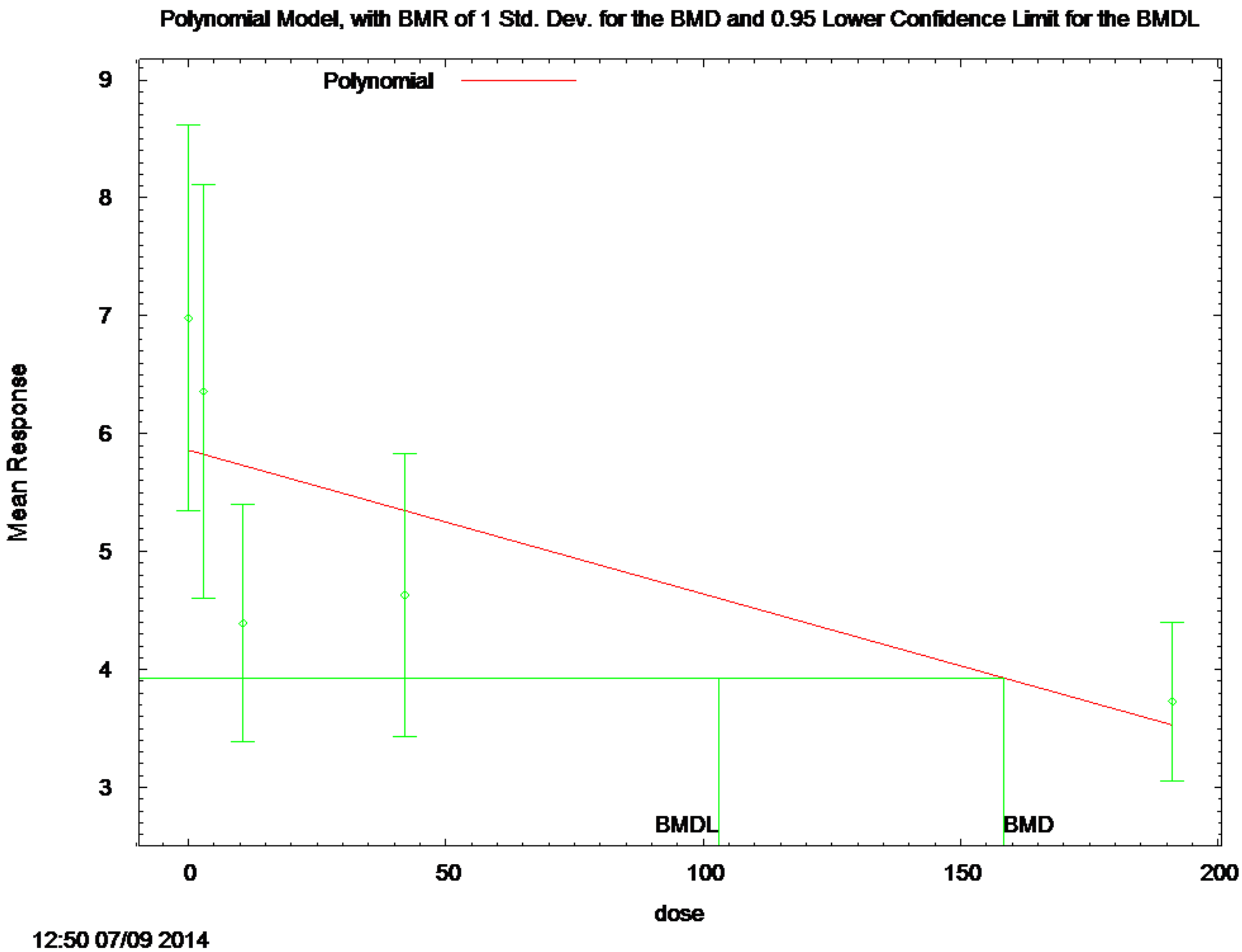
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 205.687

BMDL = 139.91


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:50 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:50:23 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      7.08617
                         beta_1 =    -0.327588
                         beta_2 =            0
                         beta_3 = -3.20797e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3

have been estimated at a boundary point, or have been specified by the user, and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-8.7e-009	2e-009
beta_0	-8.7e-009	1	-0.56
beta_1	2e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.73207	0.761806	2.23896	5.22518
beta_0	5.86108	0.337527	5.19954	6.52262
beta_1	-0.0122035	0.00378272	-0.0196175	-0.00478945
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.29	1.93	1.83
2.9	10	6.36	5.83	2.45	1.93	0.875
10.6	9	4.39	5.73	1.31	1.93	-2.08
42	9	4.63	5.35	1.56	1.93	-1.12
191.1	10	3.73	3.53	0.941	1.93	

0.329

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-55.607114	3	117.214227
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	10.9794	3	0.01184

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

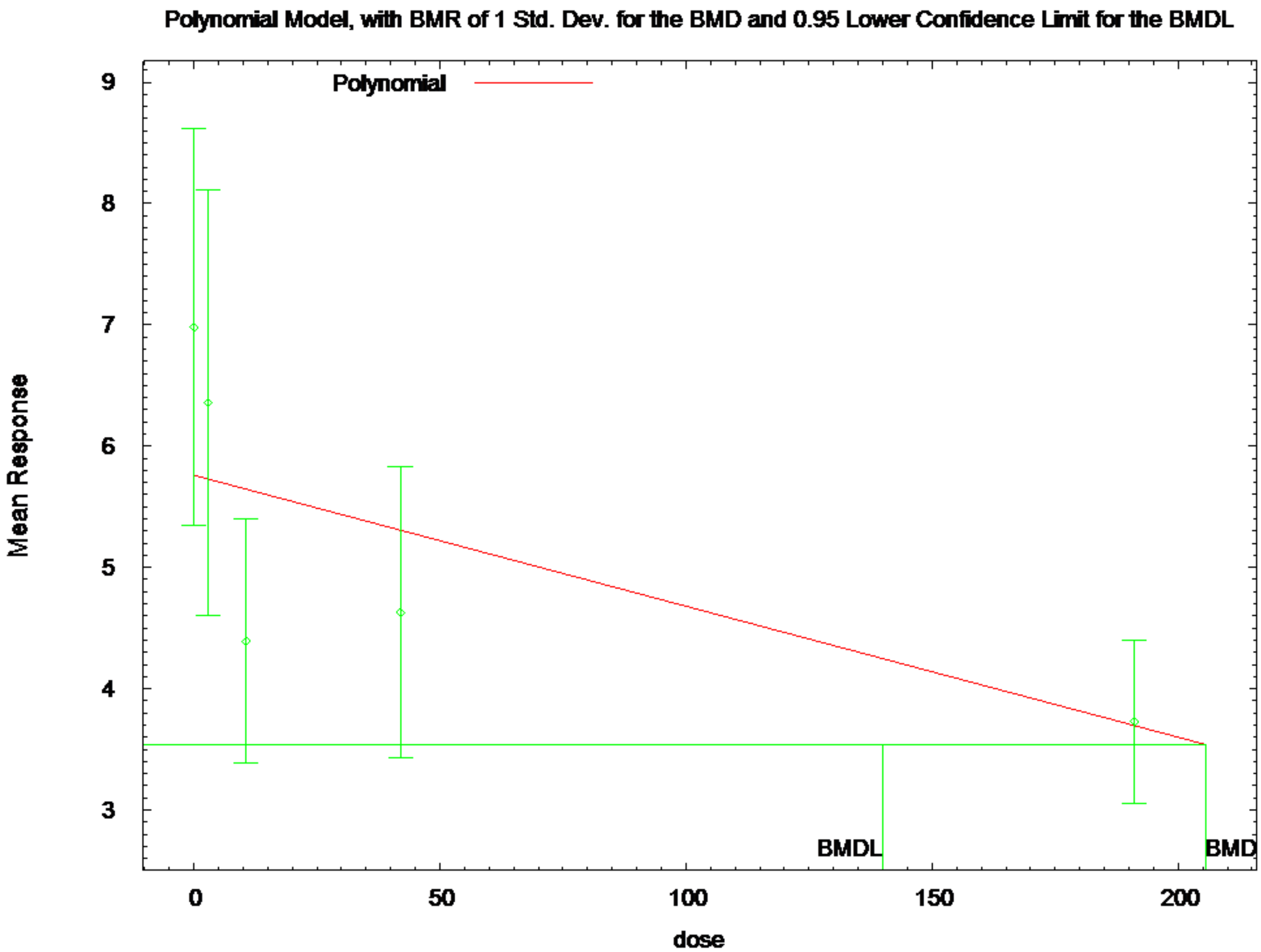
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 158.304

BMDL = 102.979



12:50 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:50:24 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =      7.08617
                         beta_1 =    -0.327588
                         beta_2 =            0
                         beta_3 = -3.20797e-005


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.041	-0.047
rho	-0.99	1	-0.042	0.048
beta_0	0.041	-0.042	1	-0.82
beta_1	-0.047	0.048	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.79278	1.89821	-9.5132	-2.07236
rho	4.22045	1.15187	1.96282	6.47807
beta_0	5.76177	0.371198	5.03424	6.48931
beta_1	-0.0108106	0.00250705	-0.0157243	-0.00589686
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound implied by some inequality constraint and thus has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.29	2.22	1.73
2.9	10	6.36	5.73	2.45	2.2	0.906
10.6	9	4.39	5.65	1.31	2.13	-1.77

```
  42     9       4.63         5.31         1.56         1.87
-1.09
191.1    10       3.73          3.7        0.941        0.871
0.124
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-50.932591	4	109.865181
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157

Test 4	12.4599	3	0.005963

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

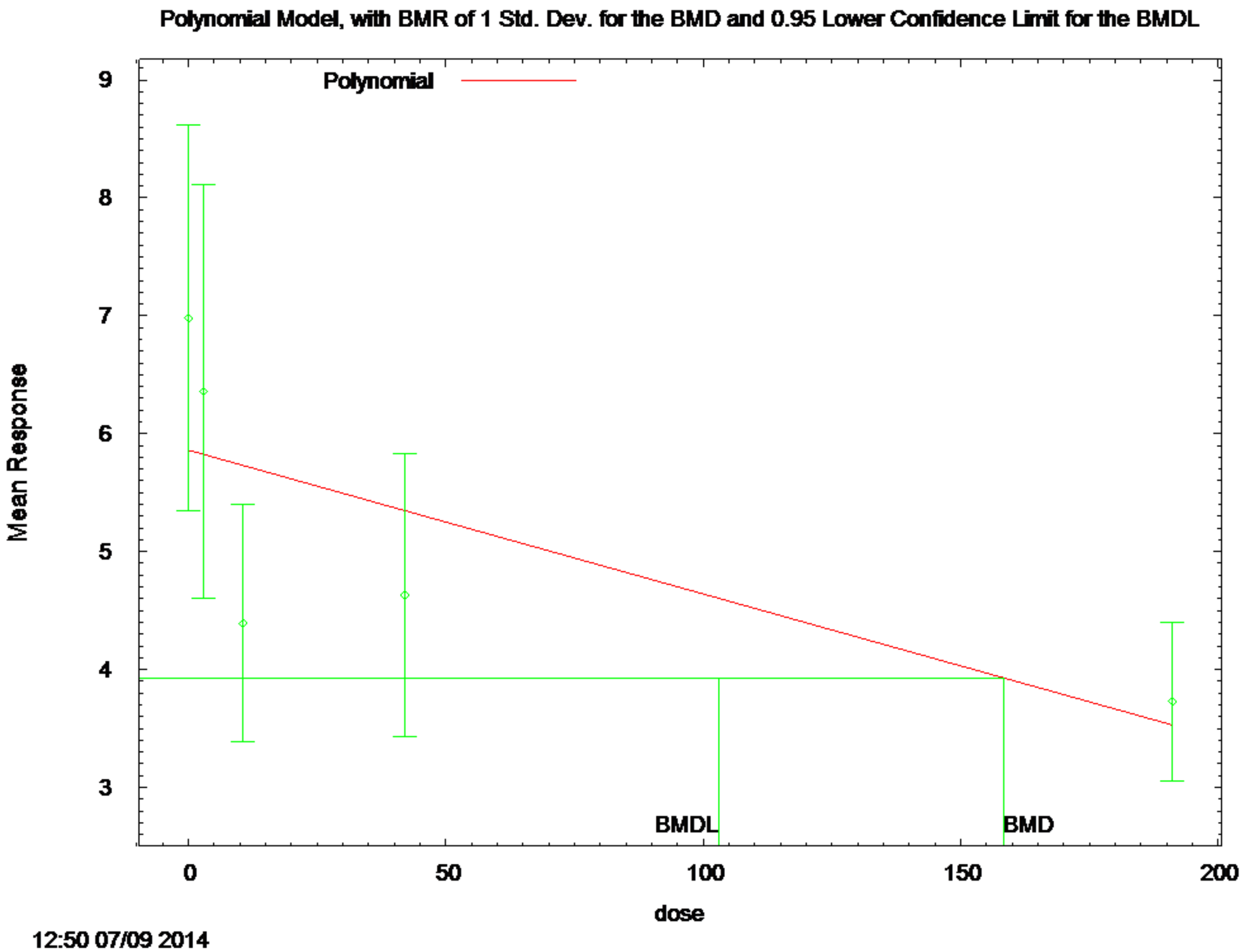
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 205.687

BMDL = 139.91



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
50
100
150
200
dose
12:50 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:50:23 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =         6.98
                         beta_1 =    -0.192486
                         beta_2 =  -0.00831882
                         beta_3 =            0
                         beta_4 = -1.52335e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	8e-007	6.5e-008
beta_0	8e-007	1	-0.56
beta_1	6.5e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.73207	0.761806	2.23896	5.22518
beta_0	5.86108	0.337527	5.19954	6.52262
beta_1	-0.0122035	0.00378272	-0.0196175	-0.00478945
beta_2	-0	NA		
beta_3	0	NA		
beta_4	-7.39728e-104	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.29	1.93	1.83
2.9	10	6.36	5.83	2.45	1.93	0.875
10.6	9	4.39	5.73	1.31	1.93	-2.08
42	9	4.63	5.35	1.56	1.93	

-1.12
191.1 10 3.73 3.53 0.941 1.93
0.329

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-55.607114	3	117.214227
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	10.9794	3	0.01184

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

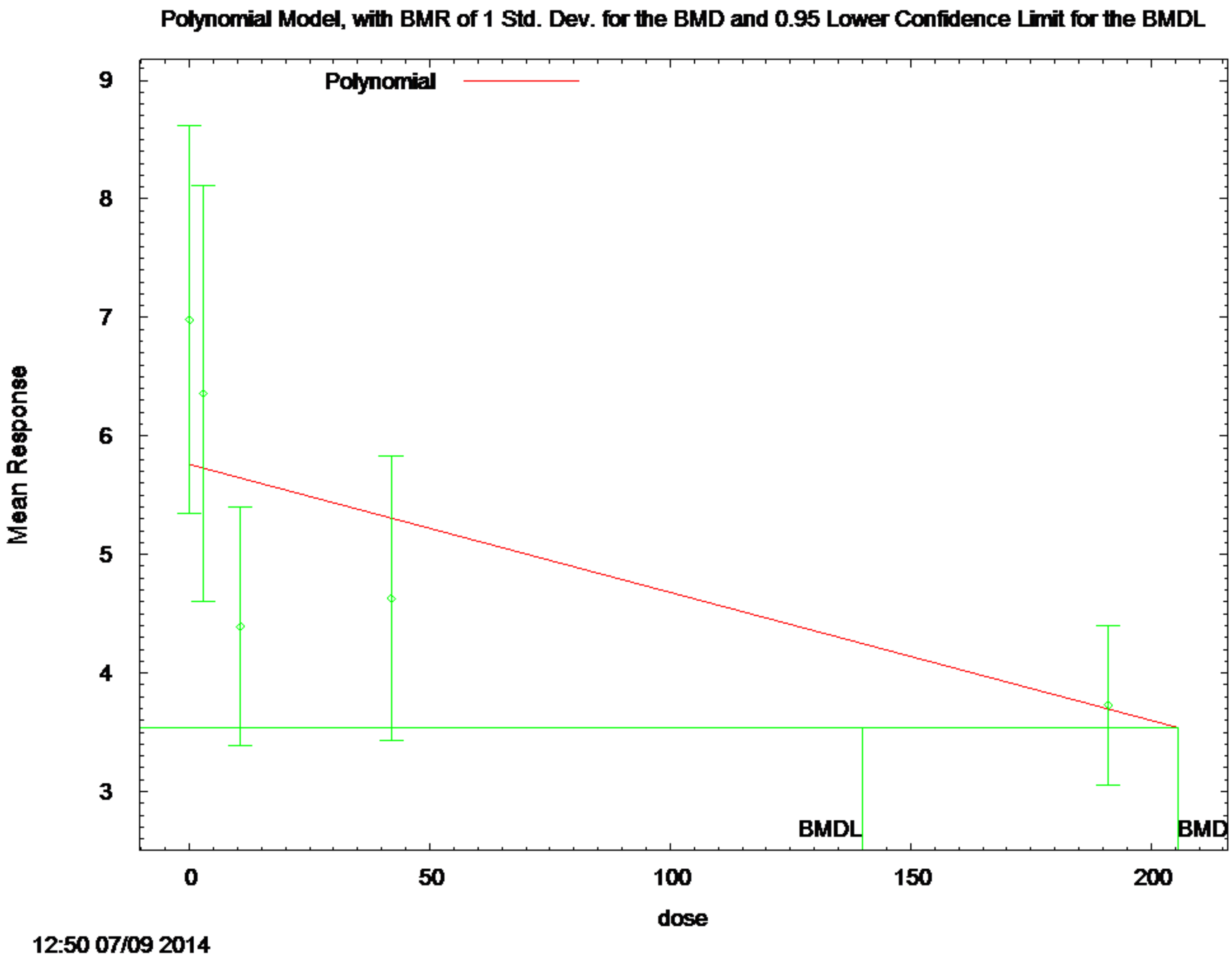
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 158.304

BMDL = 102.979


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
0
50
100
150
200
BMDL
BMD
dose
12:50 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical/Lymphocyte_H
istorical_Normal-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:50:24 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =         6.98
                         beta_1 =    -0.192486
                         beta_2 =  -0.00831882
                         beta_3 =            0
                         beta_4 = -1.52335e-006


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.041	-0.047
rho	-0.99	1	-0.042	0.048
beta_0	0.041	-0.042	1	-0.82
beta_1	-0.047	0.048	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.79277	1.89821	-9.51319	-2.07234
rho	4.22044	1.15187	1.96281	6.47807
beta_0	5.76177	0.371198	5.03424	6.48931
beta_1	-0.0108106	0.00250705	-0.0157243	-0.00589687
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.29	2.22	1.73
2.9	10	6.36	5.73	2.45	2.2	

```
0.906
 10.6     9       4.39         5.65         1.31         2.13
-1.77
   42     9       4.63         5.31         1.56         1.87
-1.09
191.1    10       3.73          3.7        0.941        0.871
0.124
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-50.932591	4	109.865181
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test   -2*log(Likelihood Ratio) Test df   p-value

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	12.4599	3	0.005963

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

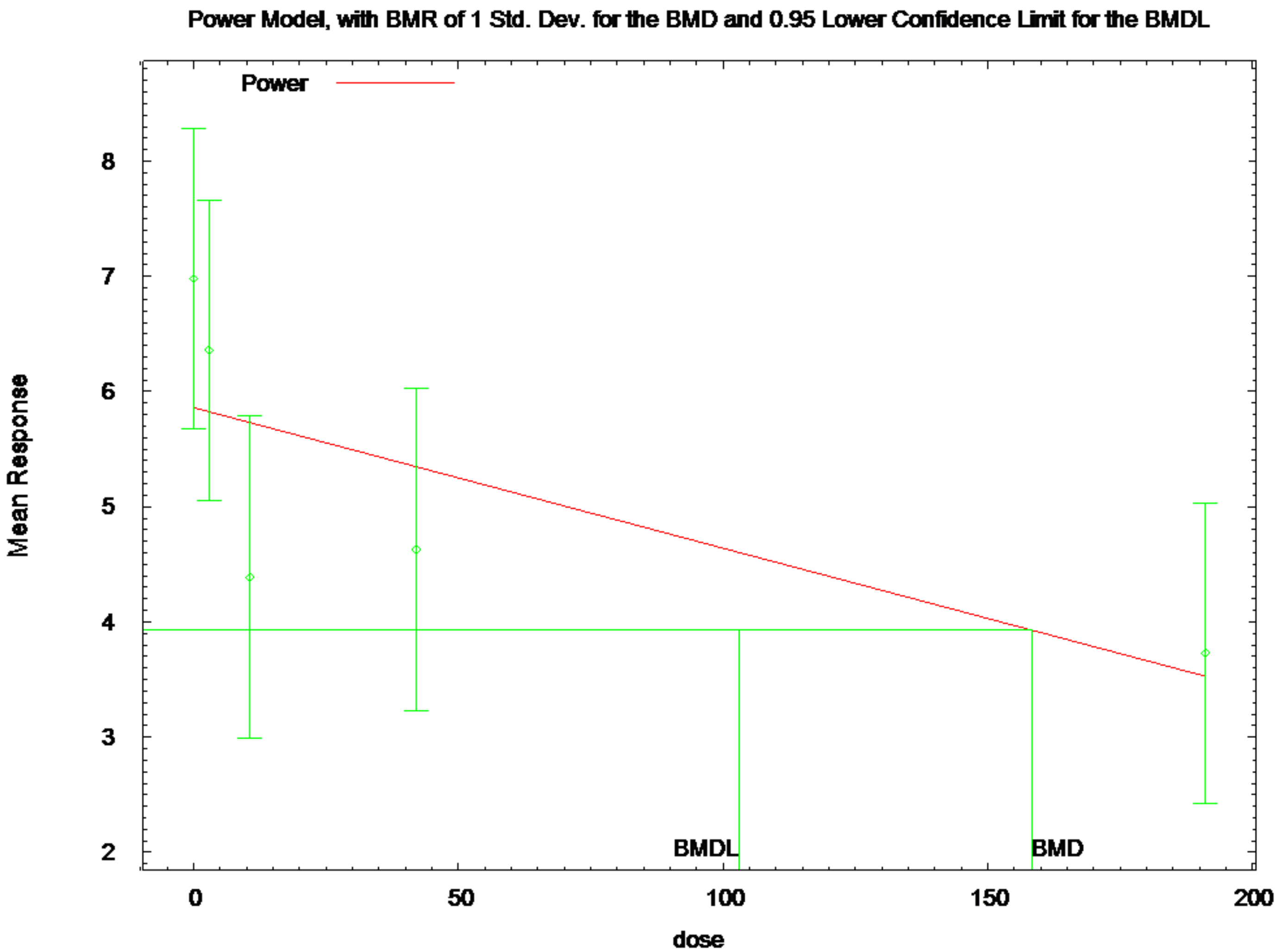
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 205.687

BMDL = 139.91



10:03 06/22 2014

```
====================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-PowerCV-1SD-5d.plt
                                        Sun Jun 22 10:03:59 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                        control =         3.73
                          slope =      2.97763
                          power =    -0.394692


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-5.8e-008	8.1e-008
control	-5.8e-008	1	-0.56
slope	8.1e-008	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.73207	0.761806	2.23896	5.22518
control	5.86108	0.337527	5.19954	6.52262
slope	-0.0122034	0.00378272	-0.0196175	-0.00478945
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.86	2.29	1.93	1.83
2.9	10	6.36	5.83	2.45	1.93	0.875
10.6	9	4.39	5.73	1.31	1.93	-2.08
42	9	4.63	5.35	1.56	1.93	-1.12
191.1	10	3.73	3.53	0.941	1.93	0.329

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-55.607114	3	117.214227
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	10.9794	3	0.01184

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

Specified effect = 1

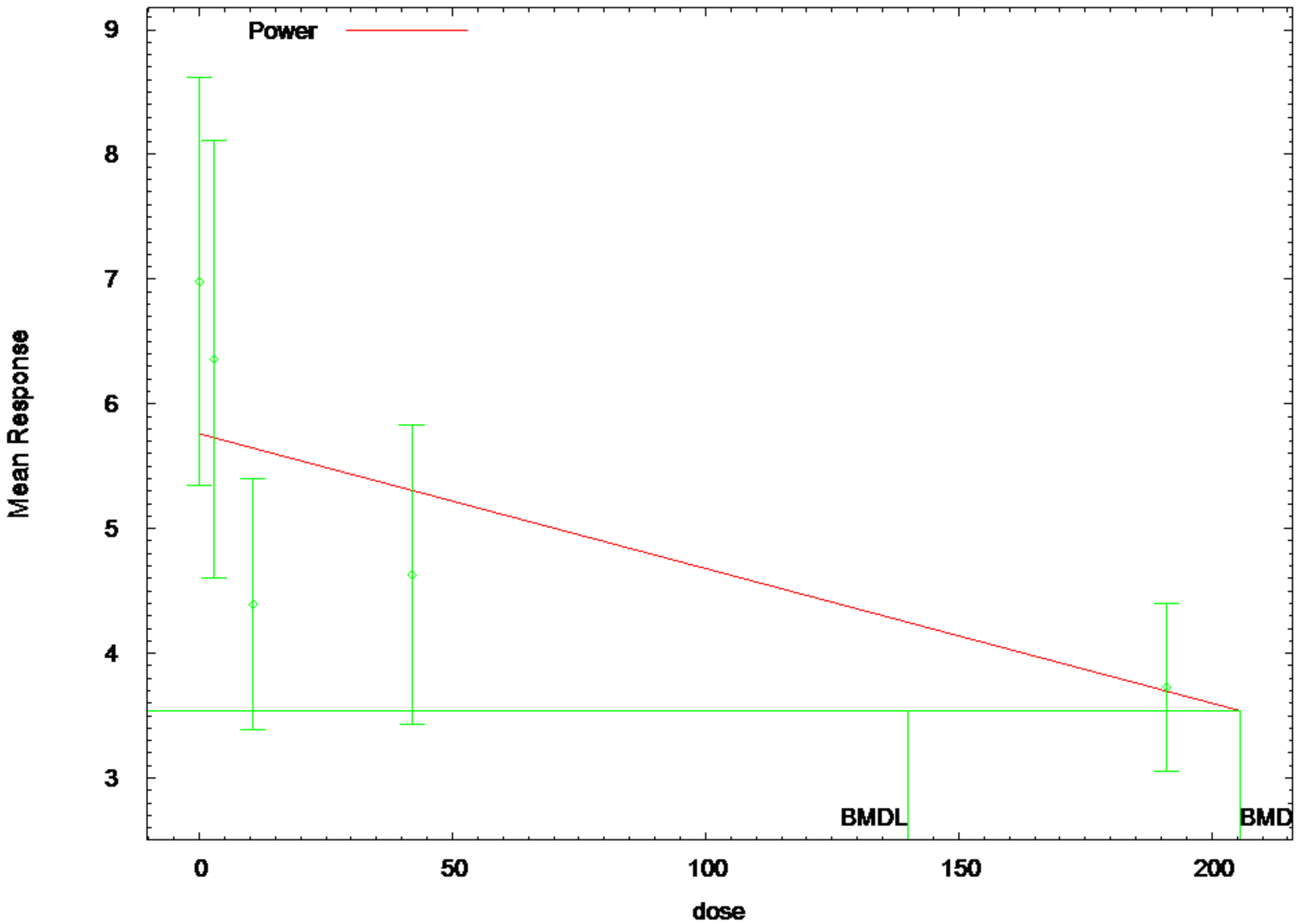
Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 158.304

BMDL = 102.979

Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



10:04 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_Normal-HLS
2001-Lymphocyte Count-PowerNCV-1SD-5d.plt
                                       Sun Jun 22 10:04:00 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                        control =         3.73
                          slope =      2.97763
                          power =    -0.394692


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-0.99	0.41	-0.64
rho	-0.99	1	-0.48	0.67
control	0.41	-0.48	1	-0.82
slope	-0.64	0.67	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-5.79276	2.54456	-10.78	-0.805511
rho	4.22044	1.57816	1.12729	7.31358
control	5.76177	0.372822	5.03106	6.49249
slope	-0.0108106	0.00250309	-0.0157166	-0.00590465
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	5.76	2.29	2.22	1.73
2.9	10	6.36	5.73	2.45	2.2	0.906
10.6	9	4.39	5.65	1.31	2.13	-1.77
42	9	4.63	5.31	1.56	1.87	-1.09

191.1	10	3.73	3.7	0.941	0.871	0.124

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-50.932591	4	109.865181
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	12.4599	3	0.005963

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

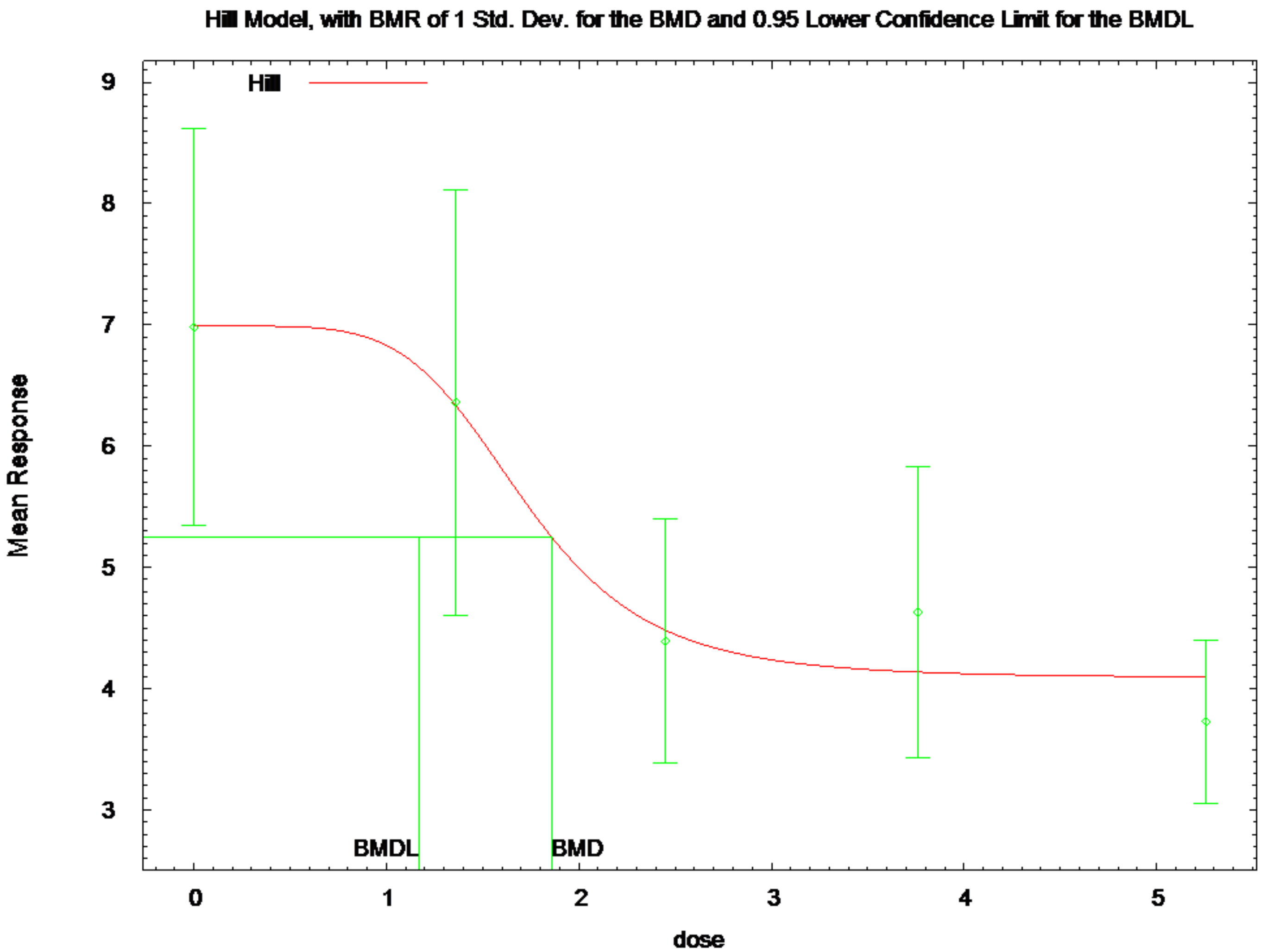
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 205.687

BMDL = 139.91

BMDS Model Results for Lymphocyte Count (Log-transformed Doses, Historical Controls)



10:10 06/22 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-HillCV-1SD-5d.plt
                                      Sun Jun 22 10:10:17 2014
=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                      intercept =         6.98
                              v =        -3.25
                              n =      3.73558
                              k =      1.91707


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	4.7e-008	6.8e-008	1.5e-007	-1.4e-007
intercept	4.7e-008	1	-0.76	-0.27	-0.35
v	6.8e-008	-0.76	1	0.63	-0.15
n	1.5e-007	-0.27	0.63	1	-0.46
k	-1.4e-007	-0.35	-0.15	-0.46	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.04453	0.621463	1.82649	4.26258
intercept	6.99164	0.54938	5.91488	8.06841
v	-2.90088	0.78628	-4.44196	-1.3598
n	5.25235	5.37316	-5.27884	15.7836
k	1.72188	0.447295	0.8452	2.59856

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.99	2.29	1.74	-0.0211

1.361	10	6.36	6.34	2.45	1.74
0.0395					
2.451	9	4.39	4.48	1.31	1.74
-0.161					
3.761	9	4.63	4.14	1.56	1.74
0.846					
5.258	10	3.73	4.1	0.941	1.74
-0.669					

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-50.720349	5	111.440698
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	1.20588	1	0.2722

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

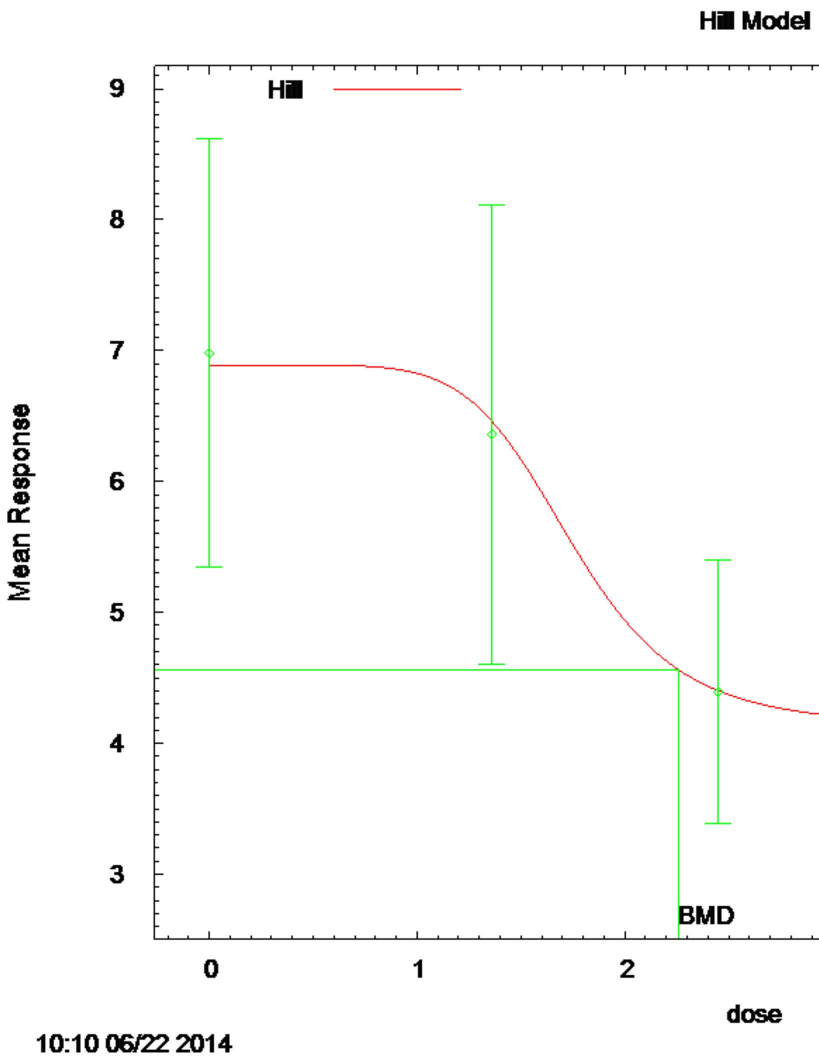
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 1.86228

BMDL = 1.17035



Hill Model
Hill
9
8
7
6
5
4
3
Mean Response
BMD
0
1
2
3
4
5
dose
10:10 06/22 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-HillNCV-1SD-5d.plt
                                      Sun Jun 22 10:10:18 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                      intercept =         6.98
                              v =        -3.25
                              n =      3.73558
                              k =      1.91707


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

n k

lalpha	1	-0.99	0.33	-0.4	-0.09	-0.032
rho	-0.99	1	-0.37	0.42	0.09	0.033
intercept	0.33	-0.37	1	-0.92	-0.44	-0.43
v	-0.4	0.42	-0.92	1	0.62	0.23
n	-0.09	0.09	-0.44	0.62	1	-0.05
k	-0.032	0.033	-0.43	0.23	-0.05	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-3.0691	1.70987	-6.42039	0.282182
rho	2.46856	1.04176	0.426739	4.51038
intercept	6.89077	0.705601	5.50782	8.27372
v	-2.75193	0.840902	-4.40007	-1.10379
n	6.70247	6.94921	-6.91773	20.3227
k	1.74805	0.392584	0.978601	2.5175

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.89	2.29	2.33	0.121

```
1.361    10       6.36         6.46         2.45         2.15
-0.143
2.451     9       4.39          4.4         1.31         1.34
-0.017
3.761     9       4.63         4.15         1.56         1.25
1.14
5.258    10       3.73         4.14        0.941         1.25
-1.04
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-46.998934	6	105.997868
R	-60.317047	2	124.634093

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	4.5926	1	0.03211

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

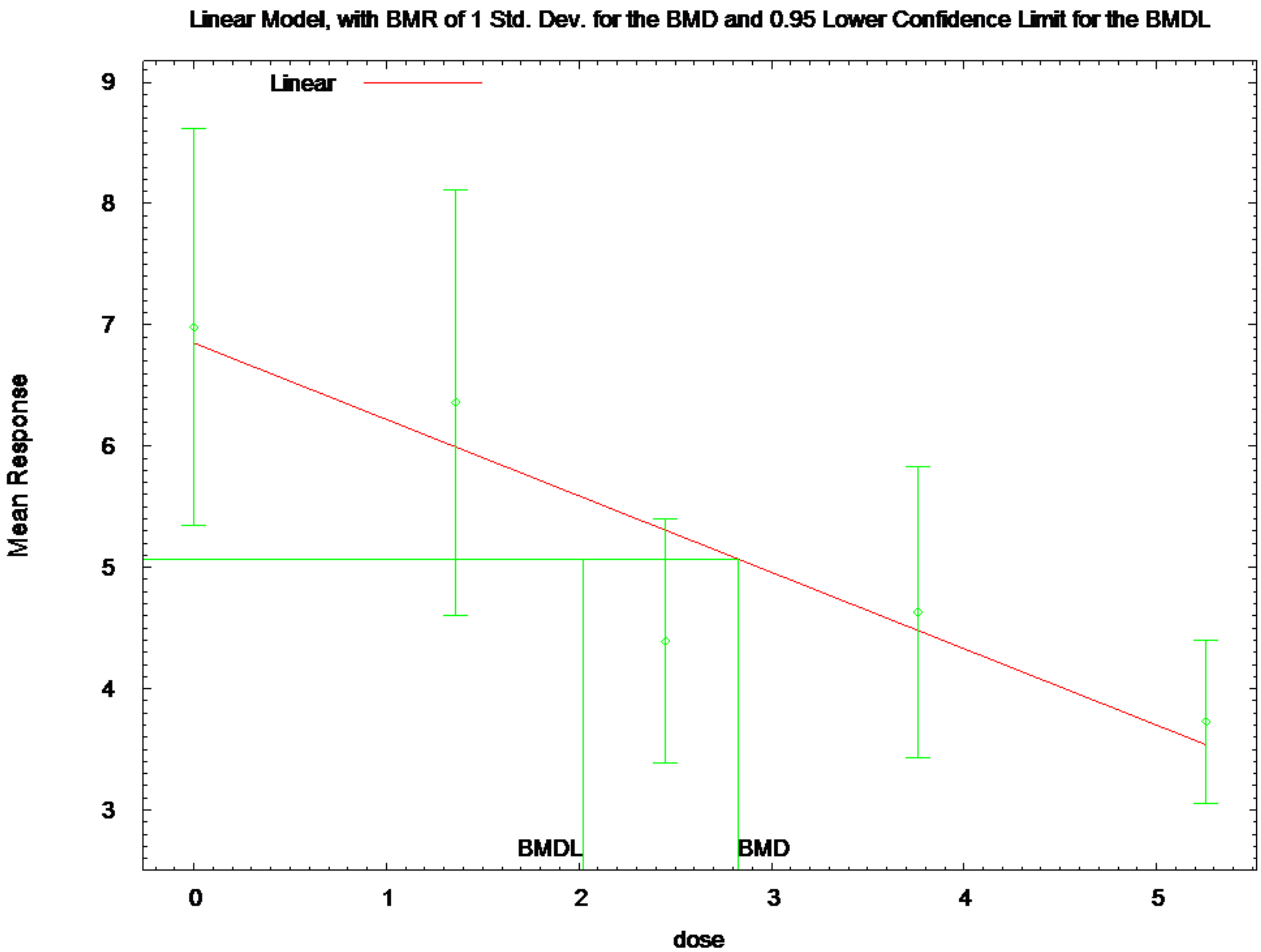
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.26002

BMDL computation failed.



12:48 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-LinearCV-1SD-5d.plt
                                         Wed Jul 09 12:48:07 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      6.83073
                         beta_1 =    -0.628452


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	2.2e-008	-8.6e-010
beta_0	2.2e-008	1	-0.81
beta_1	-8.6e-010	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.16984	0.64704	1.90166	4.43801
beta_0	6.85042	0.435612	5.99664	7.70421
beta_1	-0.630151	0.138278	-0.901171	-0.359132

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.29	1.78	0.23
1.361	10	6.36	5.99	2.45	1.78	0.652
2.451	9	4.39	5.31	1.31	1.78	-1.54
3.761	9	4.63	4.48	1.56	1.78	0.252
5.258	10	3.73	3.54	0.941	1.78	0.343

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-51.688316	3	109.376631
R	-60.317047	2	124.634093

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	3.14181	3	0.3703

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a

different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

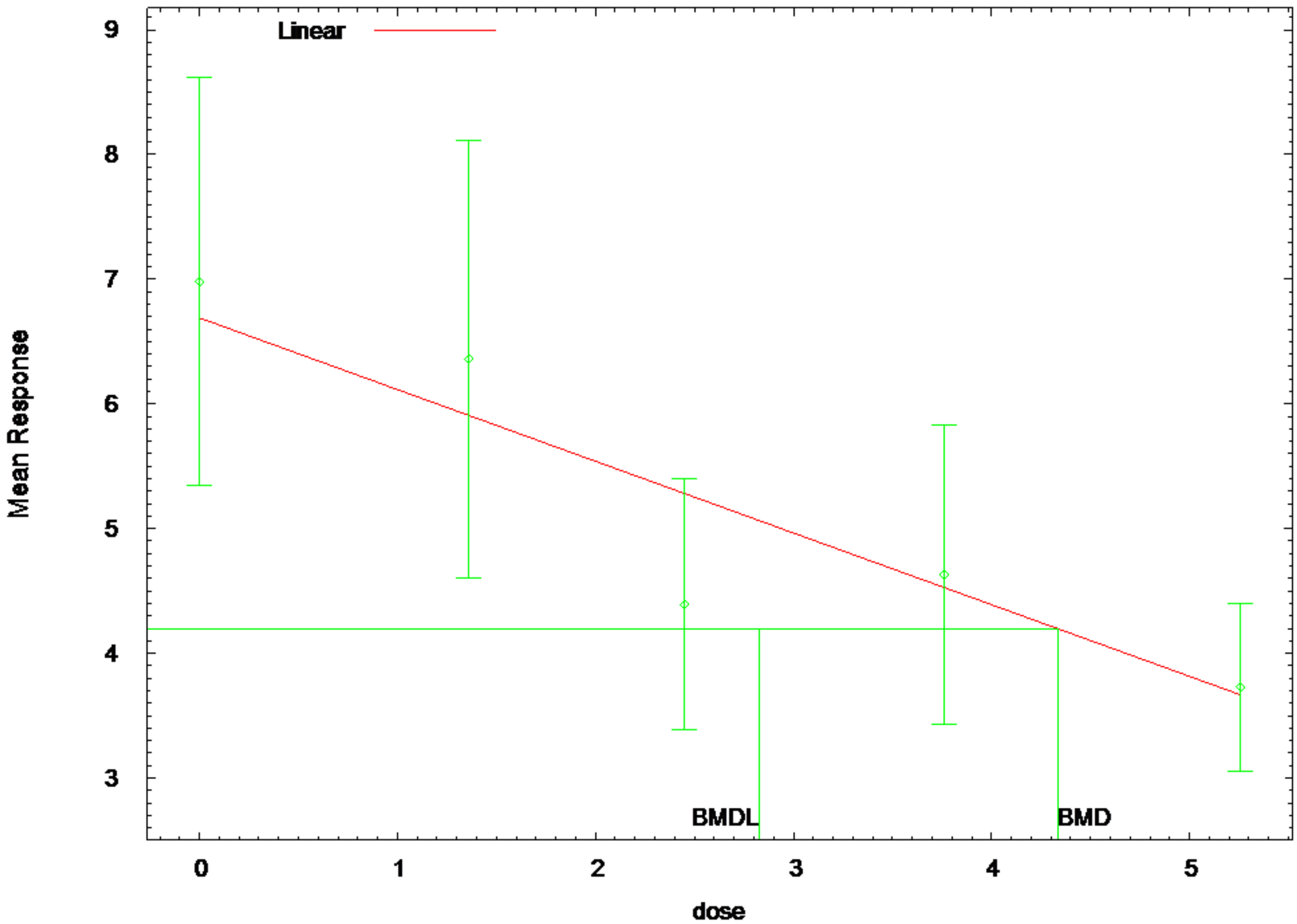
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.82536

BMDL = 2.0197

Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:48:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =       1.19823
                            rho =             0
                         beta_0 =       6.83073
                         beta_1 =     -0.628452


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1        -0.99         0.16        -0.19
```

rho	-0.99	1	-0.16	0.19
beta_0	0.16	-0.16	1	-0.91
beta_1	-0.19	0.19	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.22724	1.68476	-7.5293	-0.925178
rho	3.18577	1.02462	1.17755	5.19399
beta_0	6.68829	0.512021	5.68475	7.69183
beta_1	-0.574737	0.123483	-0.816759	-0.332715

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.69	2.29	2.49	0.37
1.361	10	6.36	5.91	2.45	2.04	0.702
2.451	9	4.39	5.28	1.31	1.71	-1.56
3.761	9	4.63	4.53	1.56	1.34	0.232
5.258	10	3.73	3.67	0.941	0.957	0.21

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-47.300760	4	102.601521
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	5.19625	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears

to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

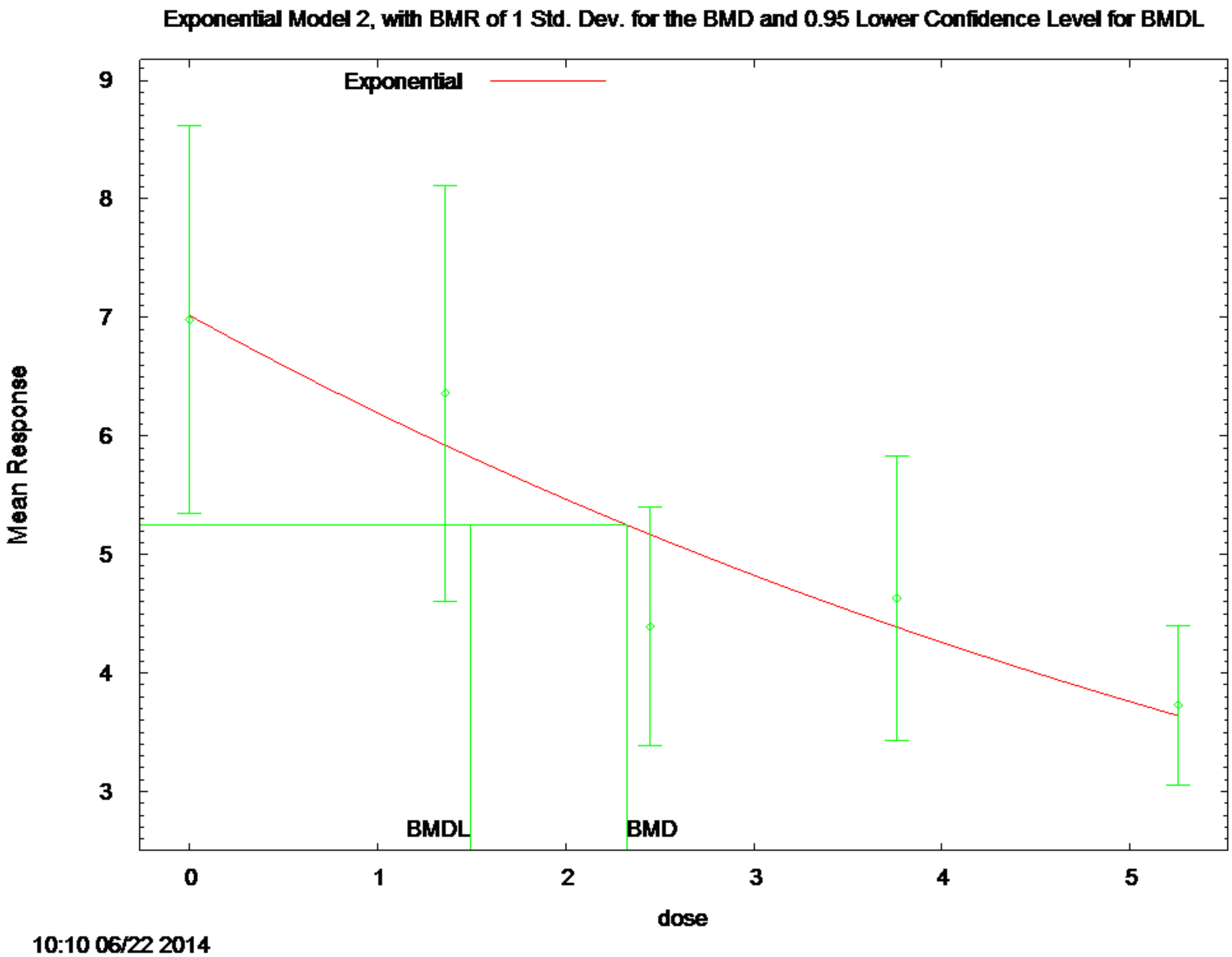
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.33739

BMDL = 2.82692



Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
10:10 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:10:17 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	1.08823
rho(S)	0
a	3.75105
b	0.120756
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	1.14279
rho	0
a	7.01811
b	0.12488
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.018	1.771	-0.06806
1.361	5.921	1.771	0.7837
2.451	5.168	1.771	-1.317
3.761	4.388	1.771	0.4104
5.258	3.64	1.771	0.1614

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
2	-51.427	3	108.854

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	

0.0001035

Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 4	2.619	3	0.4541

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

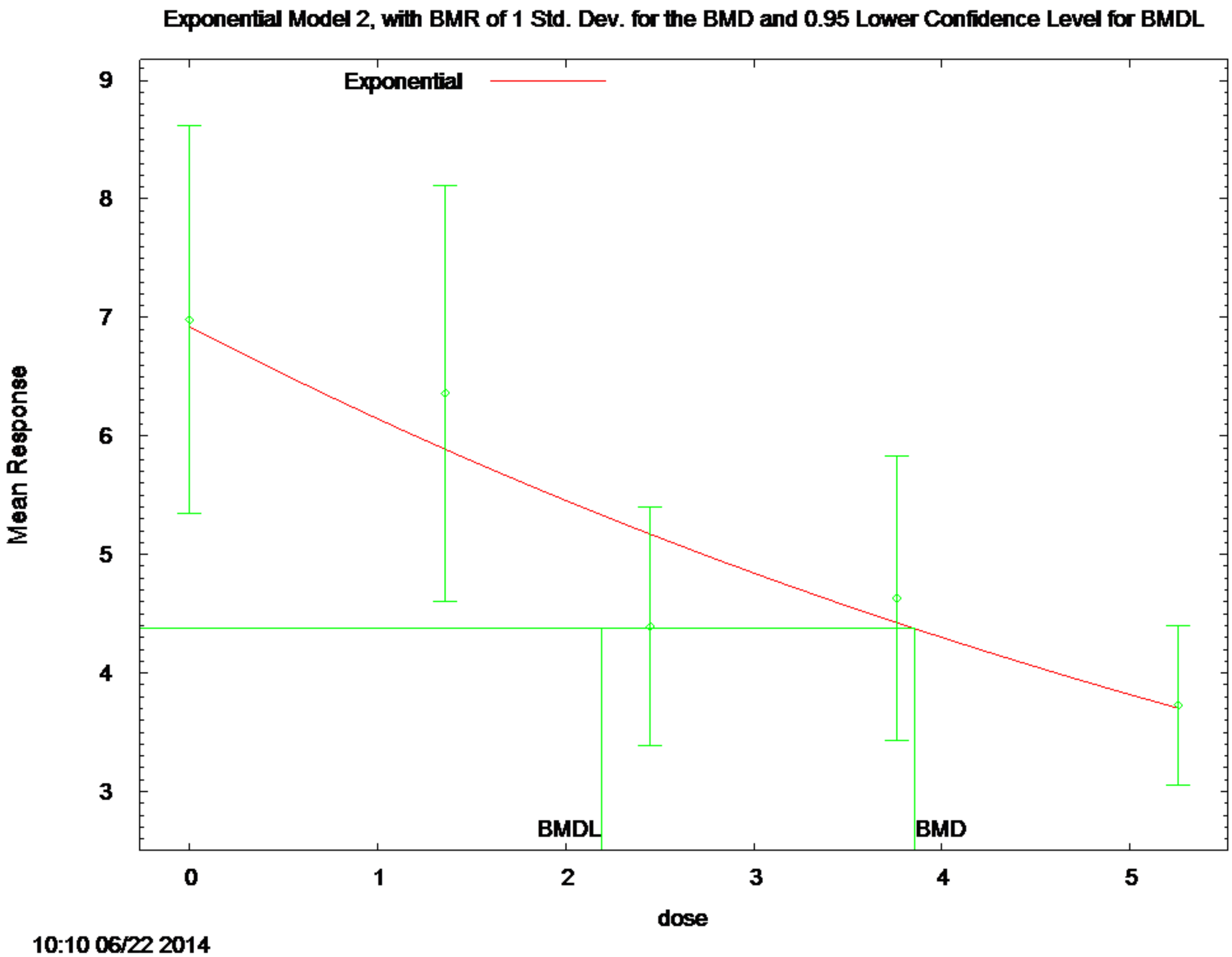
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.32836

BMDL = 1.49734


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
10:10 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 10:10:18 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-3.80501
rho	2.92874
a	3.75105
b	0.120756
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-3.90258
rho	2.98432
a	6.92193
b	0.118985
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.922	2.549	0.07205
1.361	5.887	2.002	0.7472
2.451	5.171	1.649	-1.42
3.761	4.425	1.307	0.4713
5.258	3.703	1.002	0.08605

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
2	-47.23015	4	102.4603

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035
Test 2	11.34	4	

0.02296
    Test 3 0.5142 3
0.9157
    Test 4 5.055 3
0.1678

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

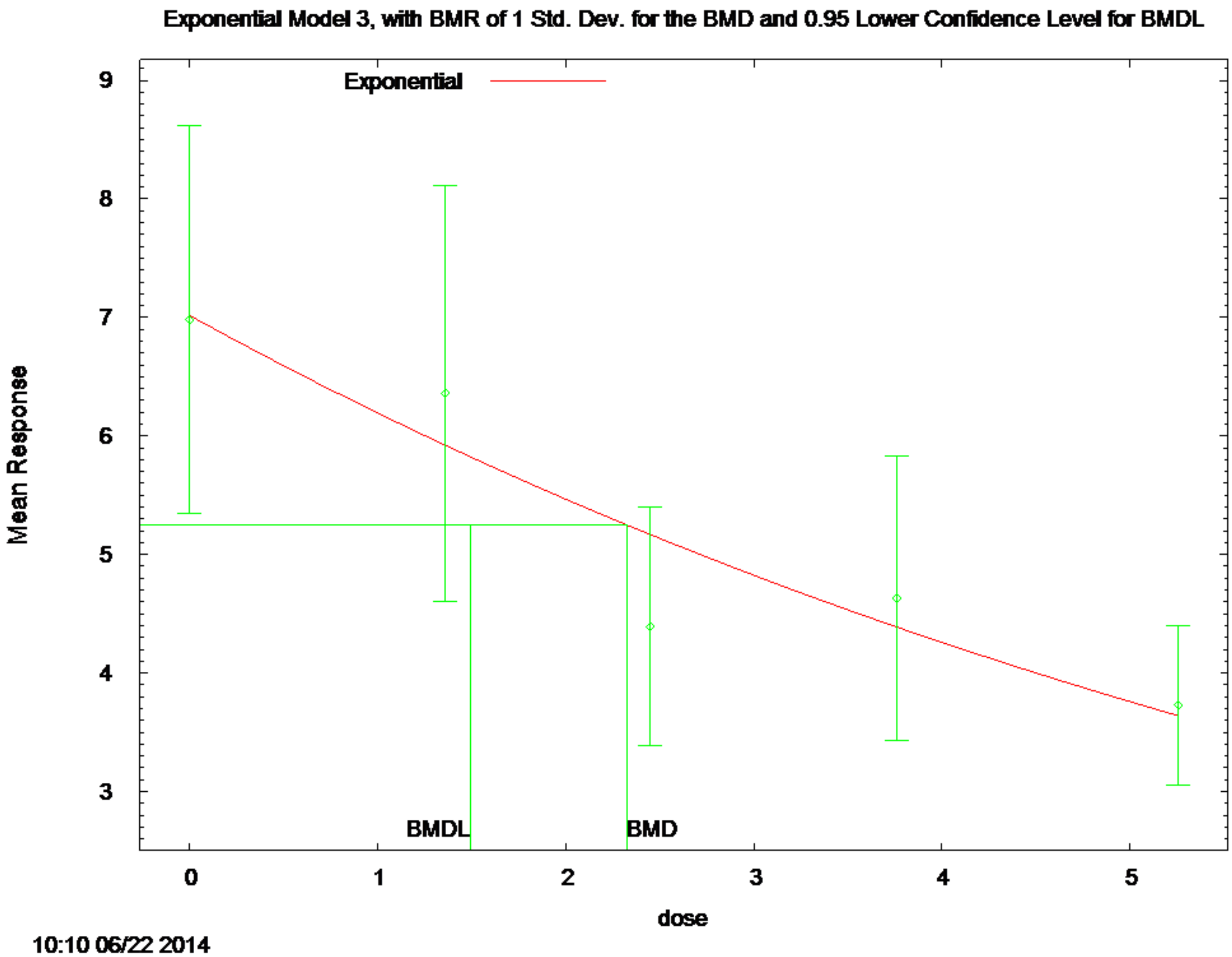
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.85924

BMDL = 2.19242



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
10:10 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:10:17 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	1.08823
rho(S)	0
a	3.75105
b	0.120756
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	1.14279
rho	0
a	7.01811
b	0.12488
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.018	1.771	-0.06806
1.361	5.921	1.771	0.7837
2.451	5.168	1.771	-1.317
3.761	4.388	1.771	0.4104
5.258	3.64	1.771	0.1614

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
3	-51.427	3	108.854

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.74	8	0.0001035
Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 5a	2.619	3	0.4541

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

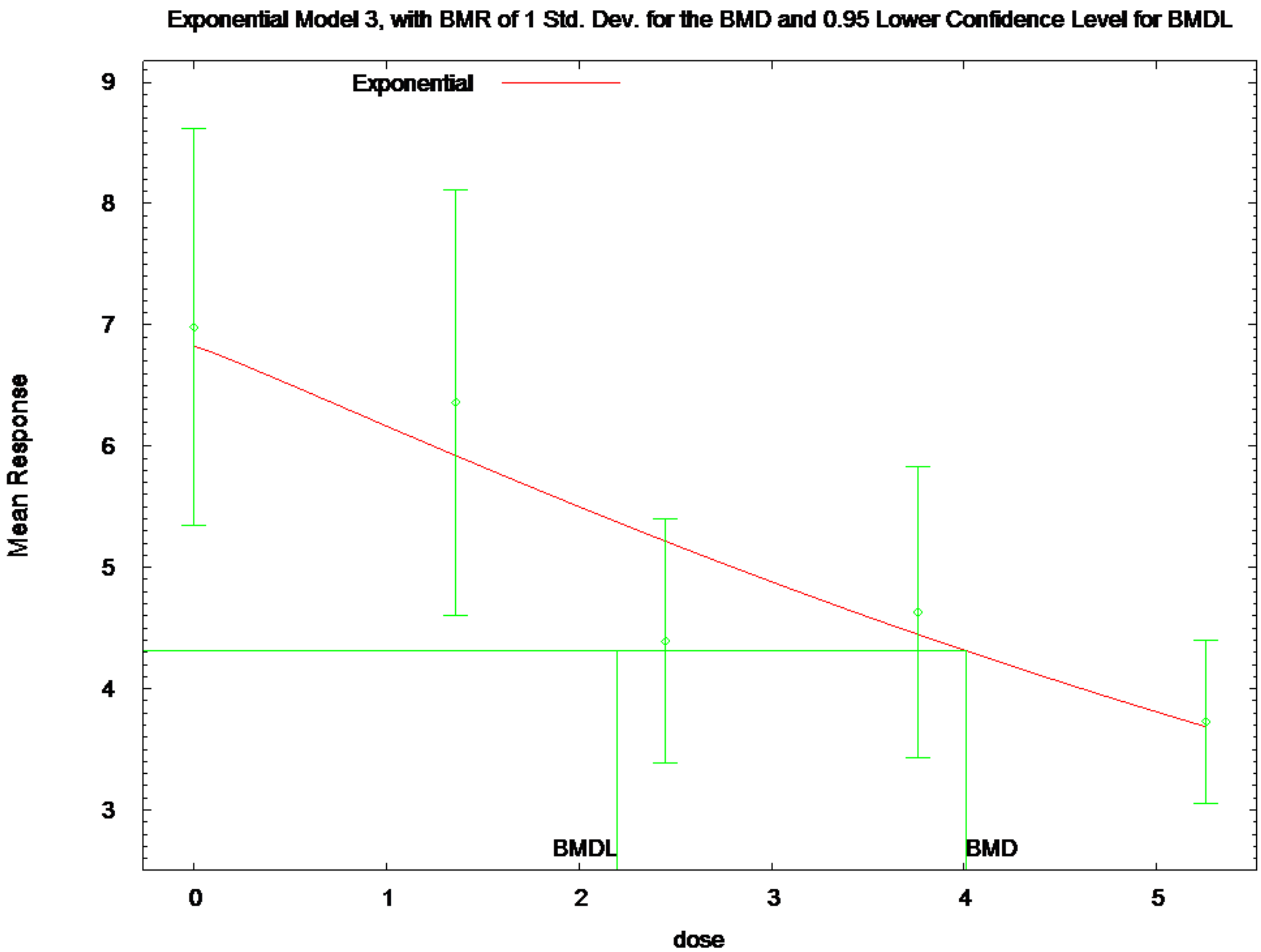
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.32836

BMDL = 1.49734



10:10 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:10:18 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-3.80501
rho	2.92874
a	3.75105
b	0.120756
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-3.99515
rho	3.04054
a	6.82645
b	0.121704
c	0
d	1.08473

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.826	2.516	0.193
1.361	5.921	2.027	0.6844
2.451	5.215	1.671	-1.482
3.761	4.448	1.312	0.4168
5.258	3.686	0.9859	0.14

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
3	-47.20826	5	104.4165

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

Test 2 11.34 4
0.02296
Test 3 0.5142 3
0.9157
Test 5a 5.011 2
0.08162

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous
variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled
variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

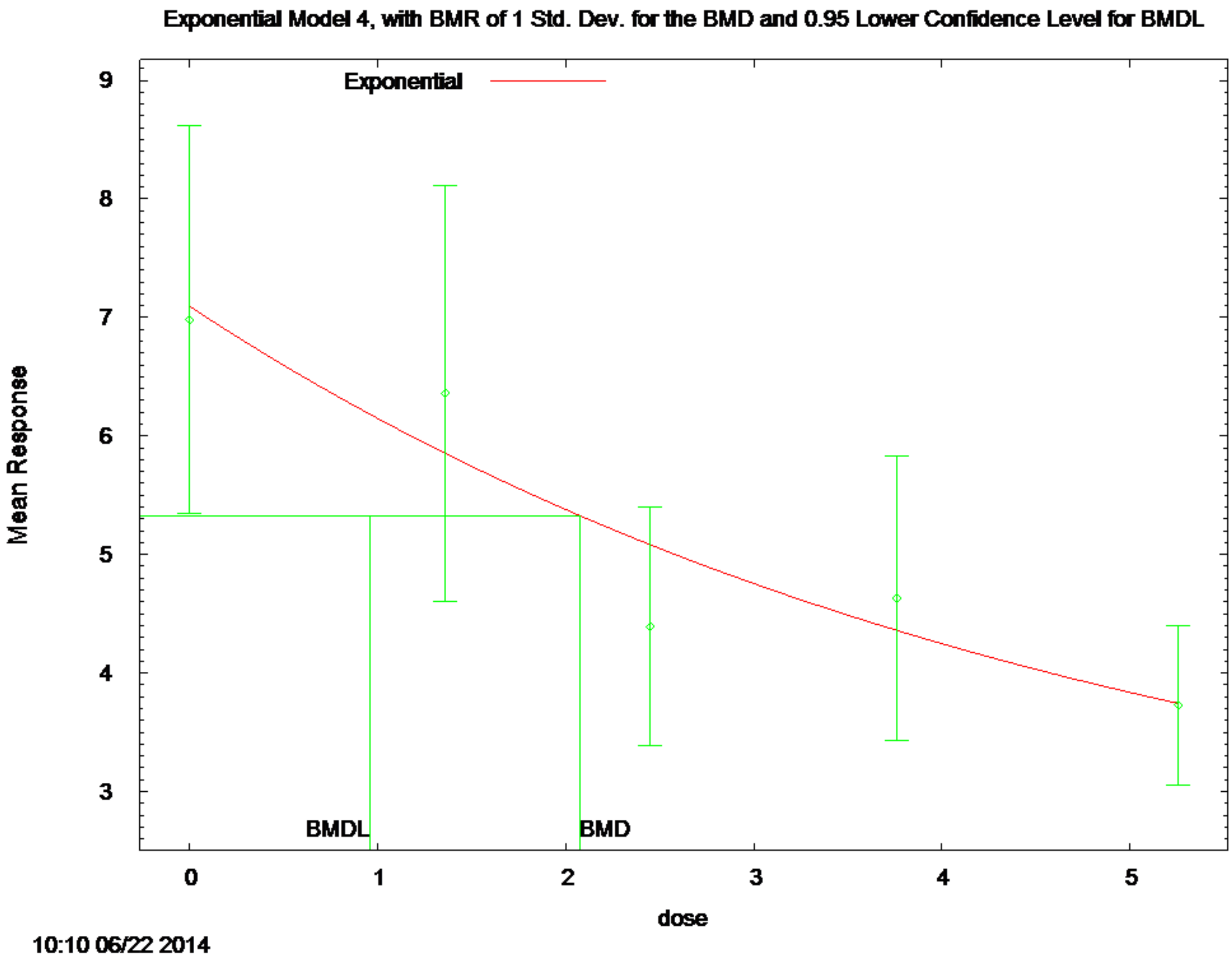
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 4.01364

BMDL = 2.20133



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
10:10 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:10:17 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	1.08823
rho(S)	0
a	7.329
b	0.208885
c	0.254469
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	1.14069
rho	0
a	7.09555
b	0.208122
c	0.289708
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	7.096	1.769	-0.2066
1.361	5.852	1.769	0.9075
2.451	5.082	1.769	-1.173
3.761	4.36	1.769	0.4586
5.258	3.743	1.769	-0.02299

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
4	-51.37665	4	110.7533

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.74	8	0.0001035
Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 6a	2.518	2	0.2839

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

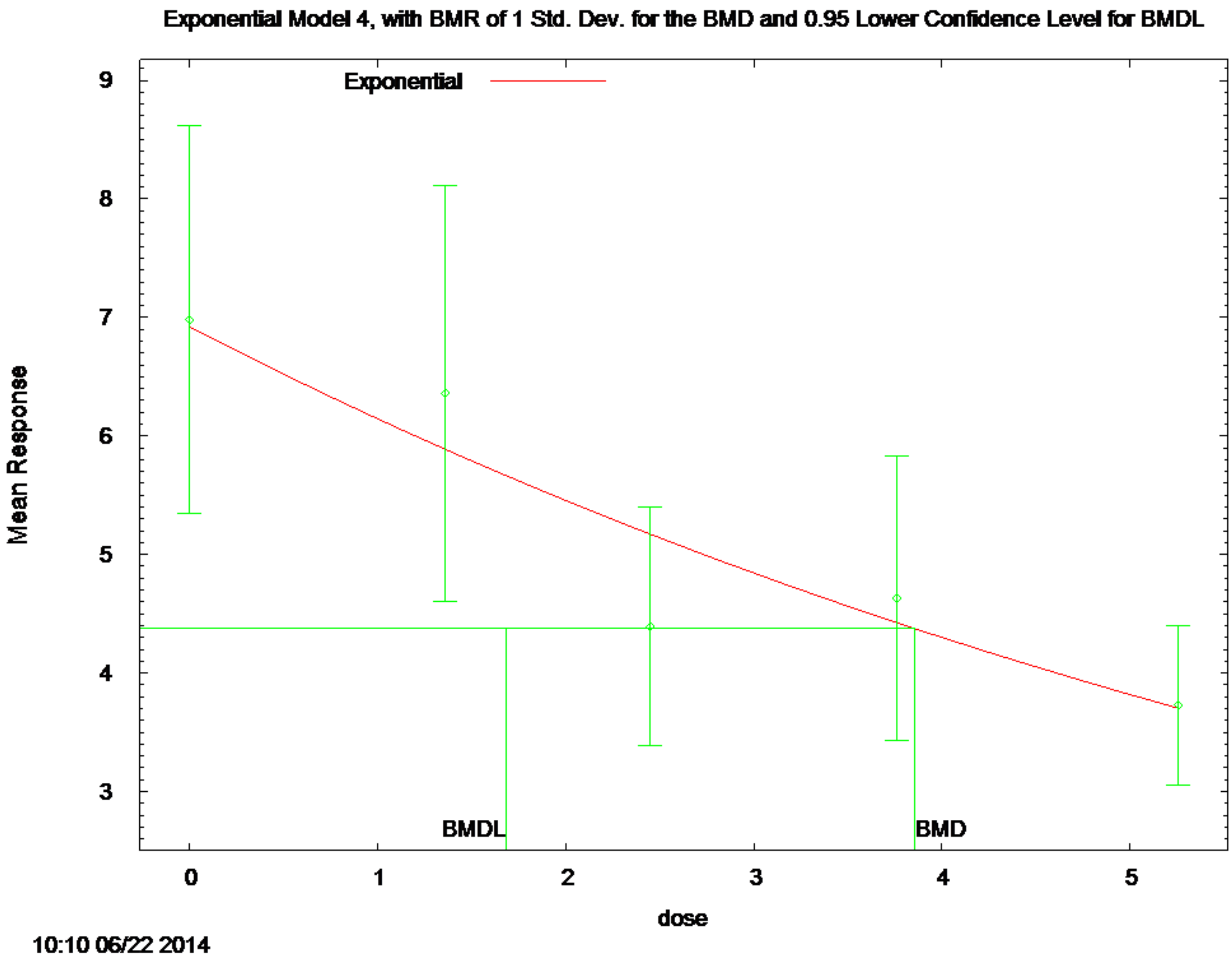
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.07707

BMDL = 0.956572


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
10:10 06/22 2014

```
====================================================================
===
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpNCV-1SD-5d.(d)
        Gnuplot Plotting File:
                                       Sun Jun 22 10:10:18 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-3.80501
rho	2.92874
a	7.329
b	0.208885
c	0.254469
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-3.90257
rho	2.98431
a	6.92193
b	0.118985
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.922	2.549	0.07205
1.361	5.887	2.002	0.7472
2.451	5.171	1.649	-1.42
3.761	4.425	1.307	0.4713
5.258	3.703	1.002	0.08604

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
4	-47.23015	4	102.4603

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

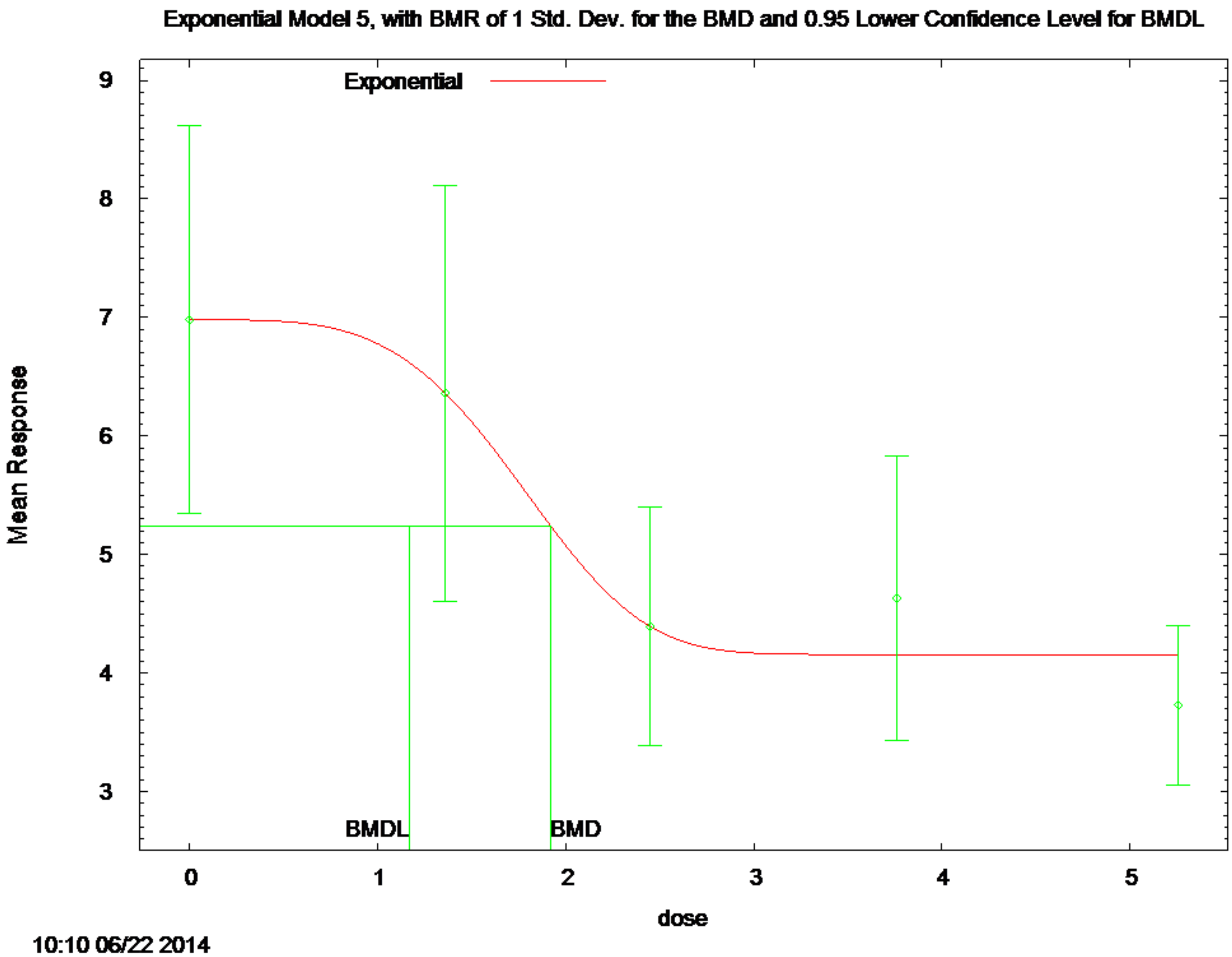
Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

```
     Test 2                              11.34           4
0.02296
     Test 3                             0.5142           3
0.9157
    Test 6a                              5.055           3
0.1678


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 6a is greater than .1.  Model 4 seems
     to adequately describe the data.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =      3.85925

                 BMDL =        1.683
```


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
10:10 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 10:10:17 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	1.08823
rho(S)	0
a	7.329
b	0.208885
c	0.254469
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	1.11479
rho	0
a	6.98002
b	0.514905
c	0.595454
d	3.92235

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.98	1.746	-3.704e-005
1.361	6.36	1.746	6.068e-005
2.451	4.39	1.746	-0.0001435
3.761	4.156	1.746	0.8139
5.258	4.156	1.746	-0.772

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-50.11741	6	112.2348
R	-60.31705	2	124.6341
5	-50.75501	5	111.51

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	31.74	8	0.0001035
Test 2	11.34	4	0.02296
Test 3	11.34	4	0.02296
Test 7a	1.275	1	0.2588

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

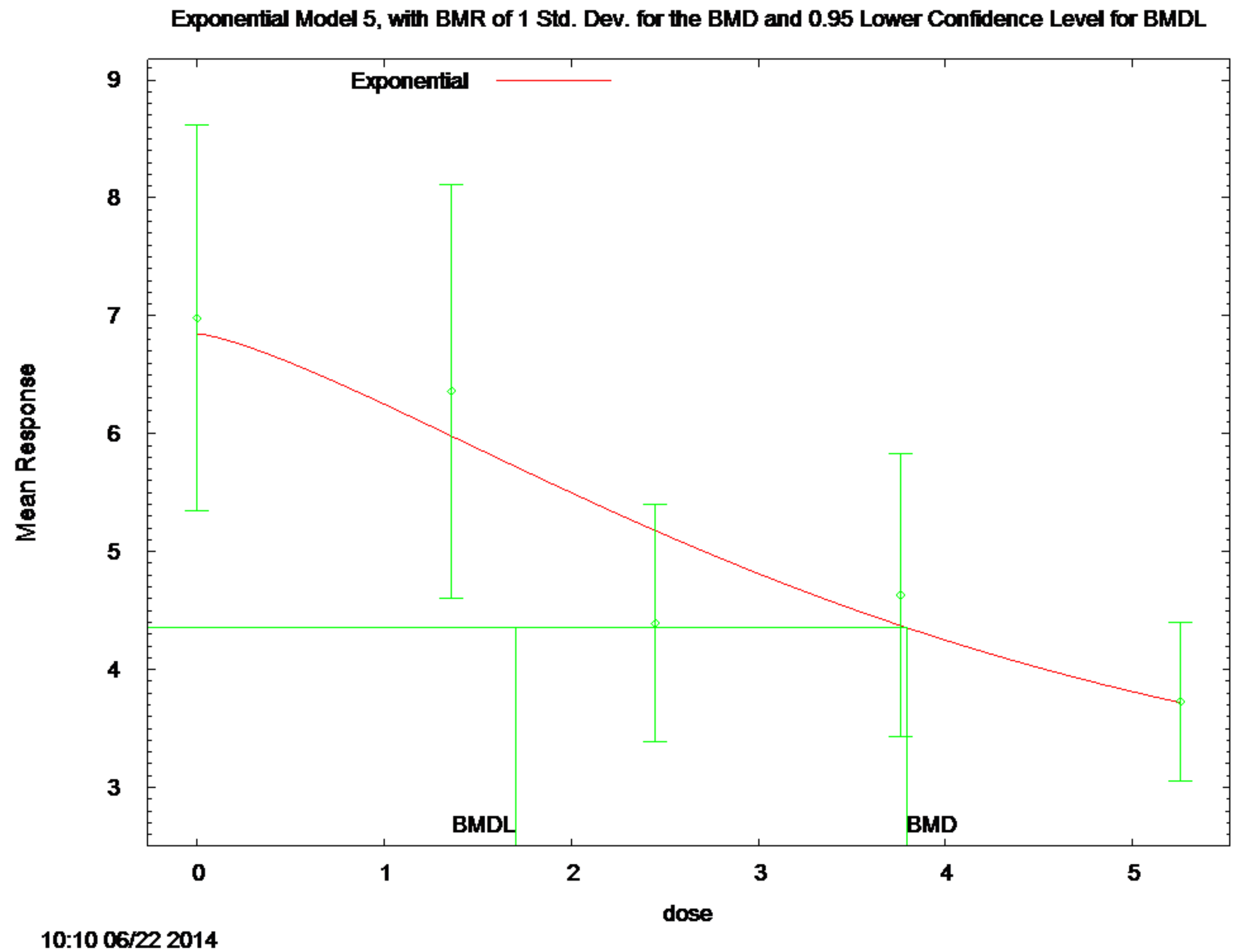
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 1.92368

BMDL = 1.16803



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
10:10 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 10:10:18 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-3.80501
rho	2.92874
a	7.329
b	0.208885
c	0.254469
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-3.85928
rho	2.95639
a	6.84831
b	0.255151
c	0.408943
d	1.34247

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.98	2.289
1.361	10	6.36	2.452
2.451	9	4.39	1.308
3.761	9	4.63	1.564
5.258	10	3.73	0.941

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	6.848	2.495	0.1669
1.361	5.979	2.042	0.5899
2.451	5.177	1.65	-1.431
3.761	4.372	1.285	0.6022
5.258	3.719	1.012	0.03544

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-50.11741	6	112.2348
A2	-44.44551	10	108.891
A3	-44.70264	7	103.4053
R	-60.31705	2	124.6341
5	-47.16672	6	106.3334

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.74	8	0.0001035

Test 2	11.34	4	0.02296
Test 3	0.5142	3	0.9157
Test 7a	4.928	1	0.02642

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

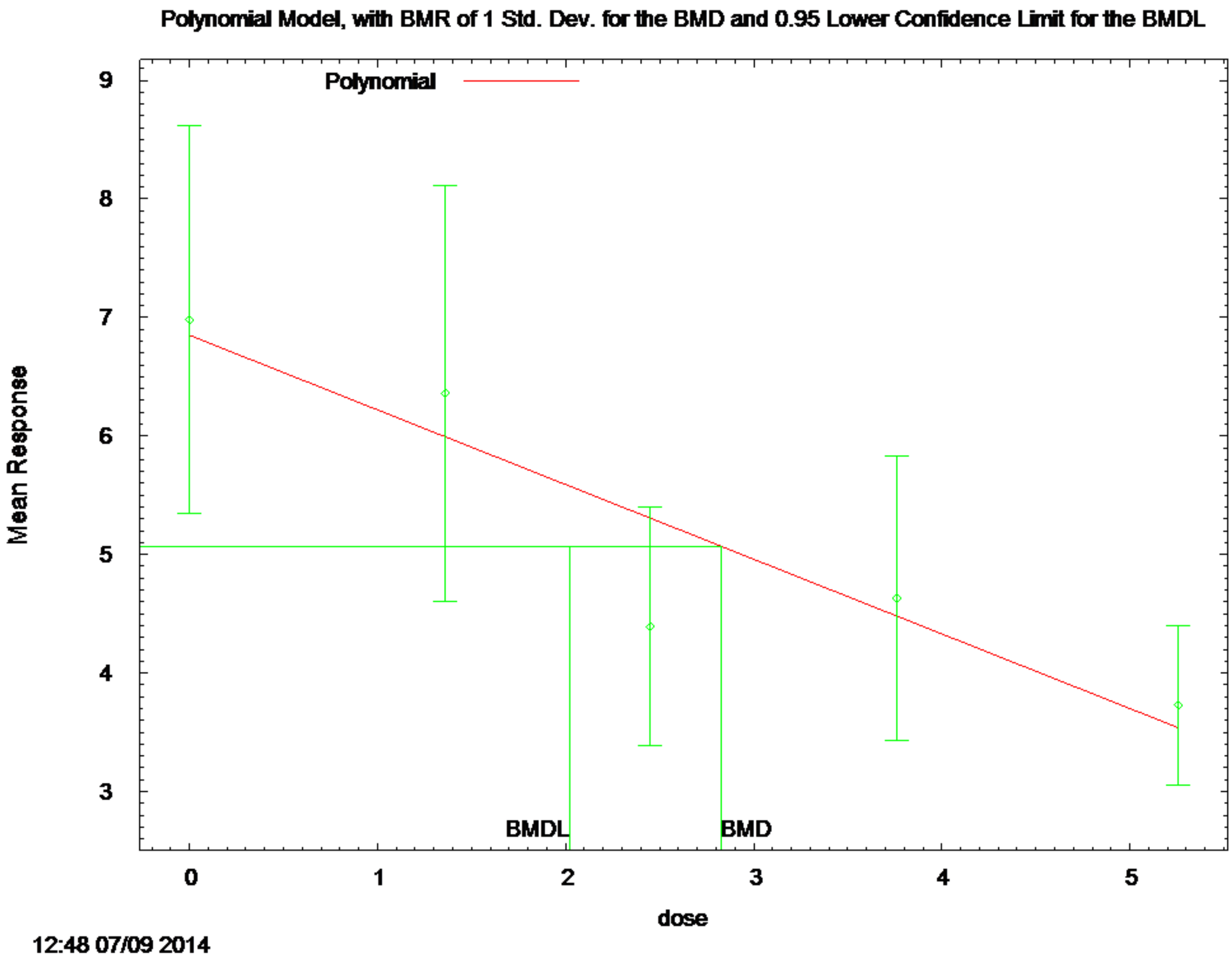
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.79695

BMDL = 1.70114



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:48:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      7.10002
                         beta_1 =     -1.02021
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.3e-007	1.2e-007
beta_0	-1.3e-007	1	-0.81
beta_1	1.2e-007	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.16984	0.64704	1.90166	4.43801
beta_0	6.85042	0.435612	5.99664	7.70421
beta_1	-0.630151	0.138278	-0.901171	-0.359132
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.29	1.78	0.23
1.361	10	6.36	5.99	2.45	1.78	0.652
2.451	9	4.39	5.31	1.31	1.78	-1.54
3.761	9	4.63	4.48	1.56	1.78	0.252
5.258	10	3.73	3.54	0.941	1.78	0.343

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-51.688316	3	109.376631
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	3.14181	3	0.3703

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

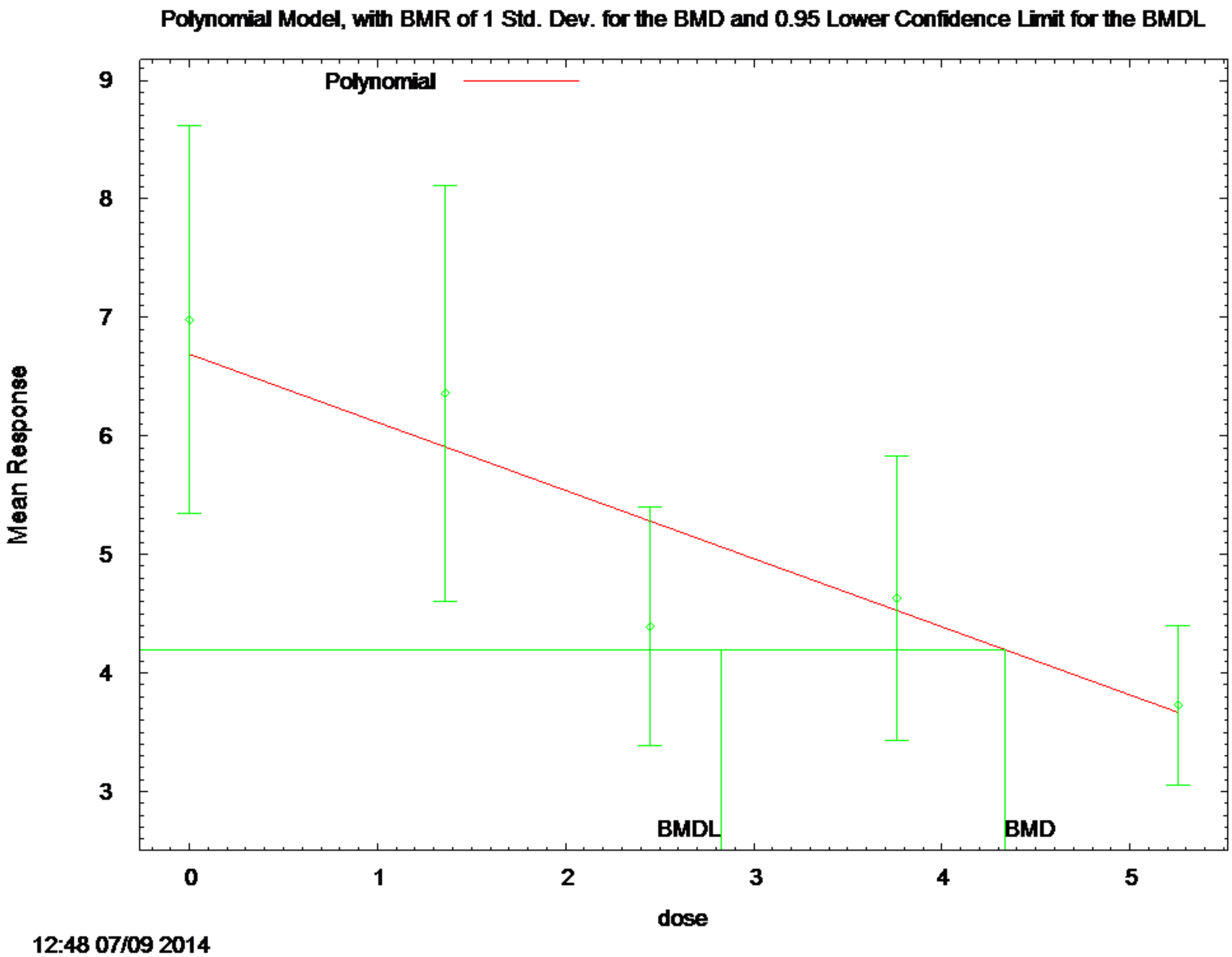
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.82536

BMDL = 2.0197



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:48:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =      7.10002
                         beta_1 =     -1.02021
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.16	-0.19
rho	-0.99	1	-0.16	0.19
beta_0	0.16	-0.16	1	-0.91
beta_1	-0.19	0.19	-0.91	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.22724	1.68476	-7.5293	-0.925178
rho	3.18577	1.02462	1.17755	5.19399
beta_0	6.68829	0.512021	5.68475	7.69183
beta_1	-0.574737	0.123483	-0.816759	-0.332715
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.69	2.29	2.49	0.37
1.361	10	6.36	5.91	2.45	2.04	0.702
2.451	9	4.39	5.28	1.31	1.71	-1.56
3.761	9	4.63	4.53	1.56	1.34	0.232

5.258 10 3.73 3.67 0.941 0.957
0.21

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-47.300760	4	102.601521
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	5.19625	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

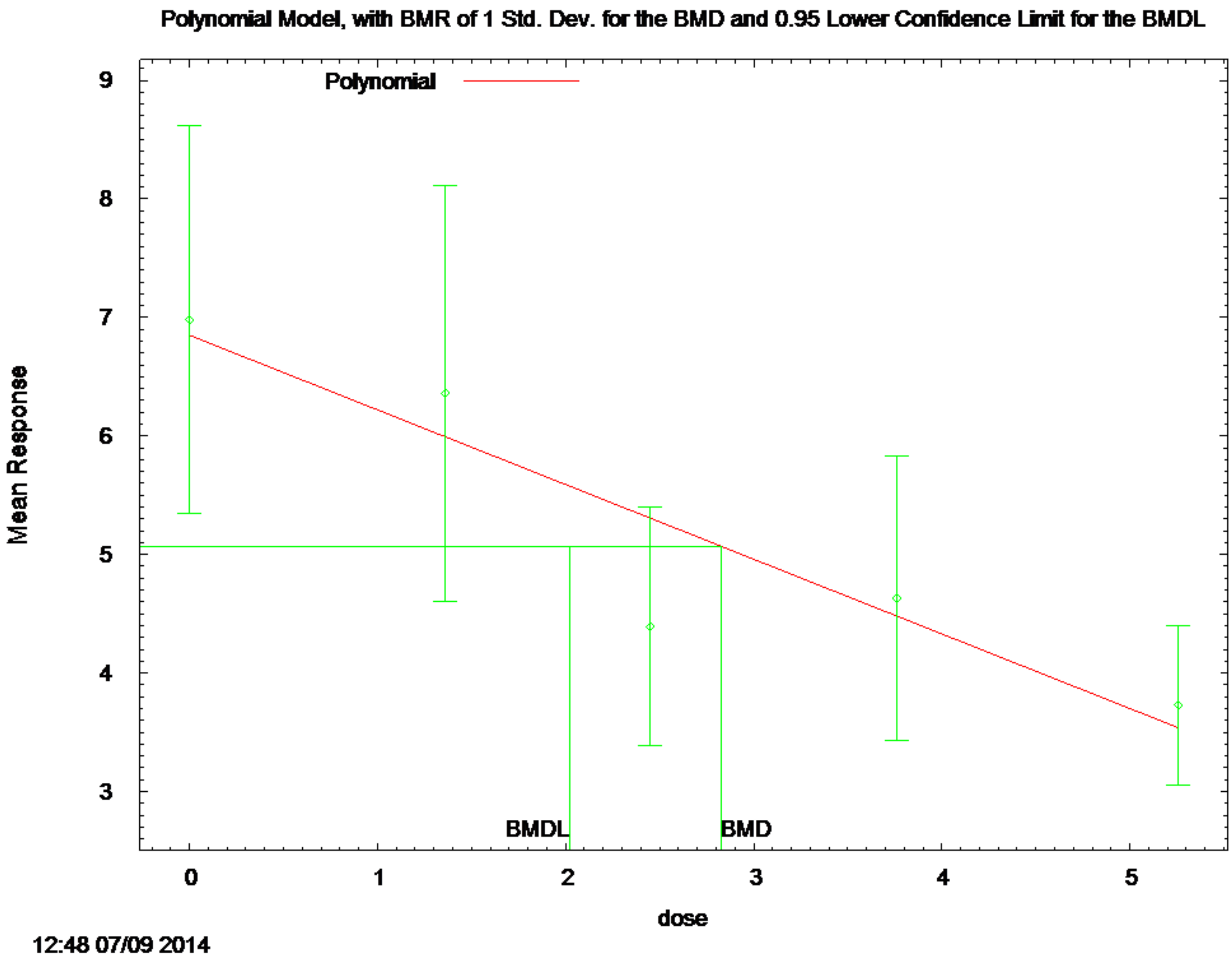
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.33739

BMDL = 2.82692


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
0
1
2
3
4
5
3
4
5
6
7
8
9
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly3CV-1SD-5d.plt
                                        Wed Jul 09 12:48:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =      7.07831
                         beta_1 =    -0.897602
                         beta_2 =            0
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	4.6e-008	3.4e-009
beta_0	4.6e-008	1	-0.81
beta_1	3.4e-009	-0.81	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.16984	0.64704	1.90166	4.43801
beta_0	6.85042	0.435612	5.99664	7.70421
beta_1	-0.630151	0.138278	-0.901171	-0.359132
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.29	1.78	0.23
1.361	10	6.36	5.99	2.45	1.78	0.652
2.451	9	4.39	5.31	1.31	1.78	-1.54
3.761	9	4.63	4.48	1.56	1.78	0.252
5.258	10	3.73	3.54	0.941	1.78	

0.343

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-51.688316	3	109.376631
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	3.14181	3	0.3703

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

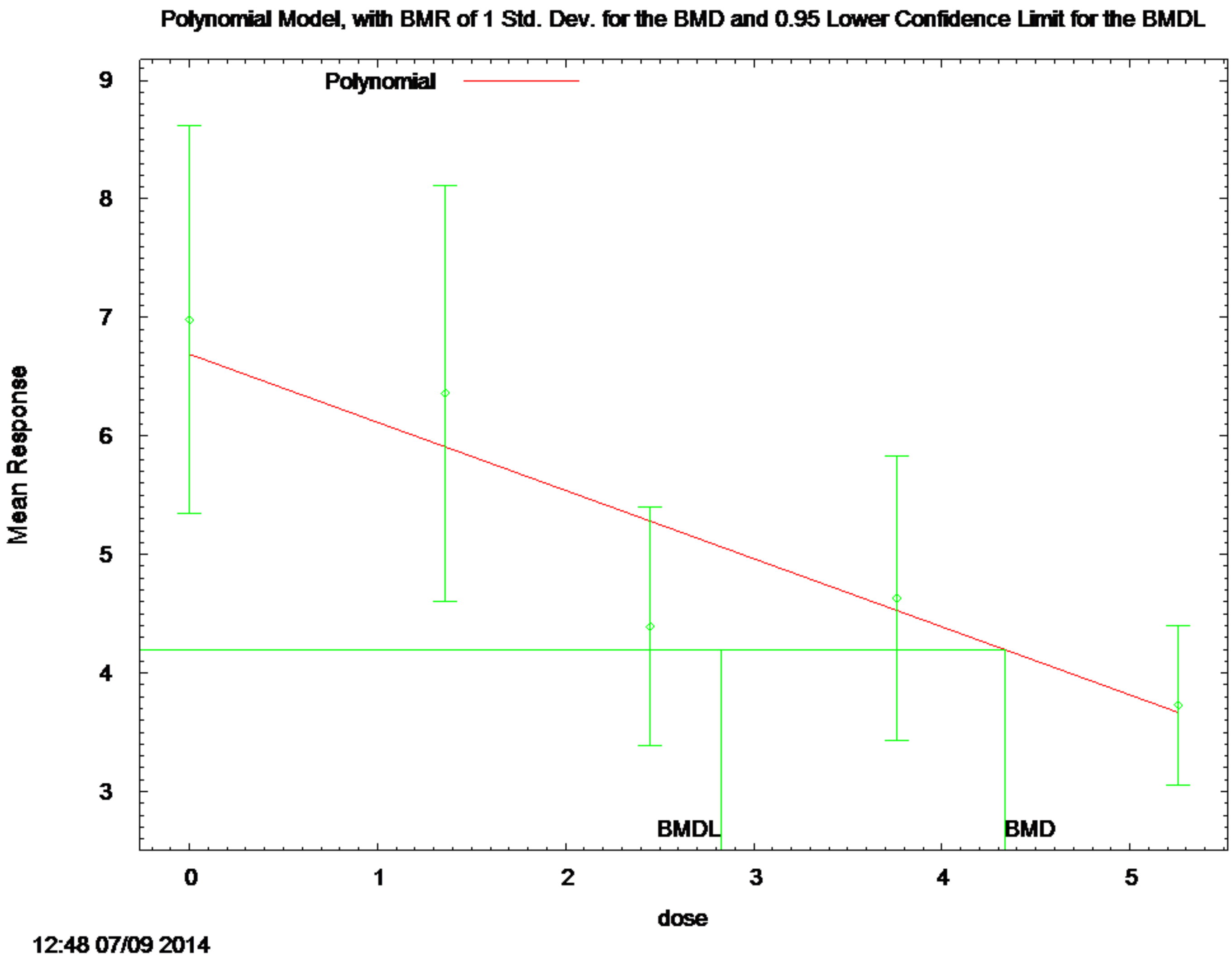
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.82536

BMDL = 2.0197


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly3NCV-1SD-5d.plt
                                        Wed Jul 09 12:48:08 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =      7.07831
                         beta_1 =    -0.897602
                         beta_2 =            0
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.16	-0.19
rho	-0.99	1	-0.16	0.19
beta_0	0.16	-0.16	1	-0.91
beta_1	-0.19	0.19	-0.91	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.22724	1.68476	-7.5293	-0.925179
rho	3.18577	1.02462	1.17755	5.19399
beta_0	6.68829	0.512021	5.68475	7.69183
beta_1	-0.574737	0.123483	-0.816759	-0.332715
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.69	2.29	2.49	0.37
1.361	10	6.36	5.91	2.45	2.04	0.702
2.451	9	4.39	5.28	1.31	1.71	-1.56

```
3.761     9       4.63          4.53          1.56          1.34
0.232
5.258    10       3.73          3.67         0.941         0.957
0.21
```

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-47.300760	4	102.601521
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157

Test 4	5.19625	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

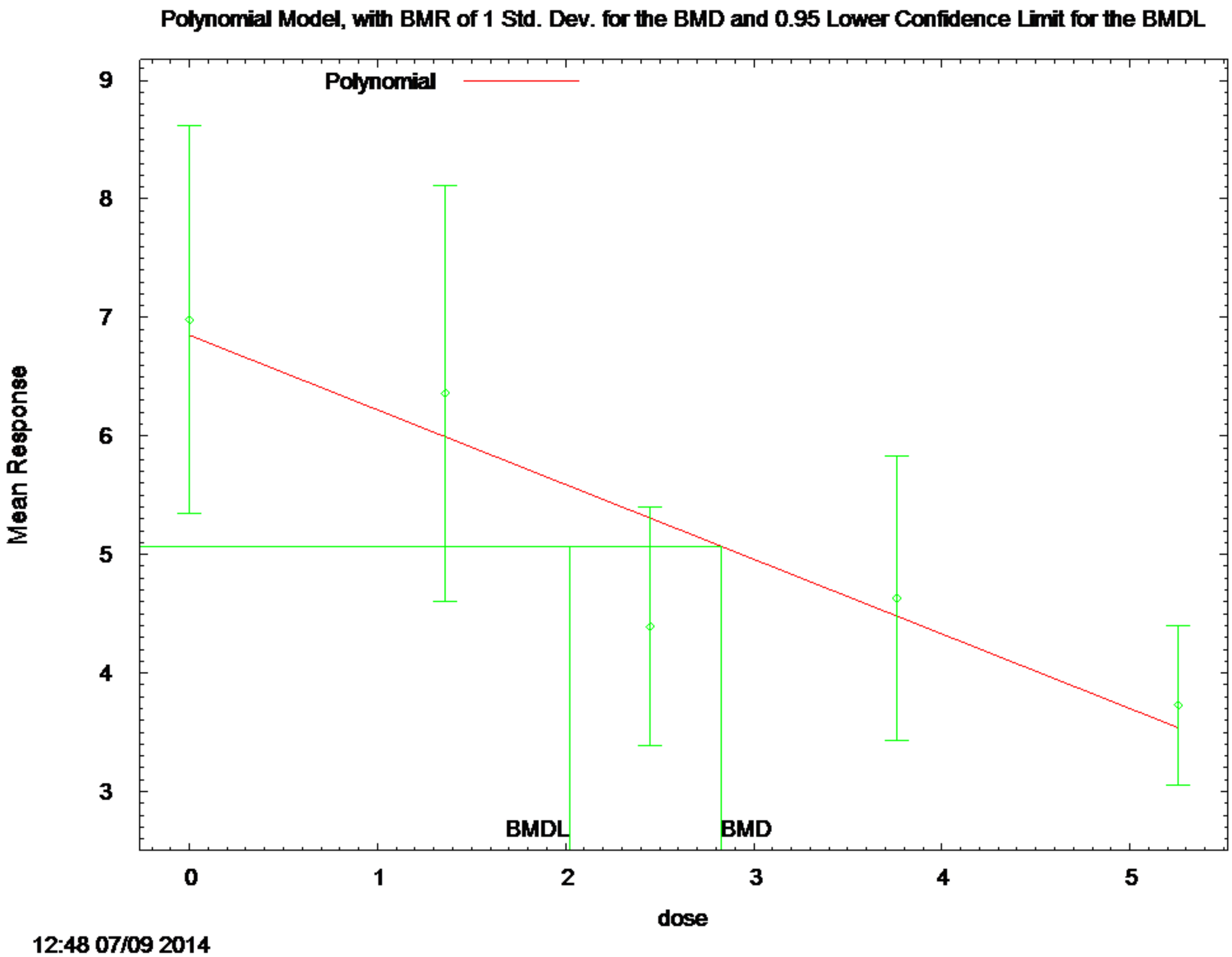
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.33739

BMDL = 2.82692



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
12:48 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:48:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                         beta_0 =         6.98
                         beta_1 =            0
                         beta_2 =     -4.14163
                         beta_3 =            0
                         beta_4 =    -0.123946


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.1e-006	8.5e-007
beta_0	-1.1e-006	1	-0.81
beta_1	8.5e-007	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	3.16984	0.64704	1.90166	4.43801
beta_0	6.85042	0.435612	5.99663	7.7042
beta_1	-0.630151	0.138278	-0.90117	-0.359131
beta_2	-8.26857e-102	NA		
beta_3	-1.22857e-104	NA		
beta_4	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.29	1.78	0.23
1.361	10	6.36	5.99	2.45	1.78	0.652
2.451	9	4.39	5.31	1.31	1.78	-1.54
3.761	9	4.63	4.48	1.56	1.78	

0.252
5.258   10   3.73   3.54   0.941   1.78
0.343

Model Descriptions for likelihoods calculated

```
Model A1:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:          Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-51.688316	3	109.376631
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	3.14181	3	0.3703

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

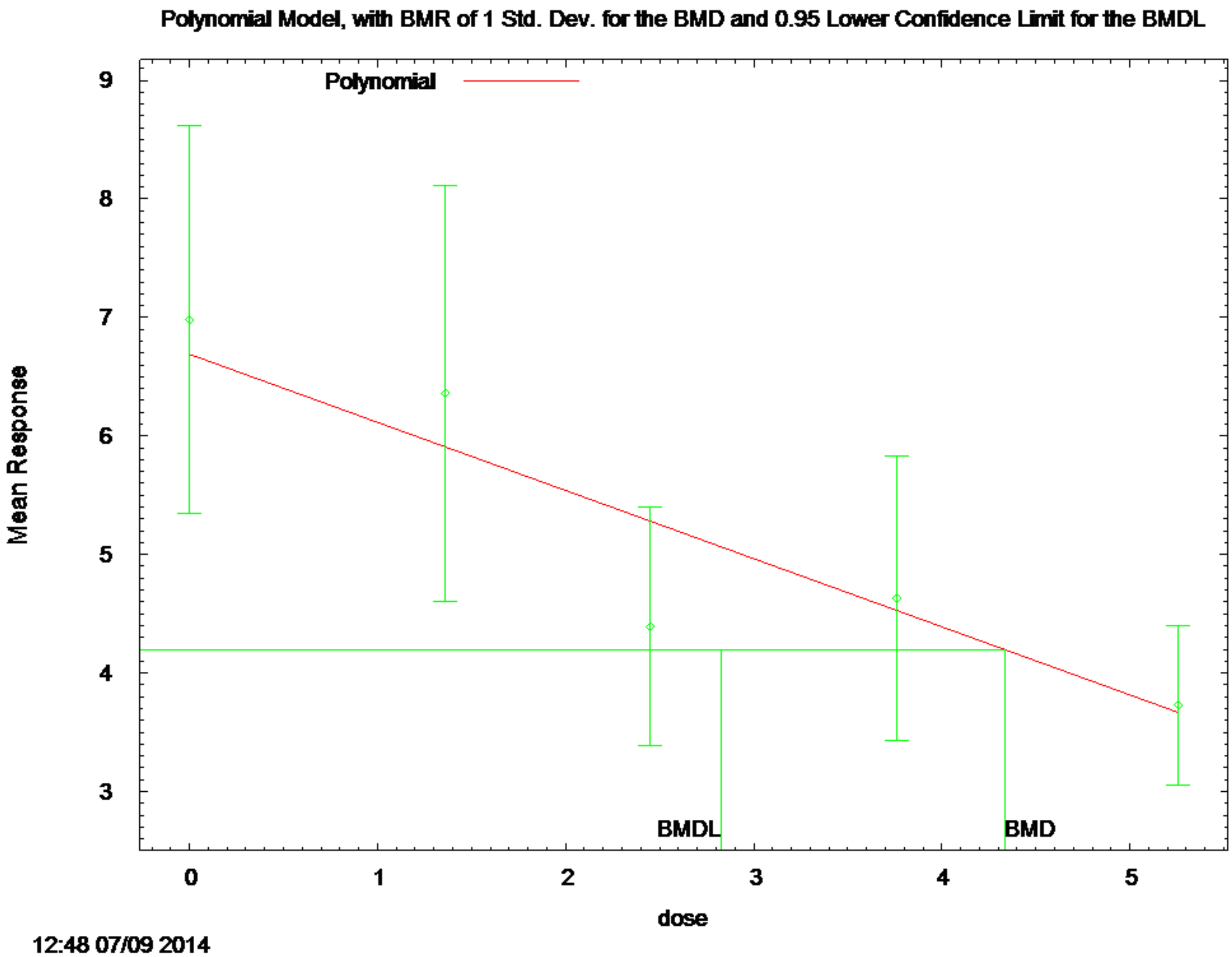
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.82536

BMDL = 2.0197


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
dose
BMDL
BMD
9
8
7
6
5
4
3
0
1
2
3
4
5
12:48 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Lymphocyte_Historical_Ln/Lymphocyt
e_Historical_LN-HLS 2001-Lymphocyte Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:48:08 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                         beta_0 =         6.98
                         beta_1 =            0
                         beta_2 =     -4.14163
                         beta_3 =            0
                         beta_4 =    -0.123946


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	-0.99	0.16	-0.19
rho	-0.99	1	-0.16	0.19
beta_0	0.16	-0.16	1	-0.91
beta_1	-0.19	0.19	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.22724	1.68476	-7.52931	-0.92518
rho	3.18577	1.02462	1.17755	5.19399
beta_0	6.68829	0.512022	5.68475	7.69183
beta_1	-0.574737	0.123483	-0.816759	-0.332715
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.69	2.29	2.49	0.37
1.361	10	6.36	5.91	2.45	2.04	

```
0.702
2.451     9       4.39          5.28          1.31          1.71
-1.56
3.761     9       4.63          4.53          1.56          1.34
0.231
5.258    10       3.73          3.67         0.941         0.957
0.21


 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          -50.117411            6     112.234822
             A2          -44.445511           10     108.891023
             A3          -44.702636            7     103.405272
          fitted         -47.300760            4     102.601521
              R          -60.317047            2     124.634093


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	5.19625	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

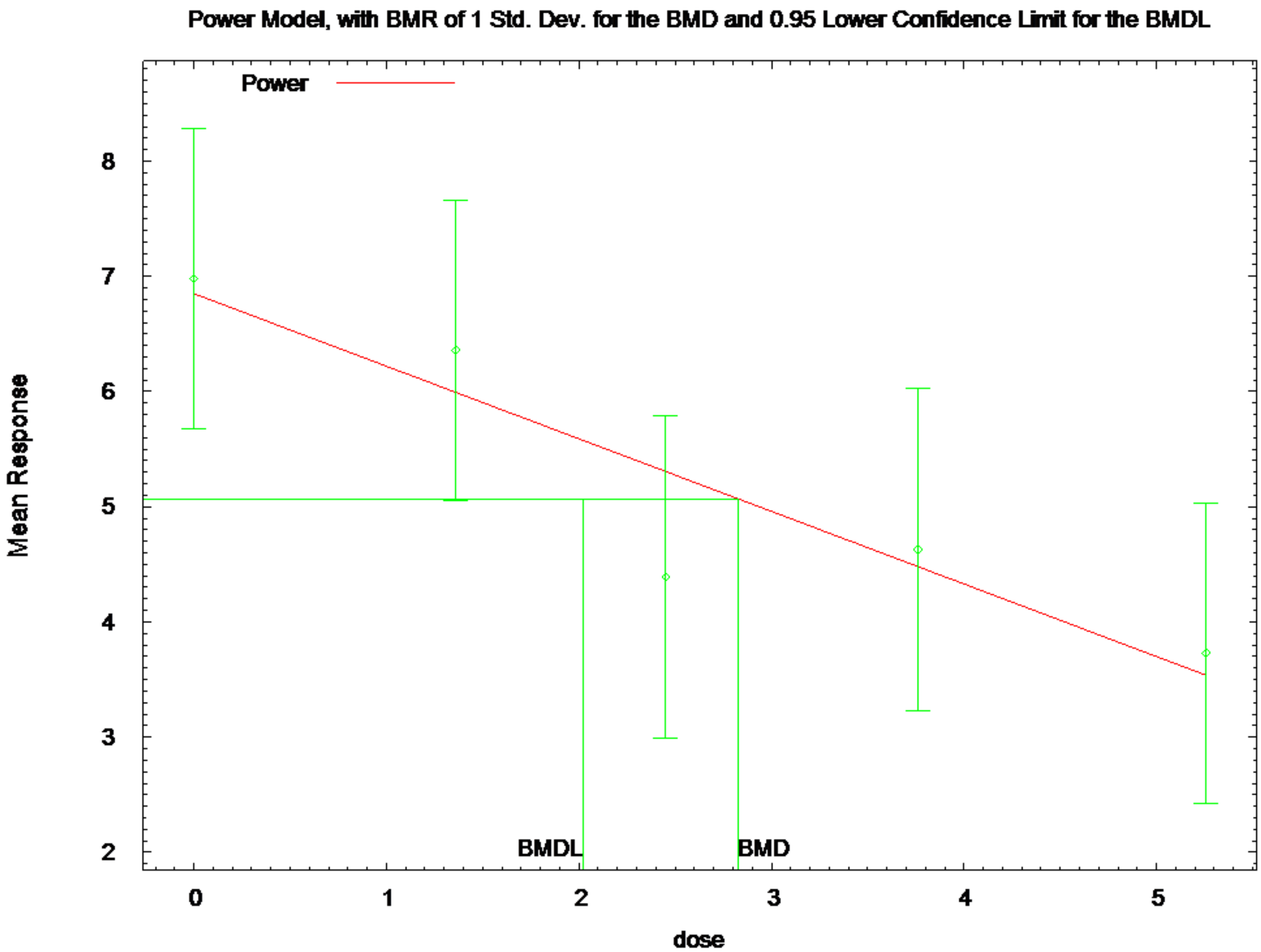
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.33739

BMDL = 2.82692



10:10 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-PowerCV-1SD-5d.plt
                                      Sun Jun 22 10:10:17 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =      3.31423
                            rho =            0   Specified
                        control =         3.73
                          slope =       3.0162
                          power =     -1.13303


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	-7.3e-008	9.3e-009
control	-7.3e-008	1	-0.81
slope	9.3e-009	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	3.16984	0.64704	1.90166	4.43801
control	6.85042	0.435612	5.99664	7.70421
slope	-0.630151	0.138278	-0.901171	-0.359132
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.85	2.29	1.78	0.23
1.361	10	6.36	5.99	2.45	1.78	0.652
2.451	9	4.39	5.31	1.31	1.78	-1.54
3.761	9	4.63	4.48	1.56	1.78	0.252
5.258	10	3.73	3.54	0.941	1.78	0.343

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-50.117411	6	112.234822
fitted	-51.688316	3	109.376631
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	11.3438	4	0.02296
Test 4	3.14181	3	0.3703

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

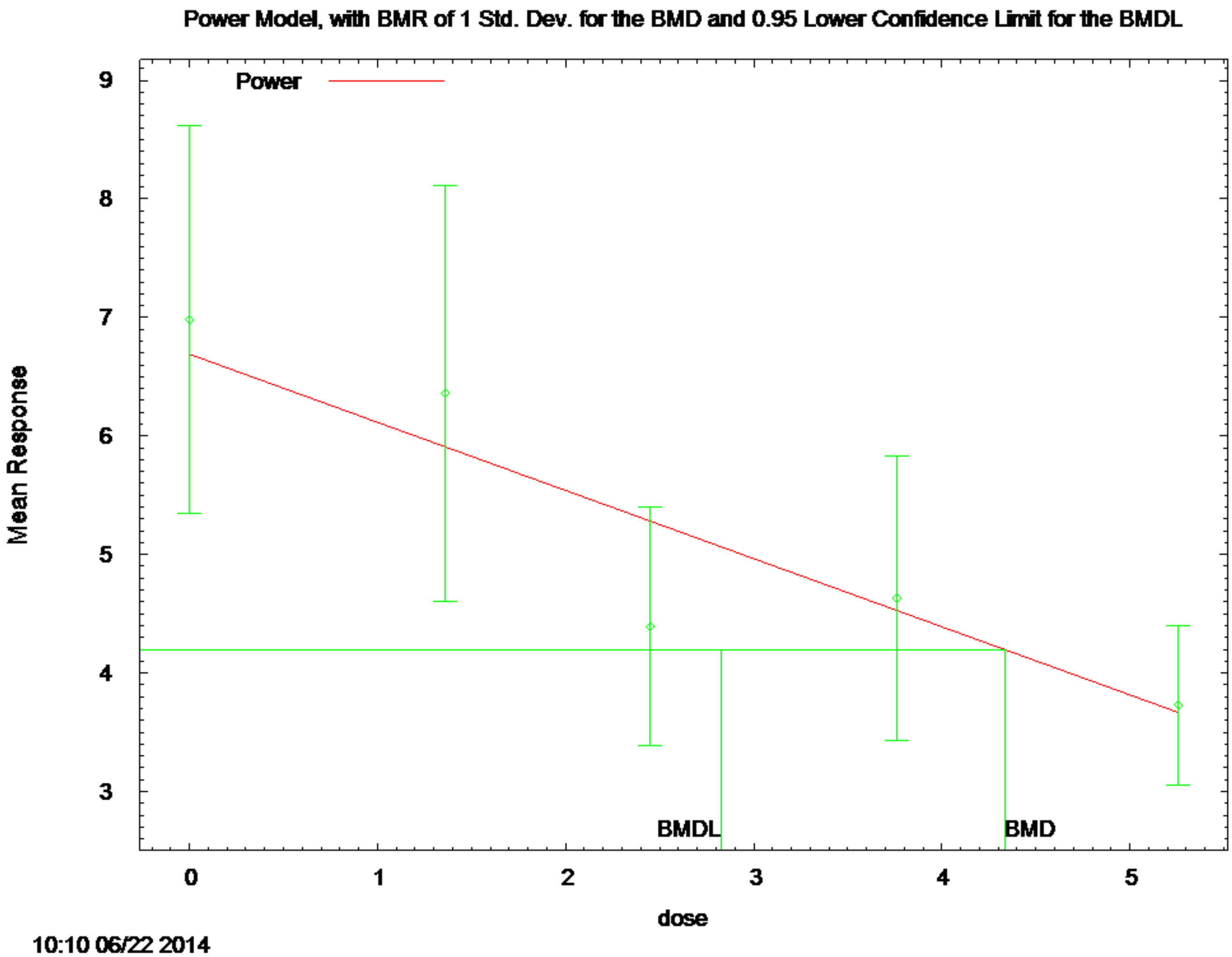
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.82536

BMDL = 2.0197



Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
9
8
7
6
5
4
3
BMDL
BMD
0
1
2
3
4
5
dose
10:10 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/Lymphocyte_Historical_LN-HLS 2001-
Lymphocyte Count-PowerNCV-1SD-5d.plt
                                      Sun Jun 22 10:10:19 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =      1.19823
                            rho =            0
                        control =         3.73
                          slope =       3.0162
                          power =     -1.13303


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	-0.99	0.45	-0.57
rho	-0.99	1	-0.5	0.6
control	0.45	-0.5	1	-0.91
slope	-0.57	0.6	-0.91	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-4.22725	2.06914	-8.28268	-0.17181
rho	3.18577	1.27347	0.689823	5.68172
control	6.68829	0.515026	5.67886	7.69772
slope	-0.574737	0.124269	-0.8183	-0.331174
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	6.98	6.69	2.29	2.49	0.37
1.361	10	6.36	5.91	2.45	2.04	0.702
2.451	9	4.39	5.28	1.31	1.71	-1.56
3.761	9	4.63	4.53	1.56	1.34	0.232

5.258	10	3.73	3.67	0.941	0.957	0.21

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	-50.117411	6	112.234822
A2	-44.445511	10	108.891023
A3	-44.702636	7	103.405272
fitted	-47.300760	4	102.601521
R	-60.317047	2	124.634093

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	31.7431	8	0.0001035
Test 2	11.3438	4	0.02296
Test 3	0.514249	3	0.9157
Test 4	5.19625	3	0.158

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

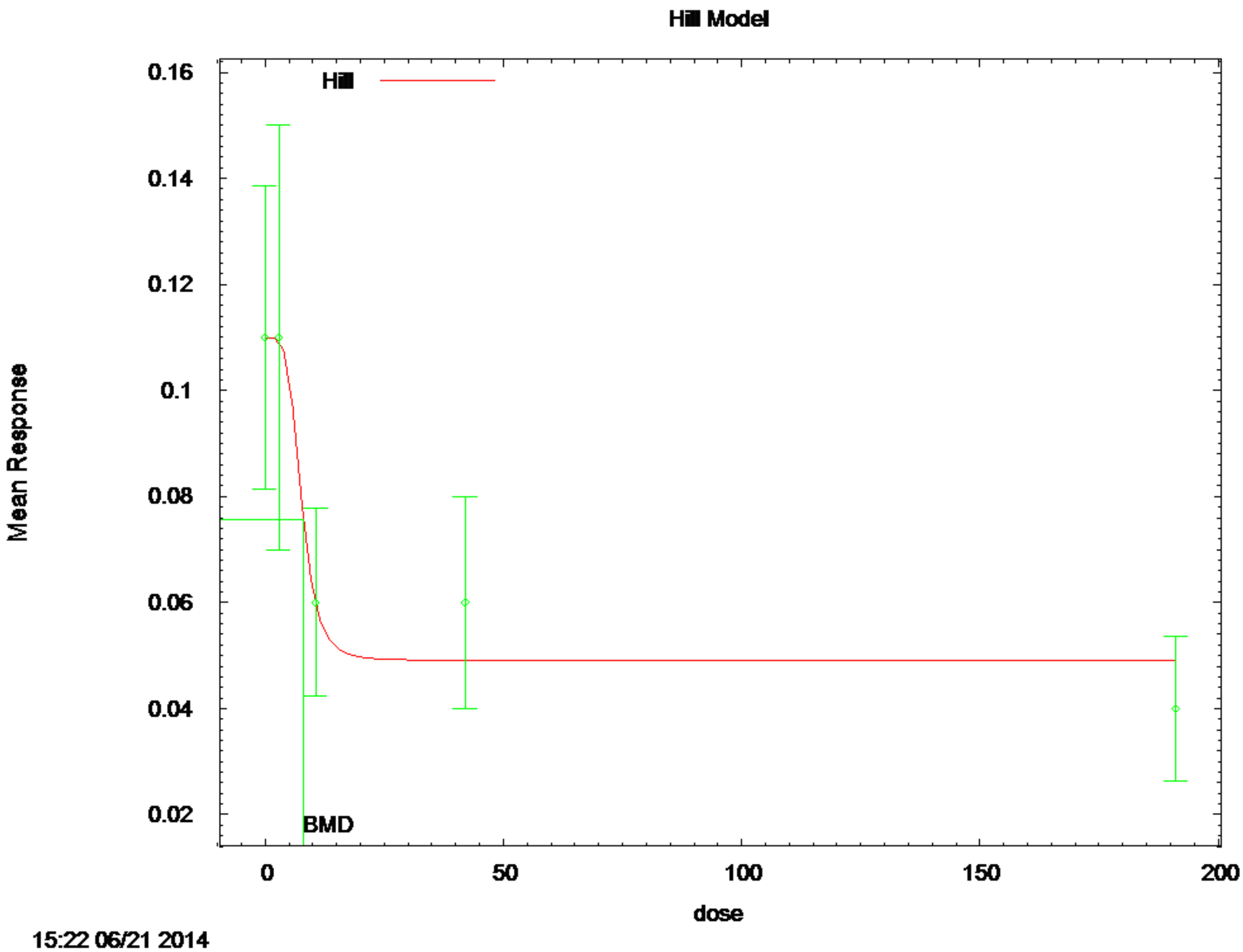
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.33739

BMDL = 2.82692

BMDS Model Results for Large Unstained Cells Count (Untransformed Doses, Concurrent Controls)



Hill Model
Hill
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
Mean Response
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-HillCV-1SD-5d.plt
                                       Sat Jun 21 15:22:11 2014
====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                      intercept =         0.11
                              v =        -0.07
                              n =      5.34555
                              k =         8.29


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-7.9e-007	5.9e-007	1.1e-006	1.1e-006
intercept	-7.9e-007	1	-0.82	-0.71	-0.71
v	5.9e-007	-0.82	1	0.62	0.56
n	1.1e-006	-0.71	0.62	1	0.97
k	1.1e-006	-0.71	0.56	0.97	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00119596	0.000244124	0.000717485	0.00167443
intercept	0.110304	0.0110773	0.0885926	0.132015
v	-0.0608572	0.0140877	-0.0884685	-0.0332458
n	4.73776	20.3397	-35.1273	44.6028
k	7.63214	10.8067	-13.5485	28.8128

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.11	0.04	0.0346	-0.0278

2.9	10	0.11	0.11	0.056	0.0346
0.0285					
10.6	9	0.06	0.06	0.023	0.0346
-0.00405					
42	9	0.06	0.0495	0.026	0.0346
0.914					
191.1	10	0.04	0.0494	0.019	0.0346
-0.864					

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	137.491343	5	-264.982687
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test   -2*log(Likelihood Ratio) Test df   p-value

Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	1.60959	1	0.2045

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

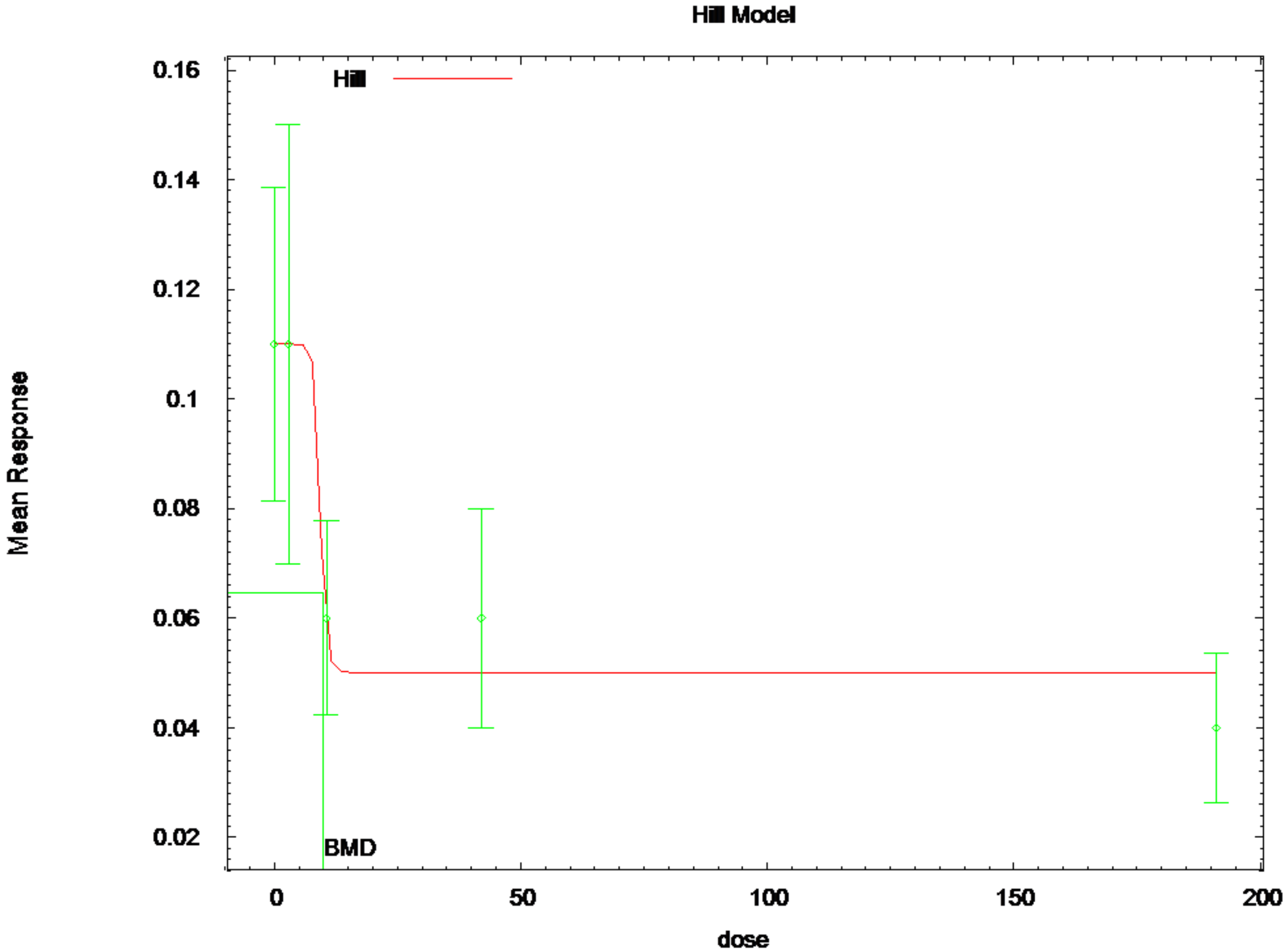
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 8.08783

BMDL computation failed.



15:22 06/21 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-HillNCV-1SD-5d.plt
                                       Sat Jun 21 15:22:13 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                      intercept =         0.11
                              v =        -0.07
                              n =      5.34555
                              k =         8.29


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	0.99	-0.38	0.47	2.7e-005	-0.00015
rho	0.99	1	-0.34	0.46	3.2e-005	-0.00015
intercept	-0.38	-0.34	1	-0.9	-0.00027	-0.00043
v	0.47	0.46	-0.9	1	0.00028	3.3e-005
n	2.7e-005	3.2e-005	-0.00027	0.00028	1	1
k	-0.00015	-0.00015	-0.00043	3.3e-005	1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-2.17483	1.65823	-5.4249	1.07524
rho	1.81244	0.62408	0.589269	3.03562
intercept	0.110329	0.0101805	0.0903753	0.130282
v	-0.0599397	0.01149	-0.0824597	-0.0374198
n	15.5198	5275.25	-10323.8	10354.8
k	9.30751	411.378	-796.979	815.594

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.11	0.04	0.0457	-0.0227

2.9	10	0.11	0.11	0.056	0.0457	-0.0227
10.6	9	0.06	0.0574	0.023	0.0253	0.306
42	9	0.06	0.0504	0.026	0.0225	1.28
191.1	10	0.04	0.0504	0.019	0.0225	-1.46

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	142.899629	6	-273.799258
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	5.18534	1	0.02278

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

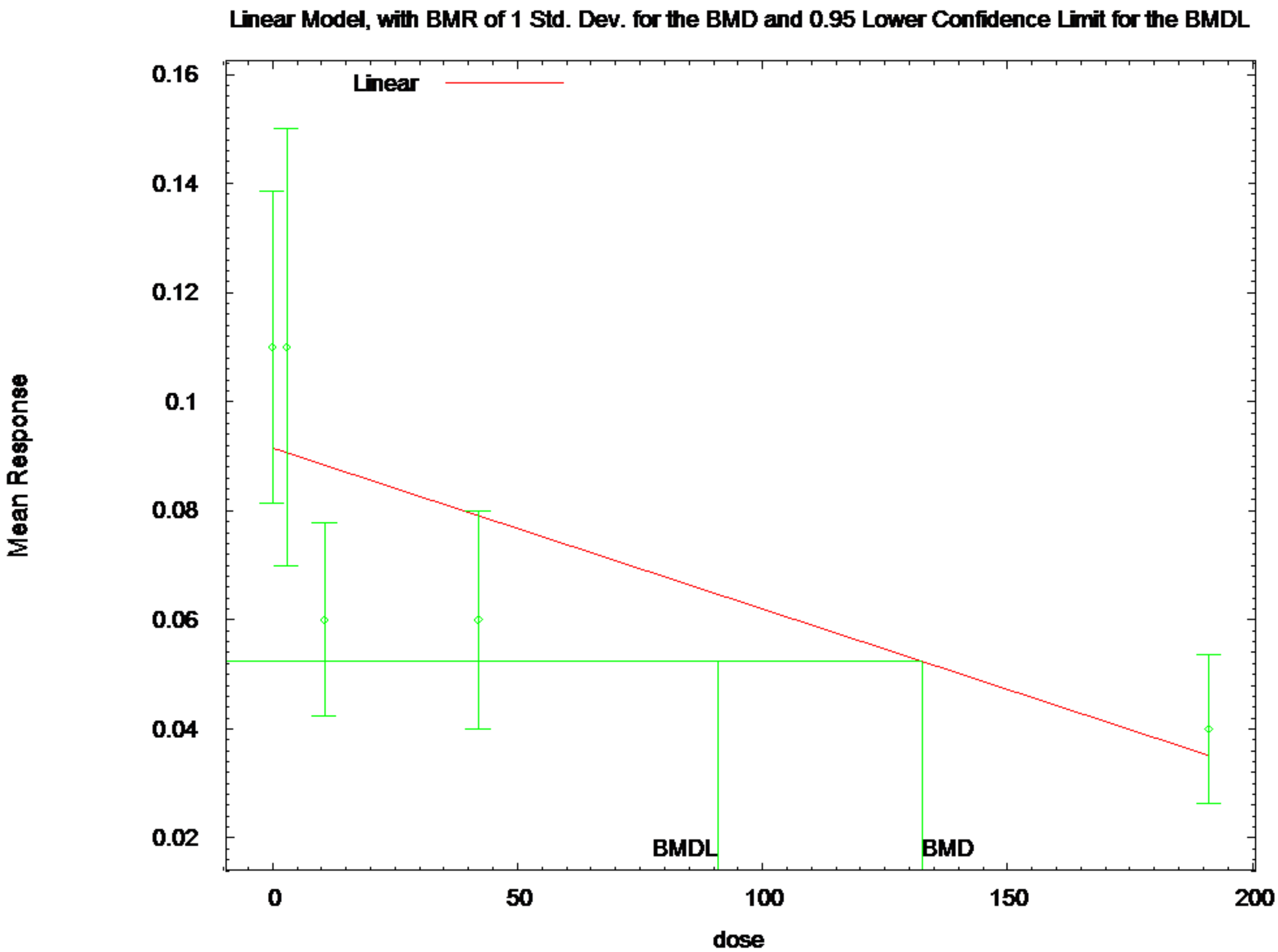
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 10.0356

BMDL computation failed.



12:40 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:40:22 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =    0.0903263
                         beta_1 = -0.000290477


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-4.4e-008	1.9e-007
beta_0	-4.4e-008	1	-0.56
beta_1	1.9e-007	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00153024	0.000312359	0.000918027	0.00214245
beta_0	0.091509	0.0068346	0.0781134	0.104905
beta_1	-0.000295197	7.65966e-005	-0.000445324	-0.000145071

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0915	0.04	0.0391	1.49
2.9	10	0.11	0.0907	0.056	0.0391	1.56
10.6	9	0.06	0.0884	0.023	0.0391	-2.18
42	9	0.06	0.0791	0.026	0.0391	-1.47
191.1	10	0.04	0.0351	0.019	0.0391	0.396

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	131.575968	3	-257.151936
R	125.105720	2	-246.211439

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	13.4403	3	0.003775

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

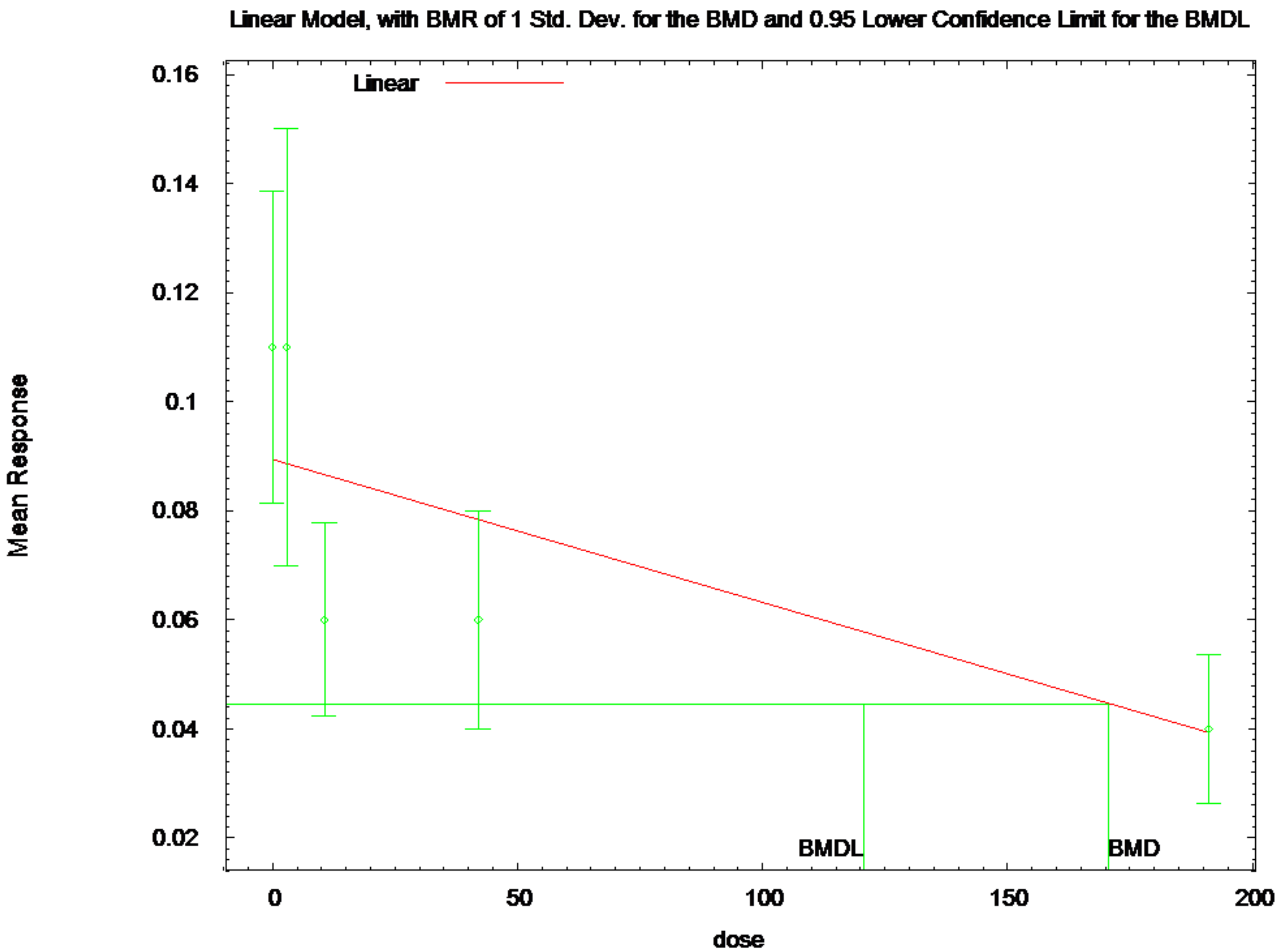
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 132.516

BMDL = 90.8103



12:40 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:40:25 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =    0.0903263
                         beta_1 = -0.000290477


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1         0.99       -0.052        0.061
```

rho	0.99	1	-0.052	0.06
beta_0	-0.052	-0.052	1	-0.82
beta_1	0.061	0.06	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.716057	1.62767	-3.90623	2.47412
rho	2.2765	0.616544	1.0681	3.48491
beta_0	0.08936	0.00749719	0.0746658	0.104054
beta_1	-0.00026225	5.03908e-005	-0.000361014	-0.000163486

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0894	0.04	0.0447	1.46
2.9	10	0.11	0.0886	0.056	0.0443	1.53
10.6	9	0.06	0.0866	0.023	0.0432	-1.85
42	9	0.06	0.0783	0.026	0.0385	-1.43
191.1	10	0.04	0.0392	0.019	0.0175	0.136

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          138.296137            6    -264.592275
             A2          146.083690           10    -272.167381
             A3          145.492300            7    -276.984600
         fitted          136.270966            4    -264.541933
              R          125.105720            2    -246.211439


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value

   Test 1              41.9559          8          <.0001
   Test 2              15.5751          4        0.003646
   Test 3              1.18278          3          0.7571
   Test 4              18.4427          3       0.0003564

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance
appears
```

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

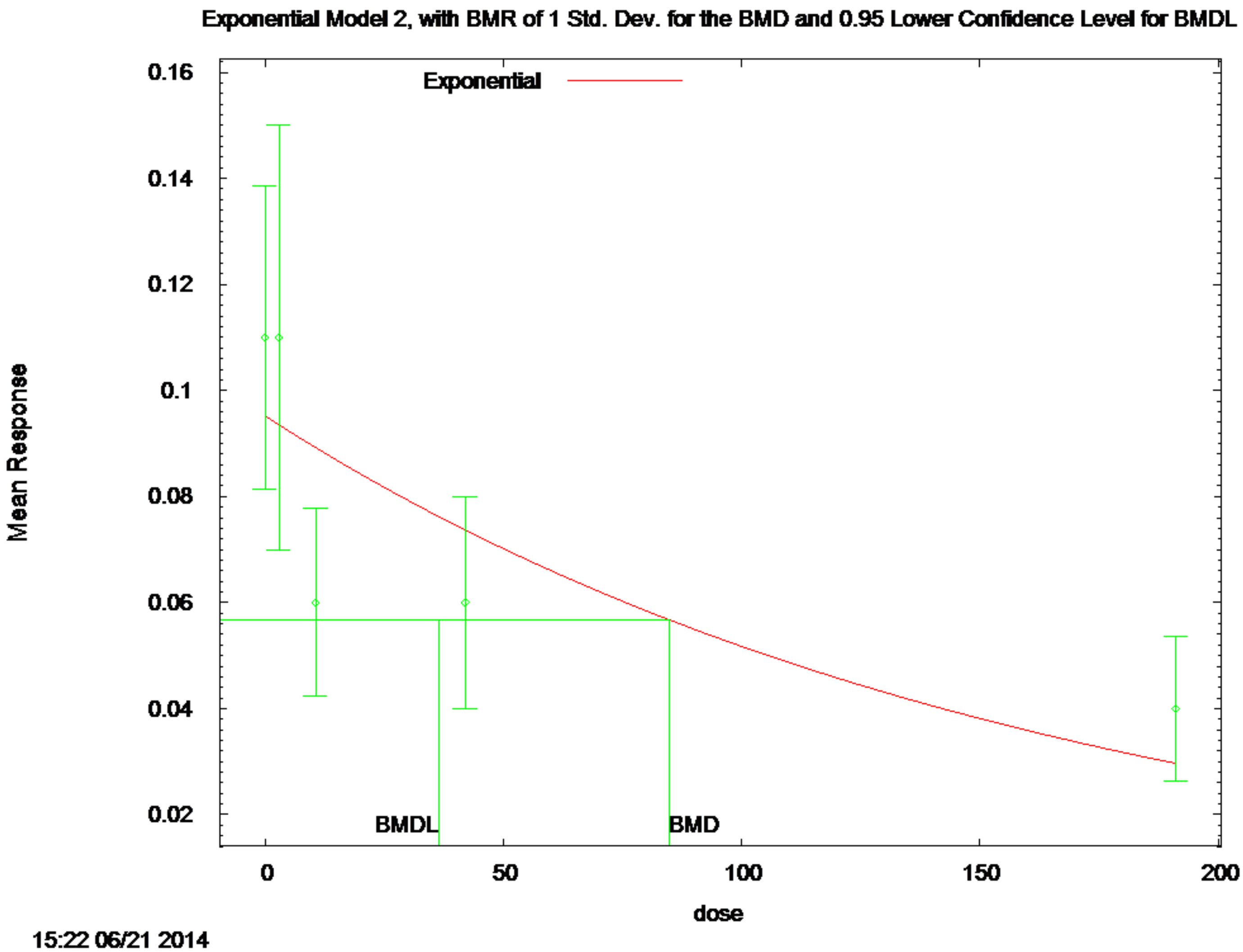
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 170.581

BMDL = 120.78


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sat Jun 21 15:22:11 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-6.76234
rho(S)	0
a	0.0567269
b	0.00445872
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	-6.51823
rho	0
a	0.0951988
b	0.00609925
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.0952	0.03842	1.218
2.9	0.09353	0.03842	1.356
10.6	0.08924	0.03842	-2.283
42	0.07368	0.03842	-1.069
191.1	0.02968	0.03842	0.8495

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
2	132.4375	3	-258.875

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	

< 0.0001
Test 2 15.58 4
0.003646
Test 3 15.58 4
0.003646
Test 4 11.72 3
0.008417

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

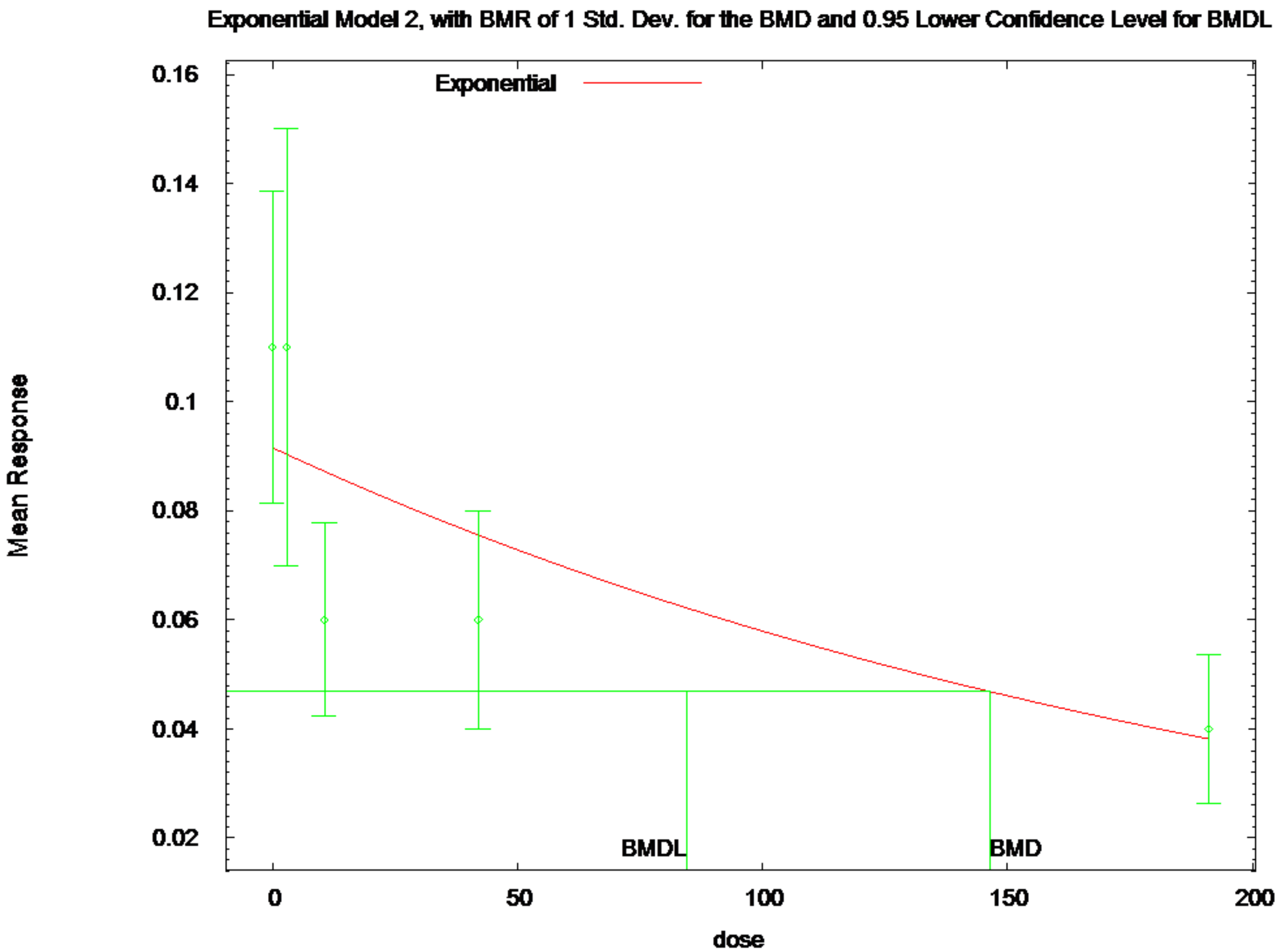
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 84.7394

BMDL = 36.554



15:22 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:22:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-1.95665
rho	1.89965
a	0.0567269
b	0.00445872
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-1.07085
rho	2.15178
a	0.0915571
b	0.00457633
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.09156	0.04471	1.305
2.9	0.09035	0.04407	1.41
10.6	0.08722	0.04243	-1.925
42	0.07555	0.03635	-1.283
191.1	0.03818	0.01745	0.3291

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
2	137.0503	4	-266.1006

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001
Test 2	15.58	4	

```
0.003646
     Test 3                              1.183           3
0.7571
     Test 4                              16.88           3
0.0007466
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

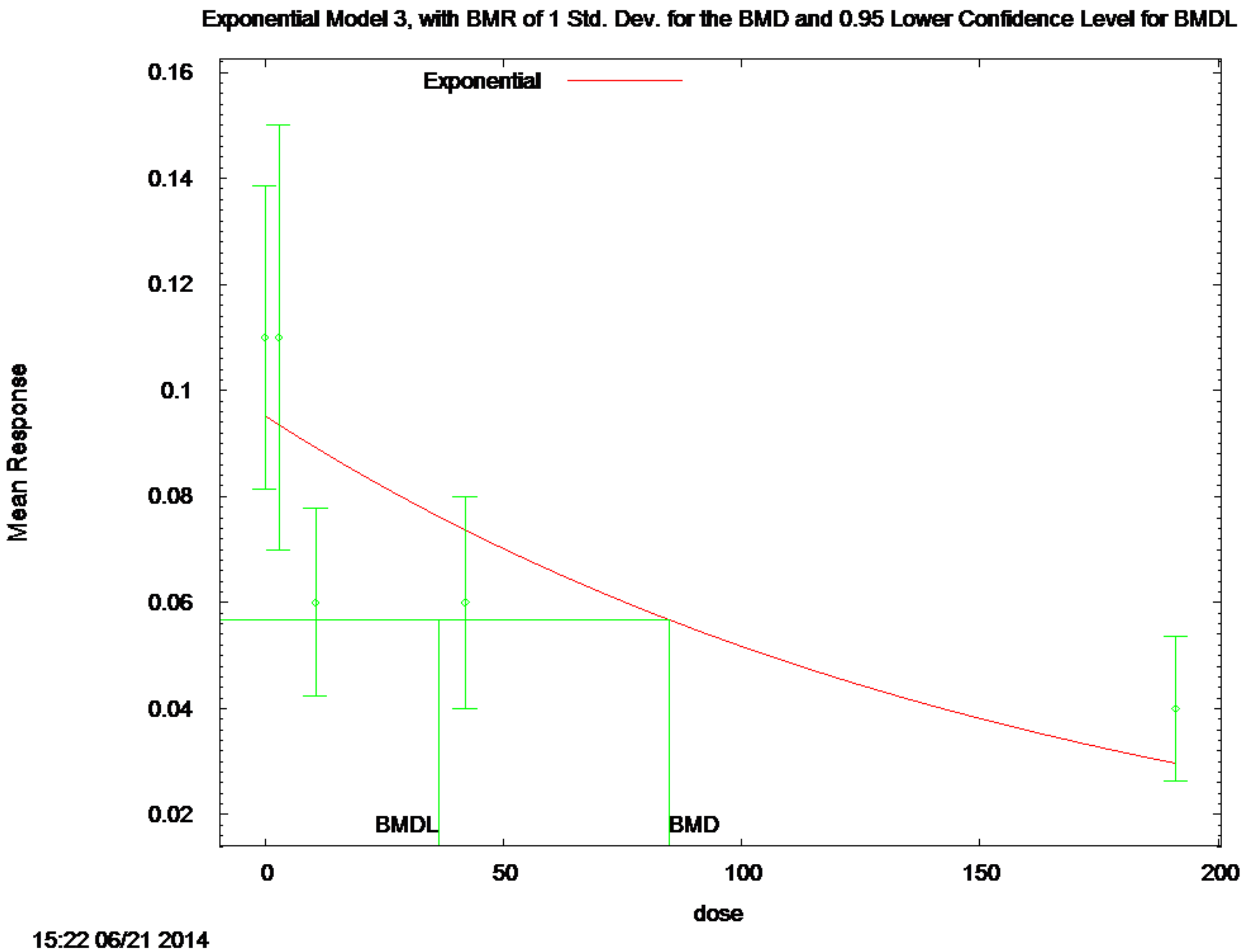
The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

```
     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from control

     Confidence Level = 0.950000

                  BMD =      146.401

                 BMDL =      84.5804
```



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:22:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-6.76234
rho(S)	0
a	0.0567269
b	0.00445872
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	-6.51823
rho	0
a	0.0951988
b	0.00609925
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.0952	0.03842	1.218
2.9	0.09353	0.03842	1.356
10.6	0.08924	0.03842	-2.283
42	0.07368	0.03842	-1.069
191.1	0.02968	0.03842	0.8495

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
3	132.4375	3	-258.875

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 5a	11.72	3	0.008417

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

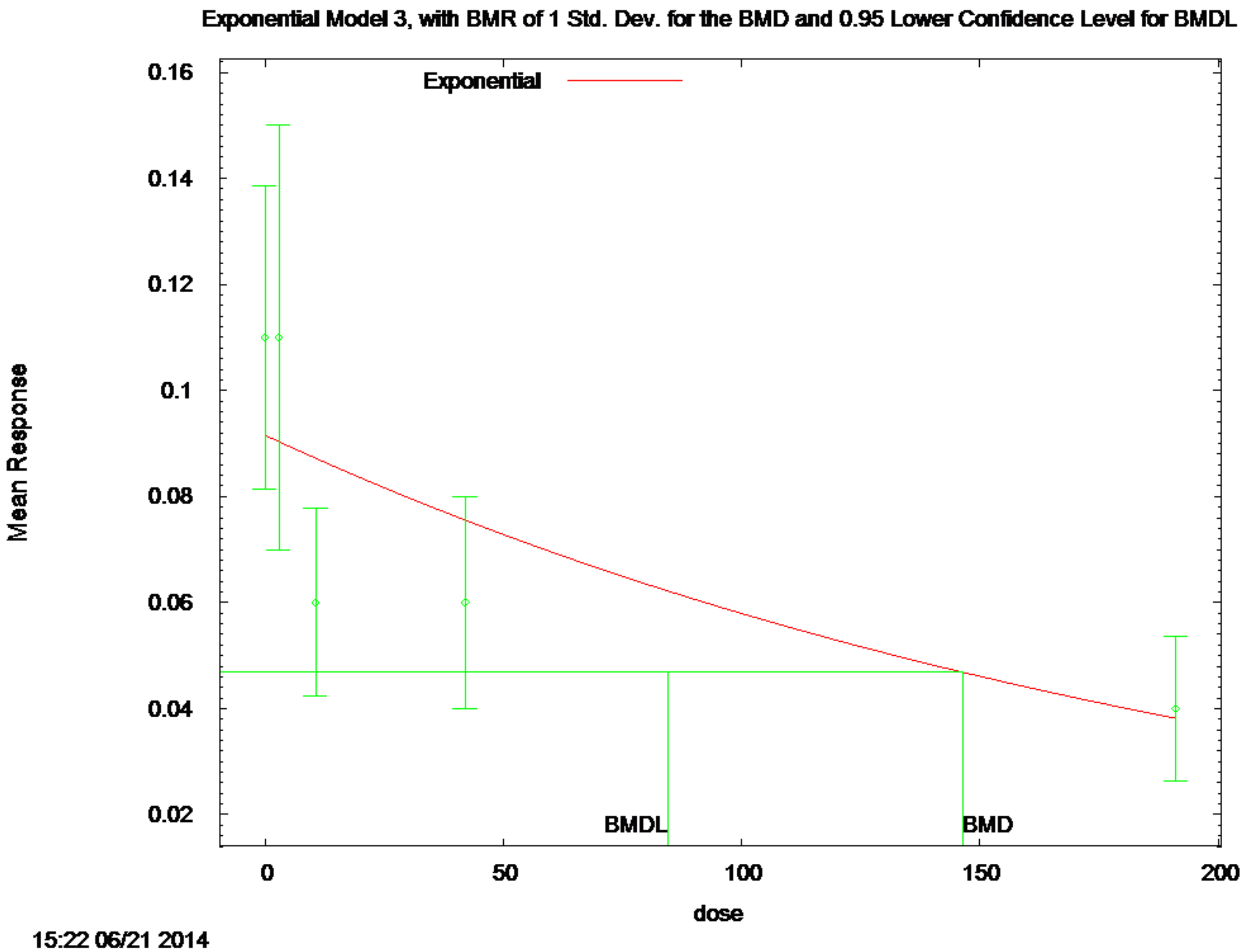
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 84.7394

BMDL = 36.554



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:22:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-1.95665
rho	1.89965
a	0.0567269
b	0.00445872
c	0
d	1

Parameter Estimates

Variable	Model 3
lnalpha	-1.07085
rho	2.15178
a	0.0915571
b	0.00457634
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.09156	0.04471	1.305
2.9	0.09035	0.04407	1.41
10.6	0.08722	0.04243	-1.925
42	0.07555	0.03635	-1.283
191.1	0.03818	0.01745	0.3291

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
3	137.0503	4	-266.1006

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 5a	16.88	3	0.0007466

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

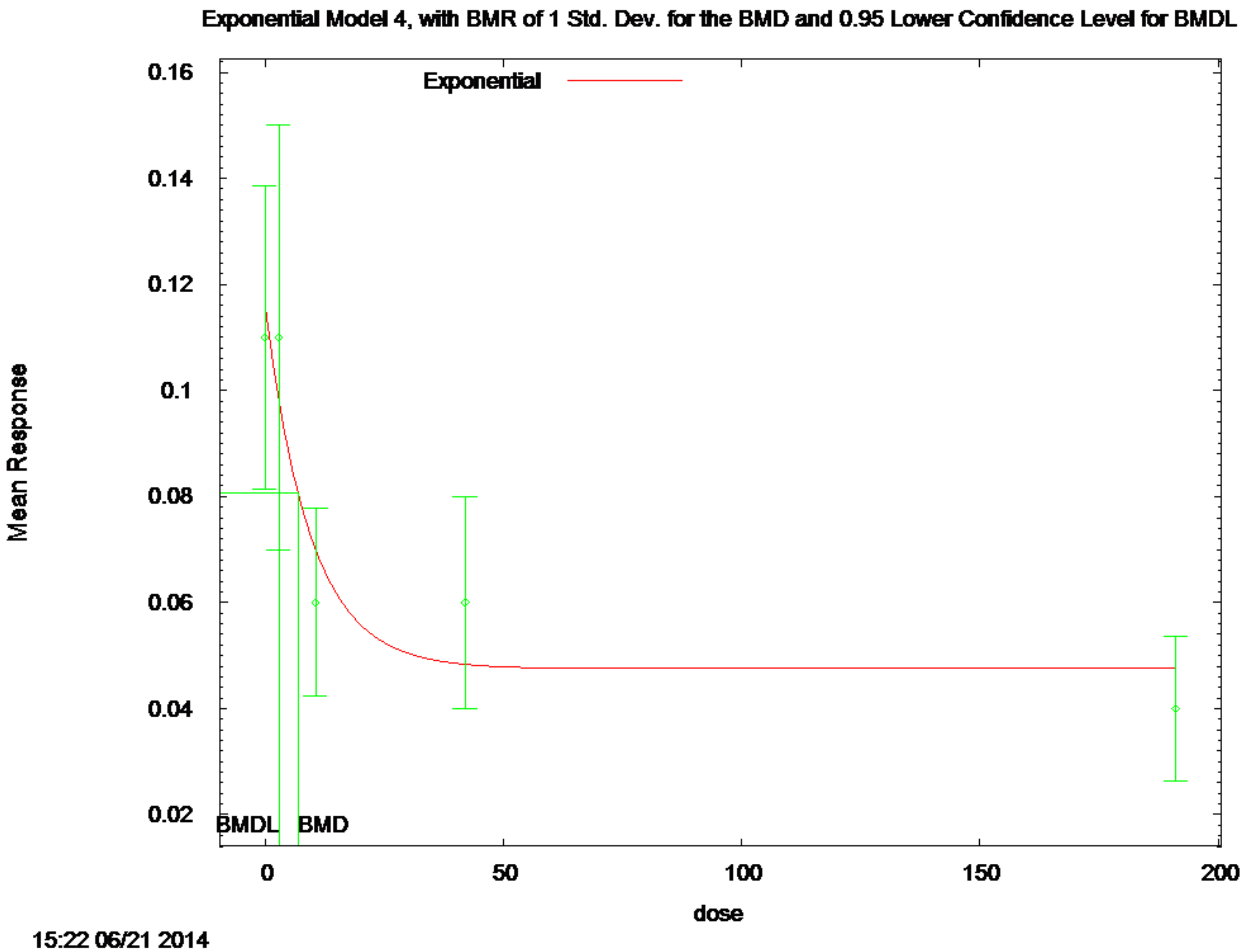
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 146.4

BMDL = 84.5804


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:22:11 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-6.76234
rho(S)	0
a	0.1155
b	0.0201693
c	0.329829
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	-6.68465
rho	0
a	0.116057
b	0.10556
c	0.409529
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1161	0.03535	-0.5418
2.9	0.09799	0.03535	1.075
10.6	0.06991	0.03535	-0.8411
42	0.04834	0.03535	0.9892
191.1	0.04753	0.03535	-0.6734

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
4	136.4317	4	-264.8634

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 6a	3.729	2	0.155

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

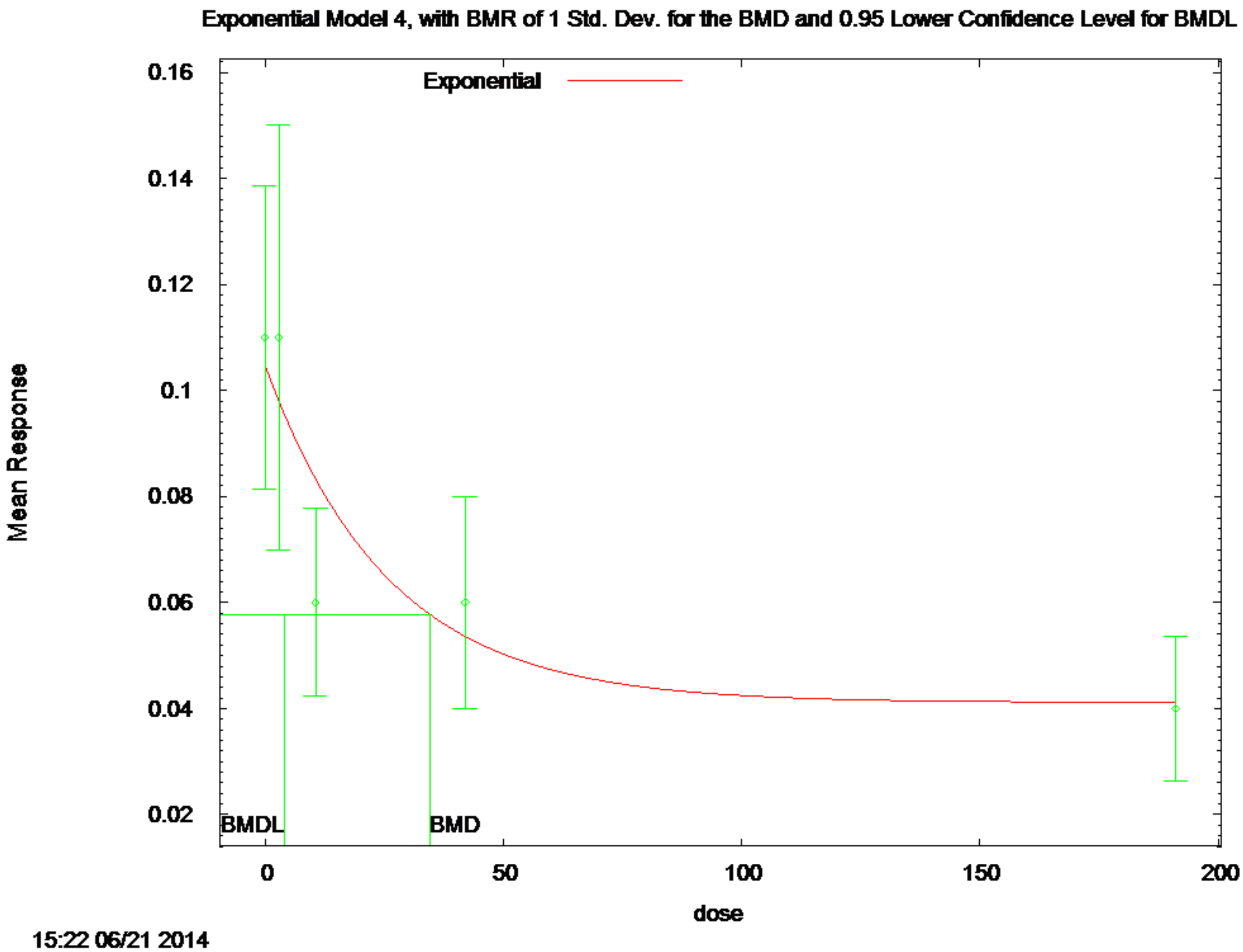
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 6.87276

BMDL = 2.97343


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:22:12 2014

================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-1.95665
rho	1.89965
a	0.1155
b	0.0201693
c	0.329829
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-1.60402
rho	1.99902
a	0.104728
b	0.0388147
c	0.392968
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1047	0.04701	0.3546
2.9	0.09796	0.04398	0.8658
10.6	0.08328	0.03739	-1.868
42	0.05361	0.02407	0.7966
191.1	0.04119	0.0185	-0.2039

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
4	140.8295	5	-271.659

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 6a	9.326	2	0.00944

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

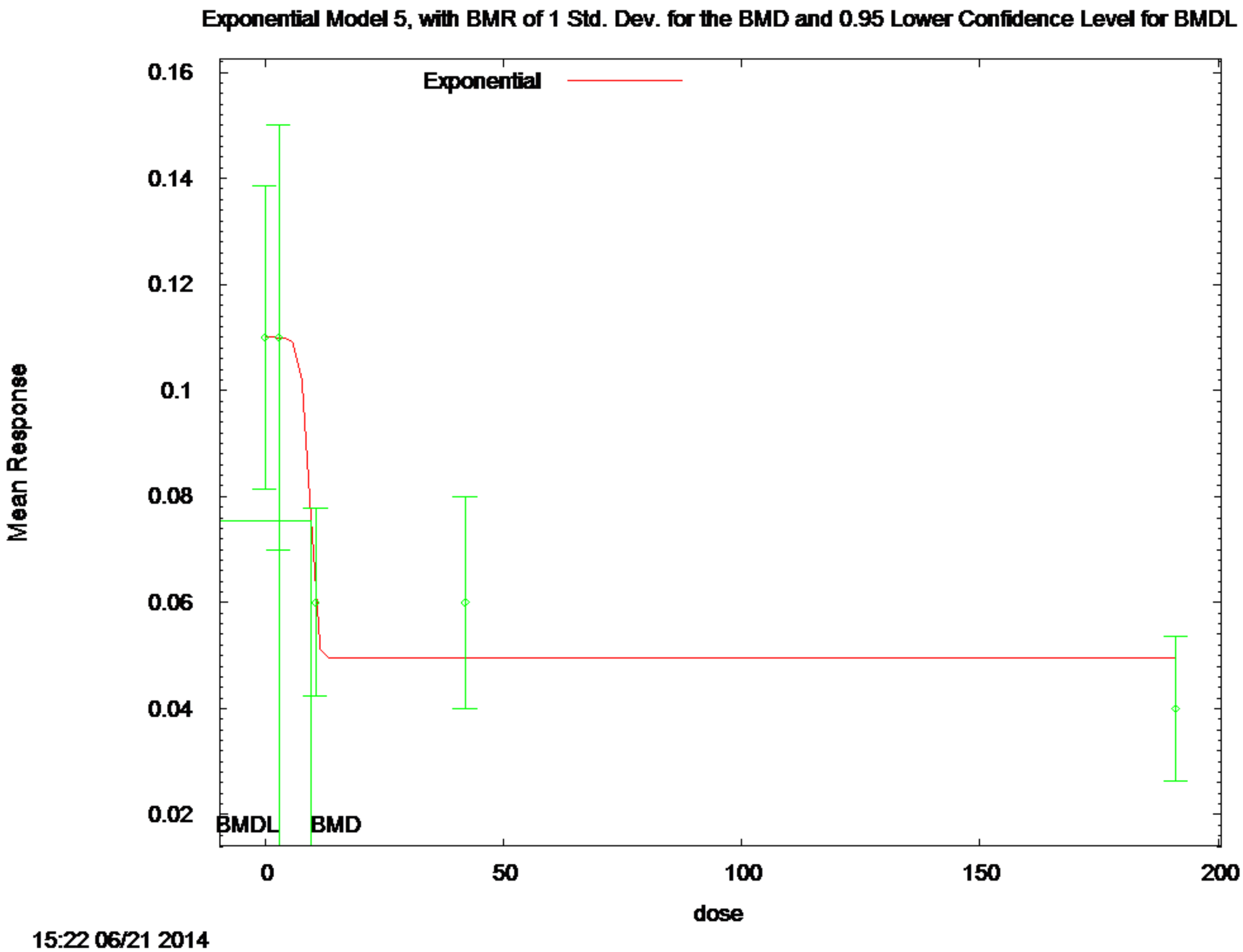
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 34.6593

BMDL = 3.93988



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:22:11 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-6.76234
rho(S)	0
a	0.1155
b	0.0201693
c	0.329829
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	-6.72878
rho	0
a	0.110002
b	0.101245
c	0.449753
d	7.91531

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.11	0.03458	-0.0001696
2.9	0.11	0.03458	0.0001695
10.6	0.06	0.03458	-3.376e-008
42	0.04947	0.03458	0.9131
191.1	0.04947	0.03458	-0.8663

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:        Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
5	137.4907	5	-264.9813

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 7a	1.611	1	0.2044

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

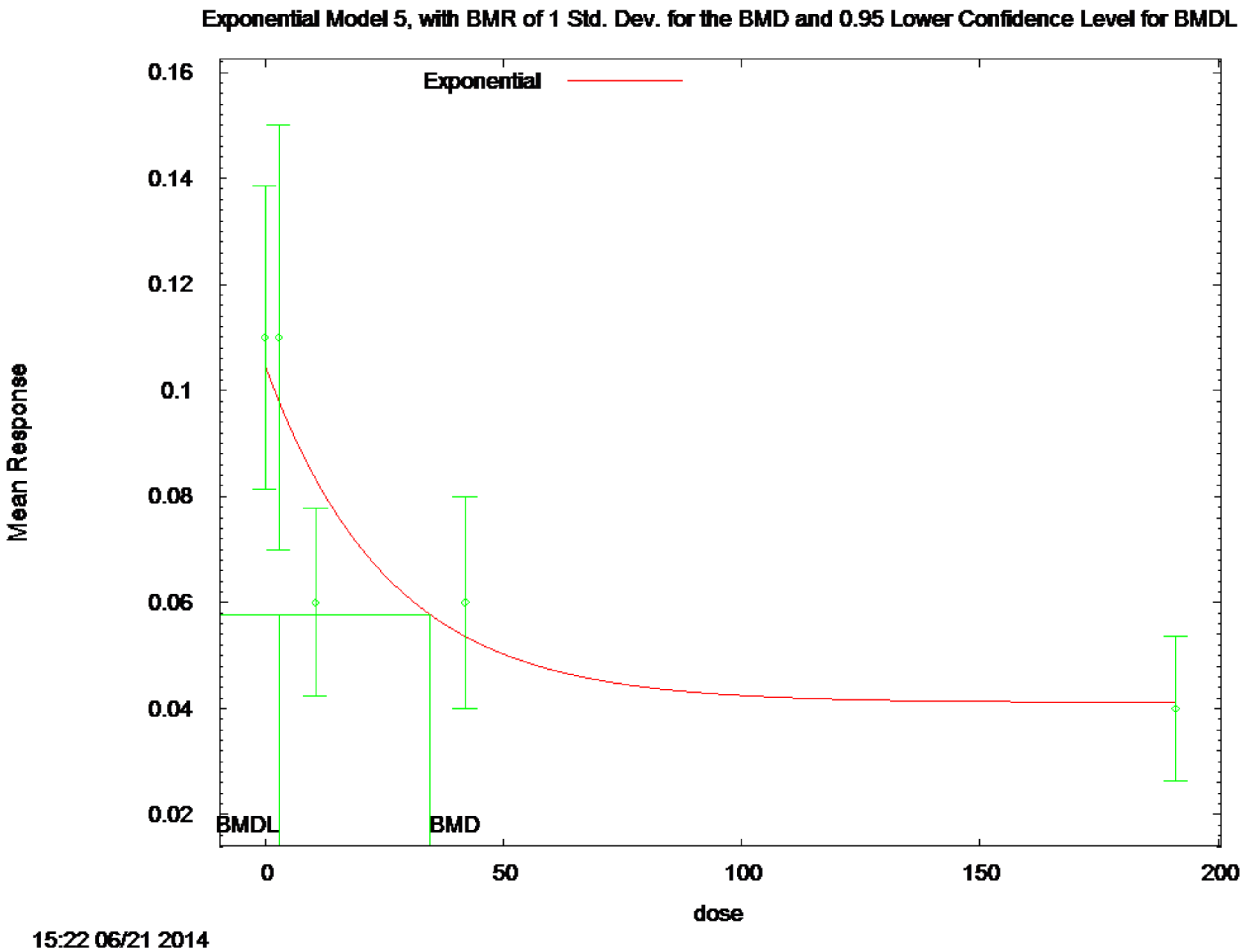
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 9.67214

BMDL = 2.99175


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:22:12 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-1.95665
rho	1.89965
a	0.1155
b	0.0201693
c	0.329829
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-1.60402
rho	1.99902
a	0.104728
b	0.0388146
c	0.392968
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
2.9	10	0.11	0.056
10.6	9	0.06	0.023
42	9	0.06	0.026
191.1	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1047	0.04701	0.3546
2.9	0.09796	0.04398	0.8658
10.6	0.08328	0.03739	-1.868
42	0.05361	0.02407	0.7966
191.1	0.04119	0.0185	-0.2039

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
5	140.8295	5	-271.659

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 7a	9.326	2	0.00944

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

Specified Effect = 1.000000

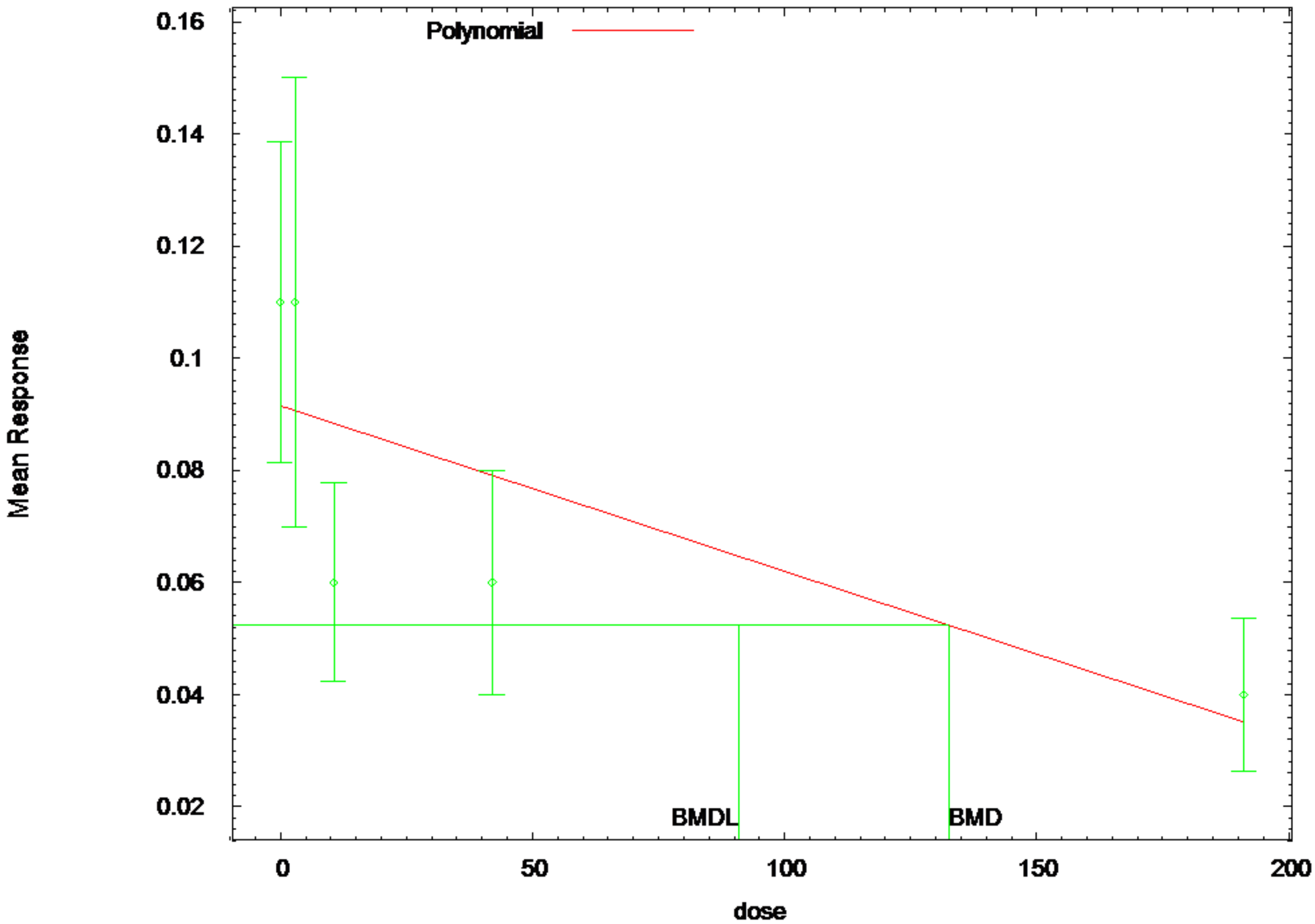
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 34.6593

BMDL = 2.96623

Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:40 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly2CV-1SD-5d.plt
                                       Wed Jul 09 12:40:22 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =     0.101799
                         beta_1 =  -0.00140875
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-2.9e-010	-2e-011
beta_0	-2.9e-010	1	-0.56
beta_1	-2e-011	-0.56	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00153024	0.000312359	0.000918027	0.00214245
beta_0	0.091509	0.0068346	0.0781134	0.104905
beta_1	-0.000295198	7.65966e-005	-0.000445324	-0.000145071
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0915	0.04	0.0391	1.49
2.9	10	0.11	0.0907	0.056	0.0391	1.56
10.6	9	0.06	0.0884	0.023	0.0391	-2.18
42	9	0.06	0.0791	0.026	0.0391	-1.47
191.1	10	0.04	0.0351	0.019	0.0391	0.396

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	131.575968	3	-257.151936
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	13.4403	3	0.003775

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

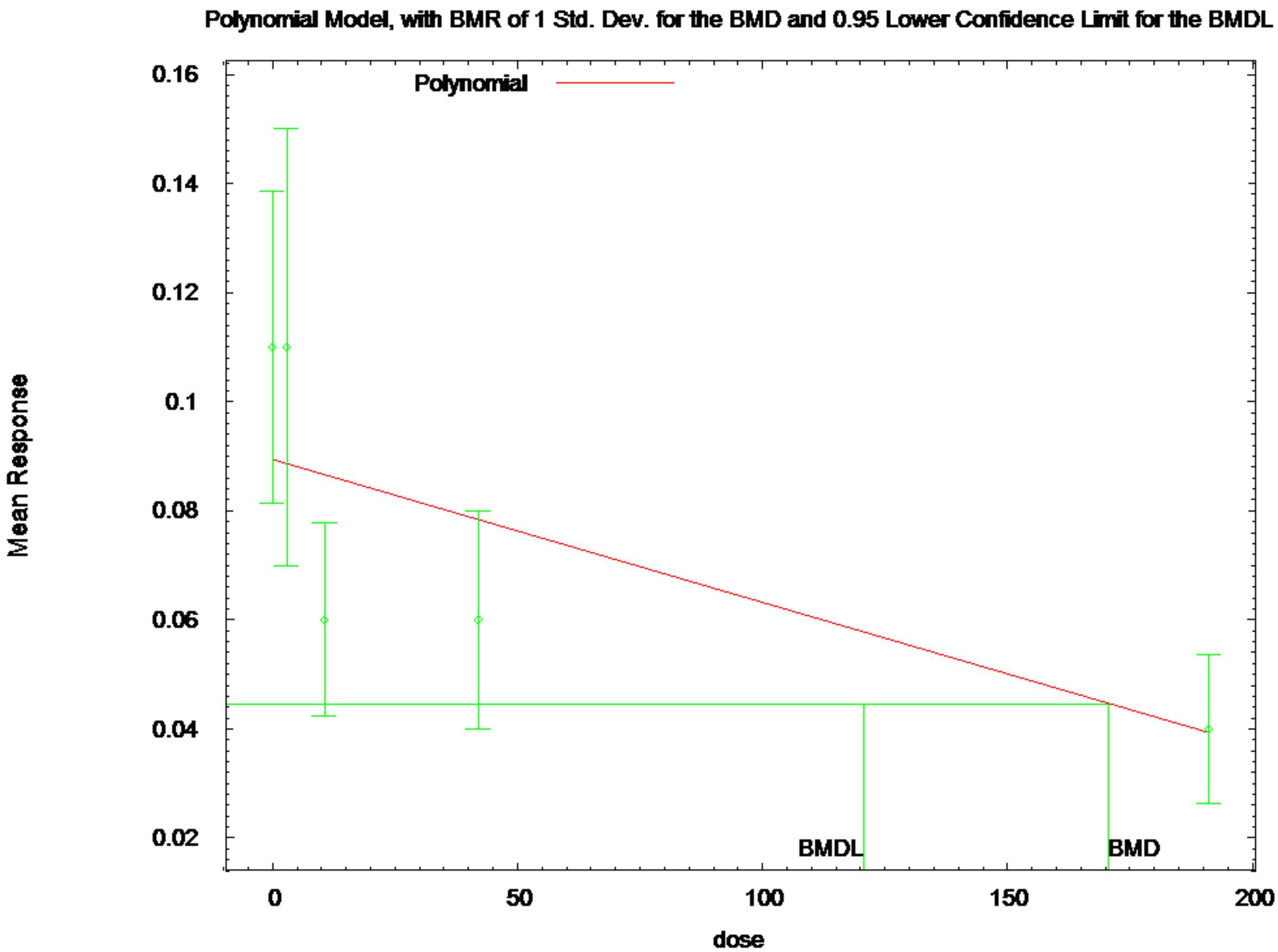
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 132.516

BMDL = 90.8103



12:40 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly2NCV-1SD-5d.plt
                                       Wed Jul 09 12:40:25 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =     0.101799
                         beta_1 =  -0.00140875
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.052	0.061
rho	0.99	1	-0.052	0.06
beta_0	-0.052	-0.052	1	-0.82
beta_1	0.061	0.06	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.716054	1.62767	-3.90623	2.47412
rho	2.2765	0.616544	1.0681	3.48491
beta_0	0.08936	0.00749719	0.0746658	0.104054
beta_1	-0.00026225	5.03908e-005	-0.000361014	-0.000163486
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0894	0.04	0.0447	1.46
2.9	10	0.11	0.0886	0.056	0.0443	1.53
10.6	9	0.06	0.0866	0.023	0.0432	-1.85
42	9	0.06	0.0783	0.026	0.0385	-1.43

191.1   10   0.04   0.0392   0.019   0.0175
0.136

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	136.270966	4	-264.541933
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	18.4427	3	0.0003564

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

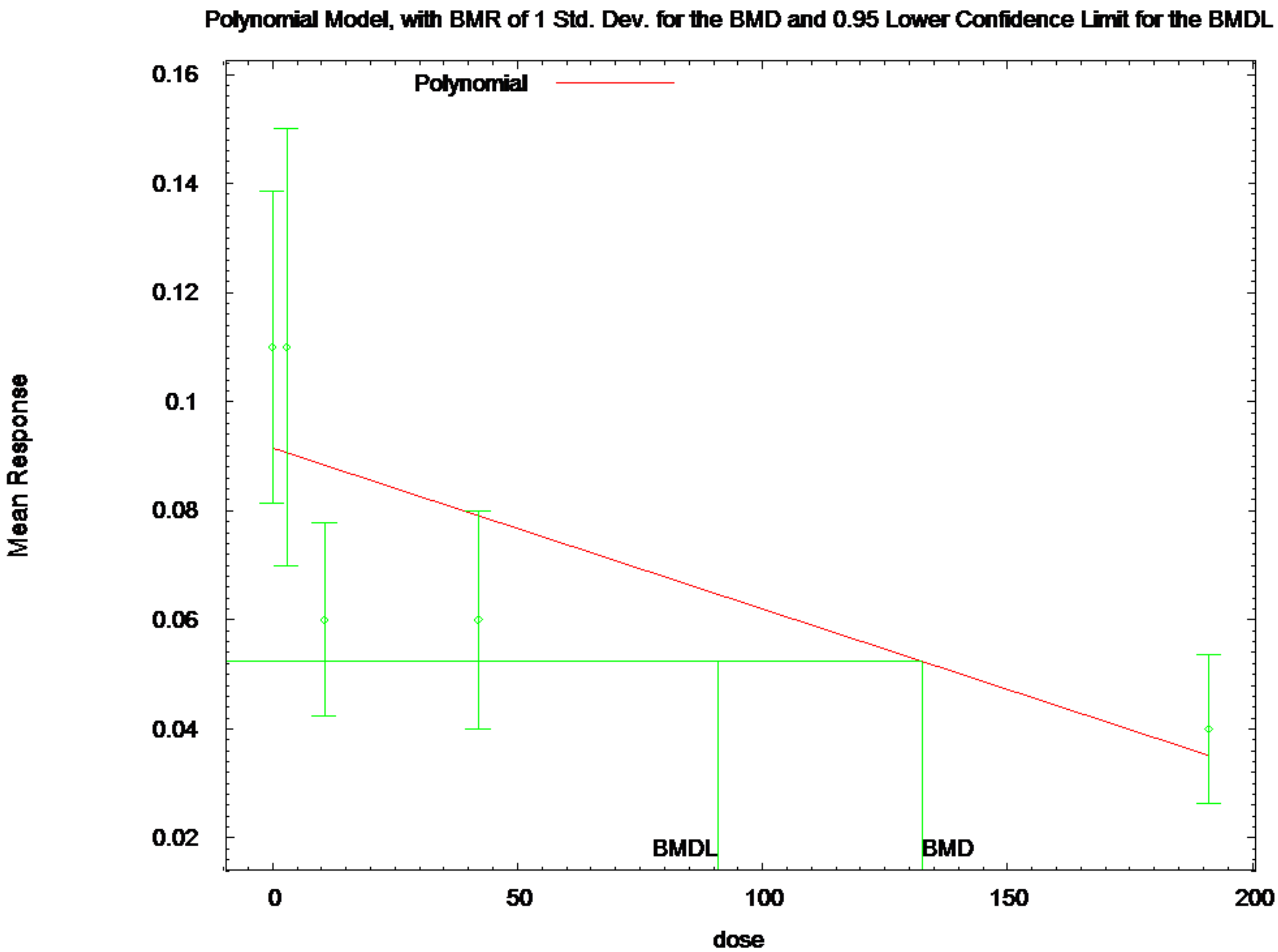
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 170.581

BMDL = 120.78



12:40 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:40:22 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =     0.117085
                         beta_1 =  -0.00653781
                         beta_2 =            0
                         beta_3 = -6.10808e-007


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-3.8e-011	-4.3e-011
beta_0	-3.8e-011	1	-0.56
beta_1	-4.3e-011	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00153024	0.000312359	0.000918027	0.00214245
beta_0	0.091509	0.0068346	0.0781134	0.104905
beta_1	-0.000295198	7.65966e-005	-0.000445324	-0.000145071
beta_2	-0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0915	0.04	0.0391	1.49
2.9	10	0.11	0.0907	0.056	0.0391	1.56
10.6	9	0.06	0.0884	0.023	0.0391	-2.18
42	9	0.06	0.0791	0.026	0.0391	-1.47
191.1	10	0.04	0.0351	0.019	0.0391	

0.396

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	131.575968	3	-257.151936
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	13.4403	3	0.003775

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

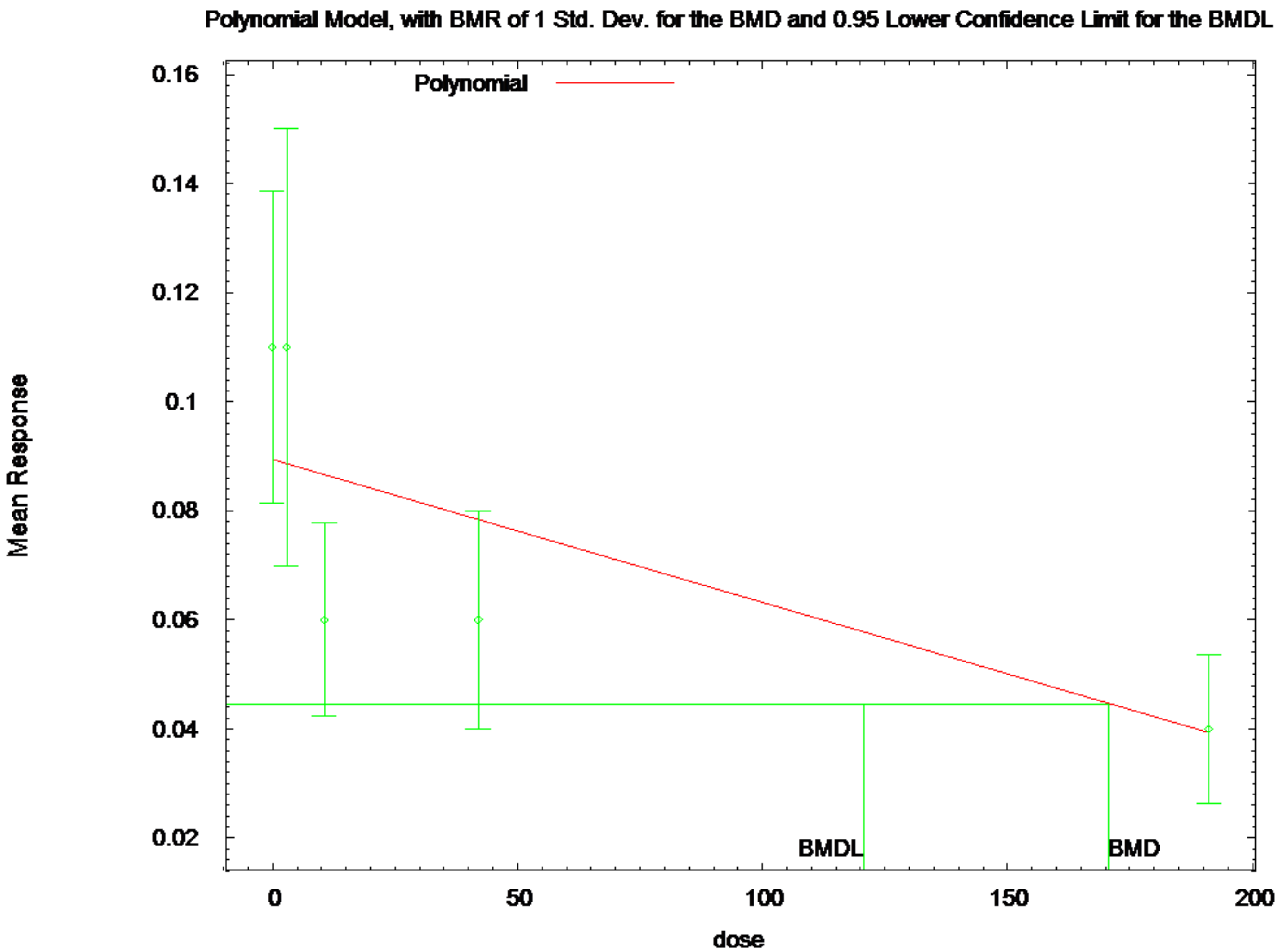
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 132.516

BMDL = 90.8103



12:40 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:40:25 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =     0.117085
                         beta_1 =  -0.00653781
                         beta_2 =            0
                         beta_3 = -6.10808e-007


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.052	0.061
rho	0.99	1	-0.052	0.06
beta_0	-0.052	-0.052	1	-0.82
beta_1	0.061	0.06	-0.82	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.716063	1.62767	-3.90624	2.47411
rho	2.2765	0.616544	1.0681	3.4849
beta_0	0.08936	0.00749719	0.0746658	0.104054
beta_1	-0.00026225	5.03908e-005	-0.000361014	-0.000163486
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0894	0.04	0.0447	1.46
2.9	10	0.11	0.0886	0.056	0.0443	1.53
10.6	9	0.06	0.0866	0.023	0.0432	-1.85

```
  42     9       0.06       0.0783        0.026       0.0385
-1.43
191.1    10       0.04       0.0392        0.019       0.0175
0.136
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	136.270966	4	-264.541933
R	125.105720	2	-246.211439

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571

Test 4	18.4427	3	0.0003564

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

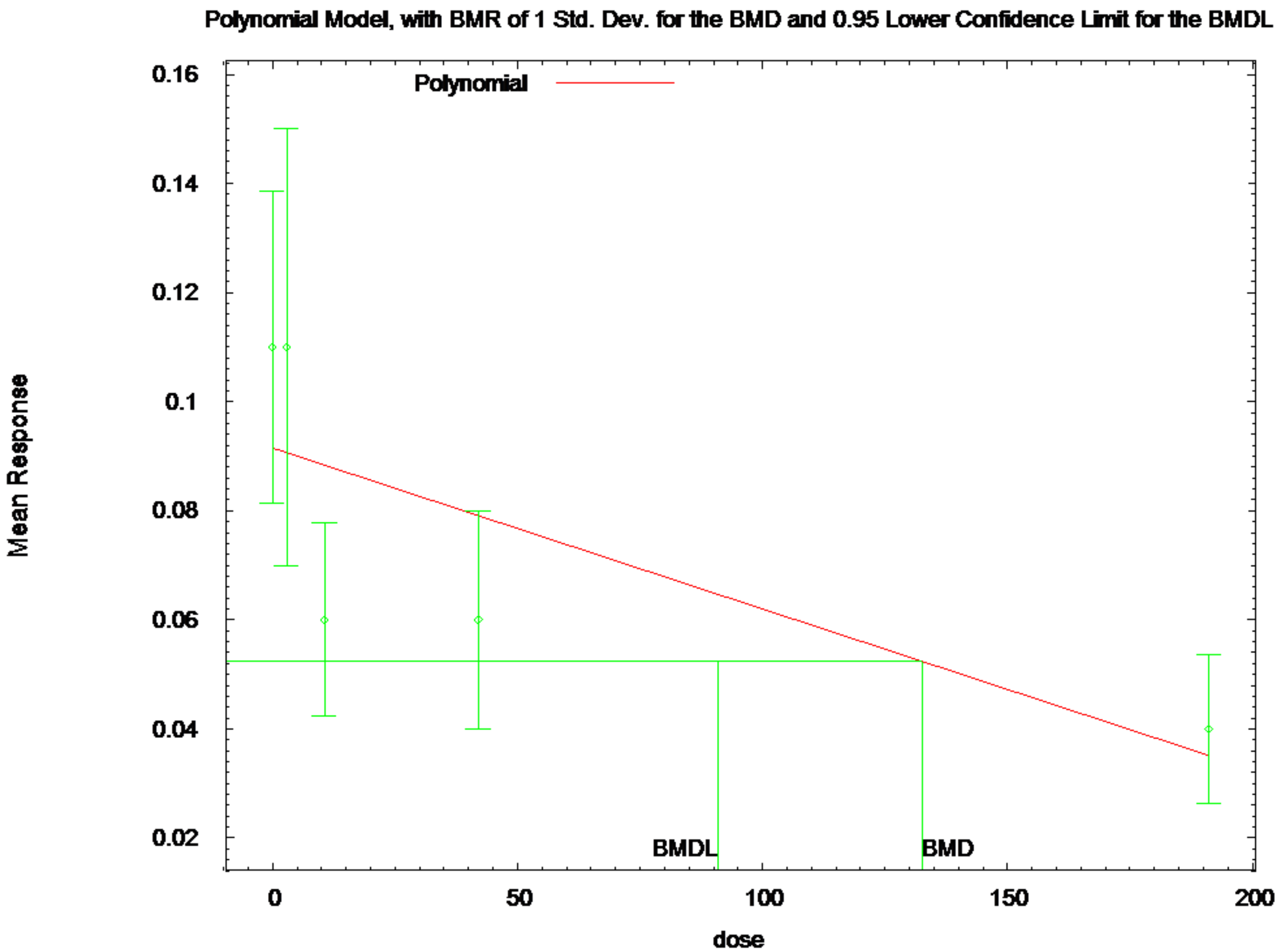
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 170.581

BMDL = 120.78



12:40 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly4CV-1SD-5d.plt
                                       Wed Jul 09 12:40:22 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =         0.11
                         beta_1 =            0
                         beta_2 = -0.000923644
                         beta_3 =            0
                         beta_4 = -1.01654e-007


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	8.5e-009	-5e-008
beta_0	8.5e-009	1	-0.56
beta_1	-5e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00153024	0.000312359	0.000918027	0.00214245
beta_0	0.091509	0.0068346	0.0781134	0.104905
beta_1	-0.000295198	7.65966e-005	-0.000445324	-0.000145071
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0915	0.04	0.0391	1.49
2.9	10	0.11	0.0907	0.056	0.0391	1.56
10.6	9	0.06	0.0884	0.023	0.0391	-2.18
42	9	0.06	0.0791	0.026	0.0391	

-1.47
191.1 10 0.04 0.0351 0.019 0.0391
0.396

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	131.575968	3	-257.151936
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	13.4403	3	0.003775

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

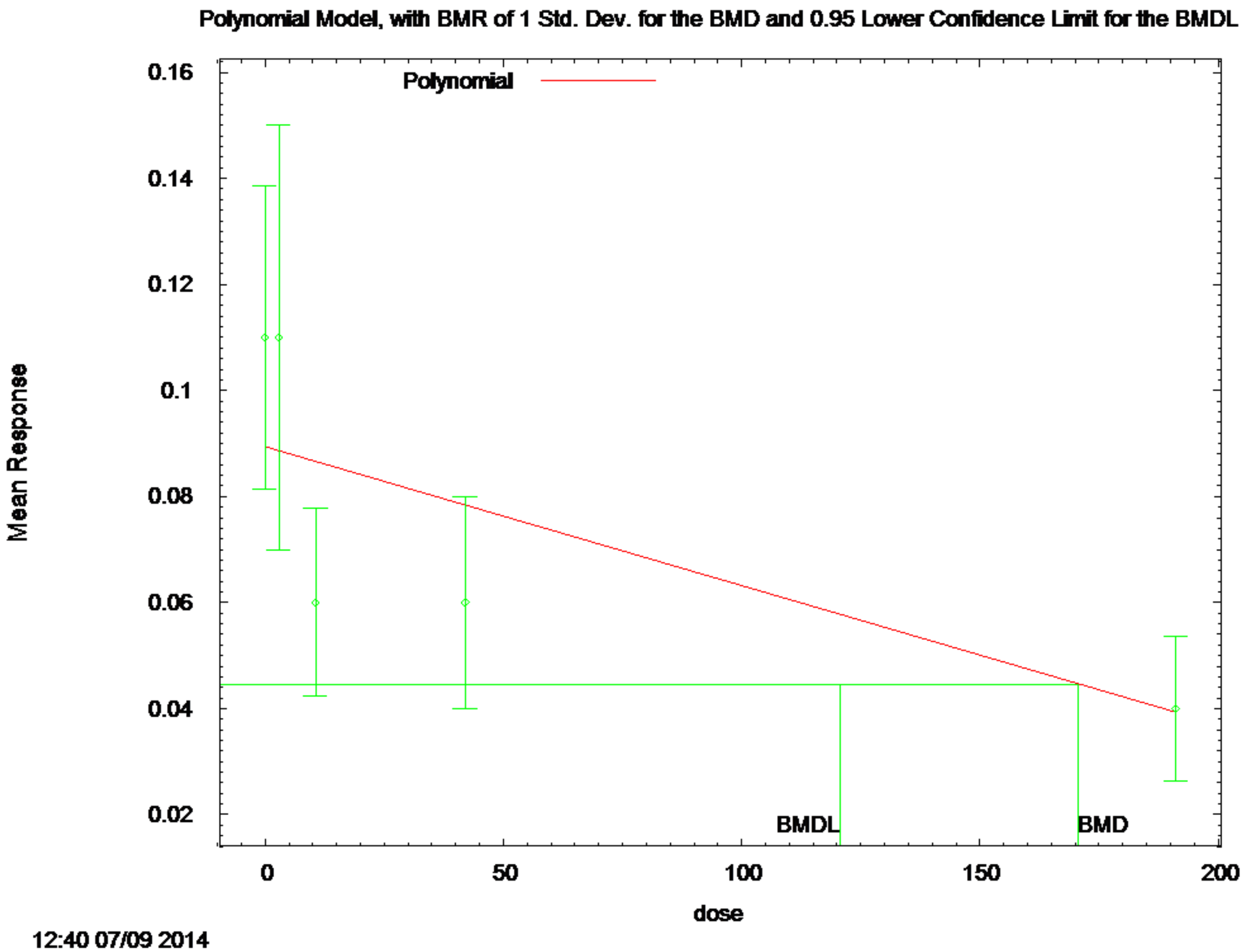
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 132.516

BMDL = 90.8103



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
12:40 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurrent/LUC_concurrent-HLS
2001-LUC count-Poly4NCV-1SD-5d.plt
                                        Wed Jul 09 12:40:24 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =         0.11
                         beta_1 =            0
                         beta_2 = -0.000923644
                         beta_3 =            0
                         beta_4 = -1.01654e-007


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.052	0.061
rho	0.99	1	-0.052	0.06
beta_0	-0.052	-0.052	1	-0.82
beta_1	0.061	0.06	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.716065	1.62767	-3.90624	2.47411
rho	2.2765	0.616544	1.0681	3.4849
beta_0	0.08936	0.00749719	0.0746658	0.104054
beta_1	-0.00026225	5.03908e-005	-0.000361015	-0.000163486
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0894	0.04	0.0447	1.46
2.9	10	0.11	0.0886	0.056	0.0443	

```
1.53
 10.6     9       0.06       0.0866        0.023       0.0432
-1.85
   42     9       0.06       0.0783        0.026       0.0385
-1.43
191.1    10       0.04       0.0392        0.019       0.0175
0.136



 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          138.296137            6    -264.592275
             A2          146.083690           10    -272.167381
             A3          145.492300            7    -276.984600
         fitted          136.270966            4    -264.541933
              R          125.105720            2    -246.211439


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	18.4427	3	0.0003564

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

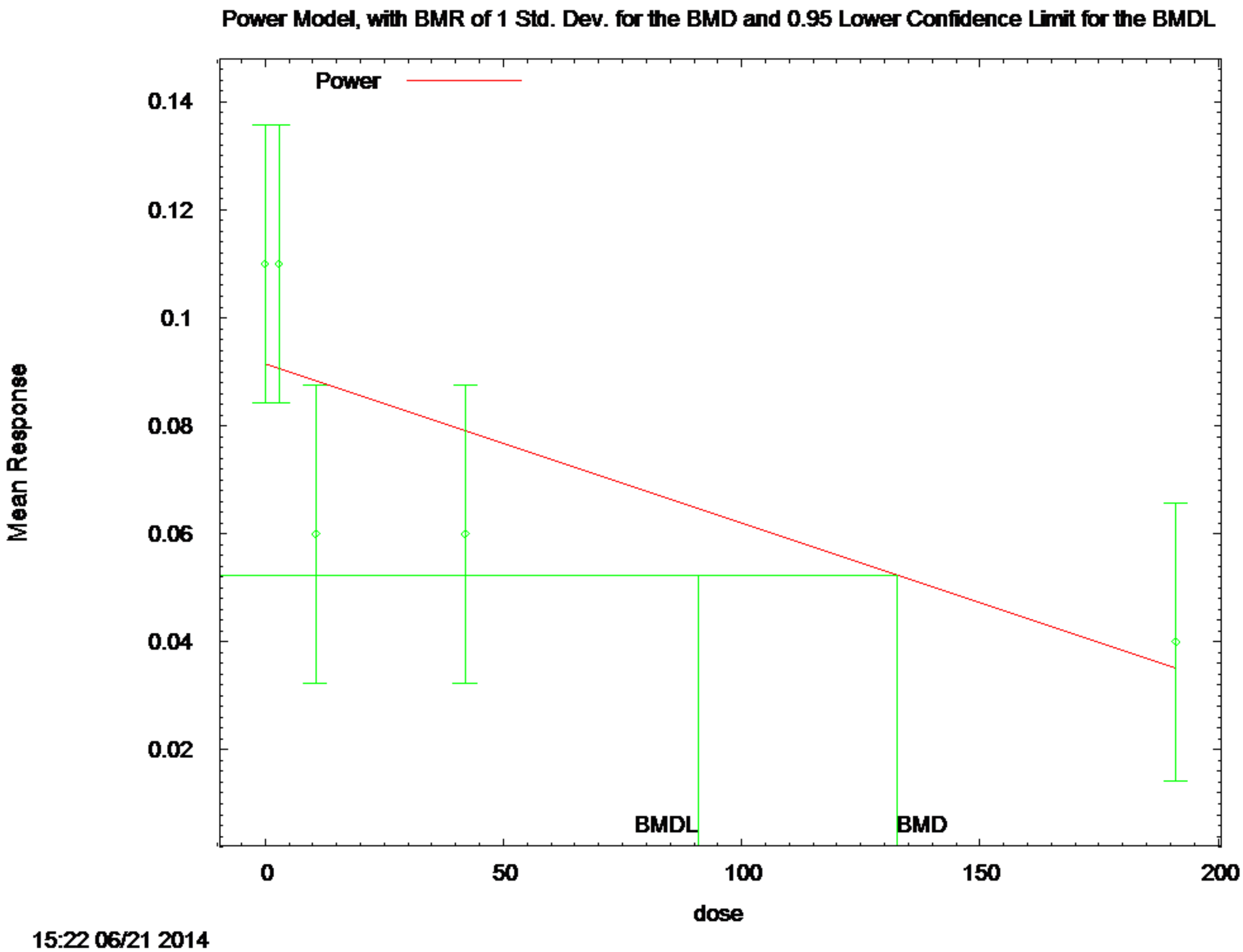
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 170.581

BMDL = 120.78


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
50
100
150
200
dose
15:22 06/21 2014

```
====================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-PowerCV-1SD-5d.plt
                                       Sat Jun 21 15:22:12 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                        control =         0.11
                          slope =    -0.800207
                          power =    -0.463824


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	1.5e-007	1.8e-008
control	1.5e-007	1	-0.56
slope	1.8e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00153024	0.000312359	0.000918027	0.00214245
control	0.091509	0.0068346	0.0781134	0.104905
slope	-0.000295198	7.65966e-005	-0.000445324	-0.000145071
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0915	0.04	0.0391	1.49
2.9	10	0.11	0.0907	0.056	0.0391	1.56
10.6	9	0.06	0.0884	0.023	0.0391	-2.18
42	9	0.06	0.0791	0.026	0.0391	-1.47
191.1	10	0.04	0.0351	0.019	0.0391	0.396

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	131.575968	3	-257.151936
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	13.4403	3	0.003775

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

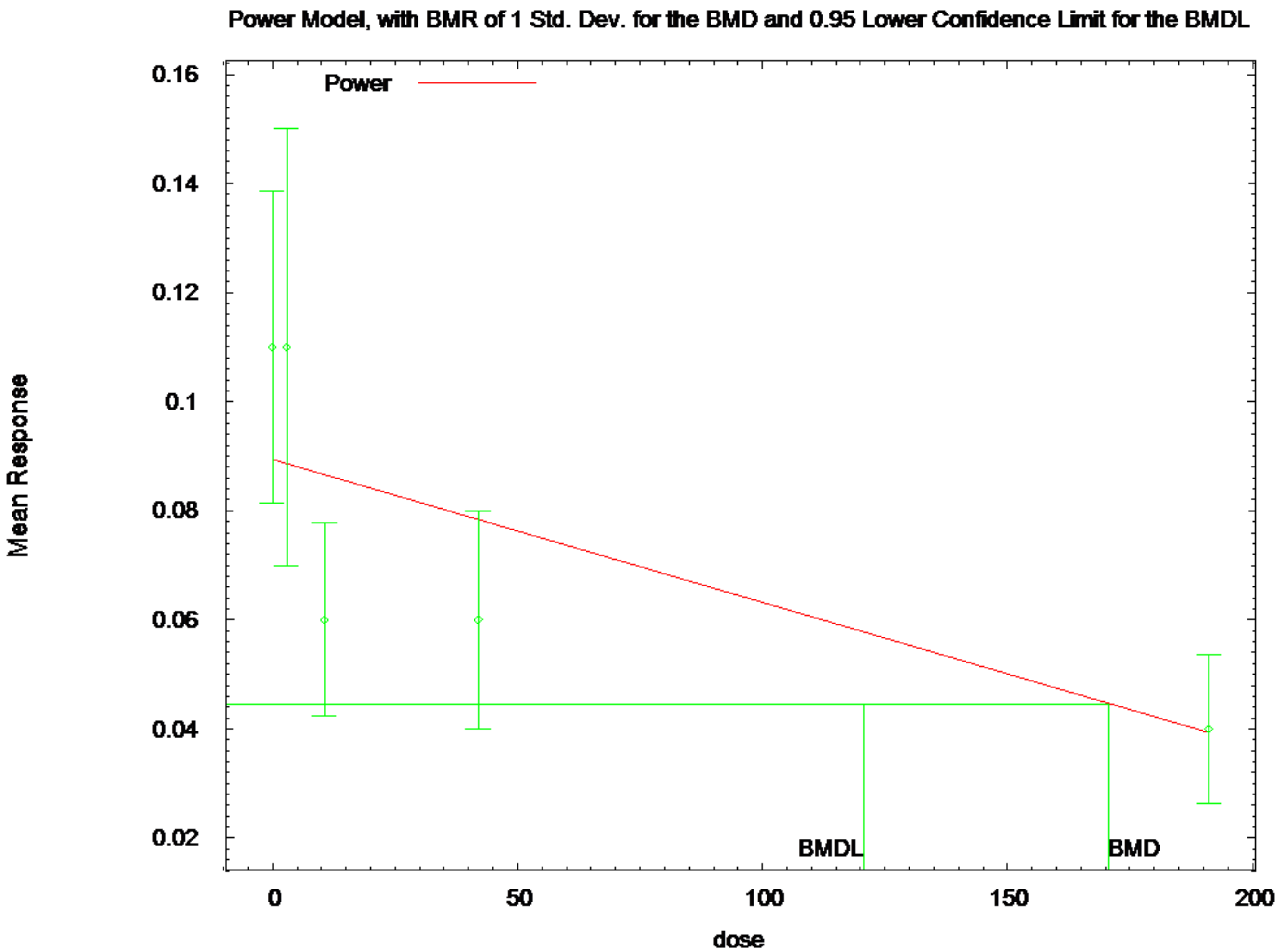
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 132.516

BMDL = 90.8103



15:22 06/21 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/LUC_concurrent-HLS 2001-LUC
count-PowerNCV-1SD-5d.plt
                                      Sat Jun 21 15:22:14 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                        control =         0.11
                          slope =    -0.800207
                          power =    -0.463824


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	0.99	-0.45	0.64
rho	0.99	1	-0.39	0.62
control	-0.45	-0.39	1	-0.82
slope	0.64	0.62	-0.82	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.716057	2.16724	-4.96376	3.53165
rho	2.2765	0.815964	0.677244	3.87576
control	0.08936	0.00757597	0.0745113	0.104209
slope	-0.00026225	5.08149e-005	-0.000361845	-0.000162655
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0894	0.04	0.0447	1.46
2.9	10	0.11	0.0886	0.056	0.0443	1.53
10.6	9	0.06	0.0866	0.023	0.0432	-1.85
42	9	0.06	0.0783	0.026	0.0385	-1.43

191.1   10   0.04   0.0392   0.019   0.0175
0.136

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	136.270966	4	-264.541933
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	18.4427	3	0.0003564

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

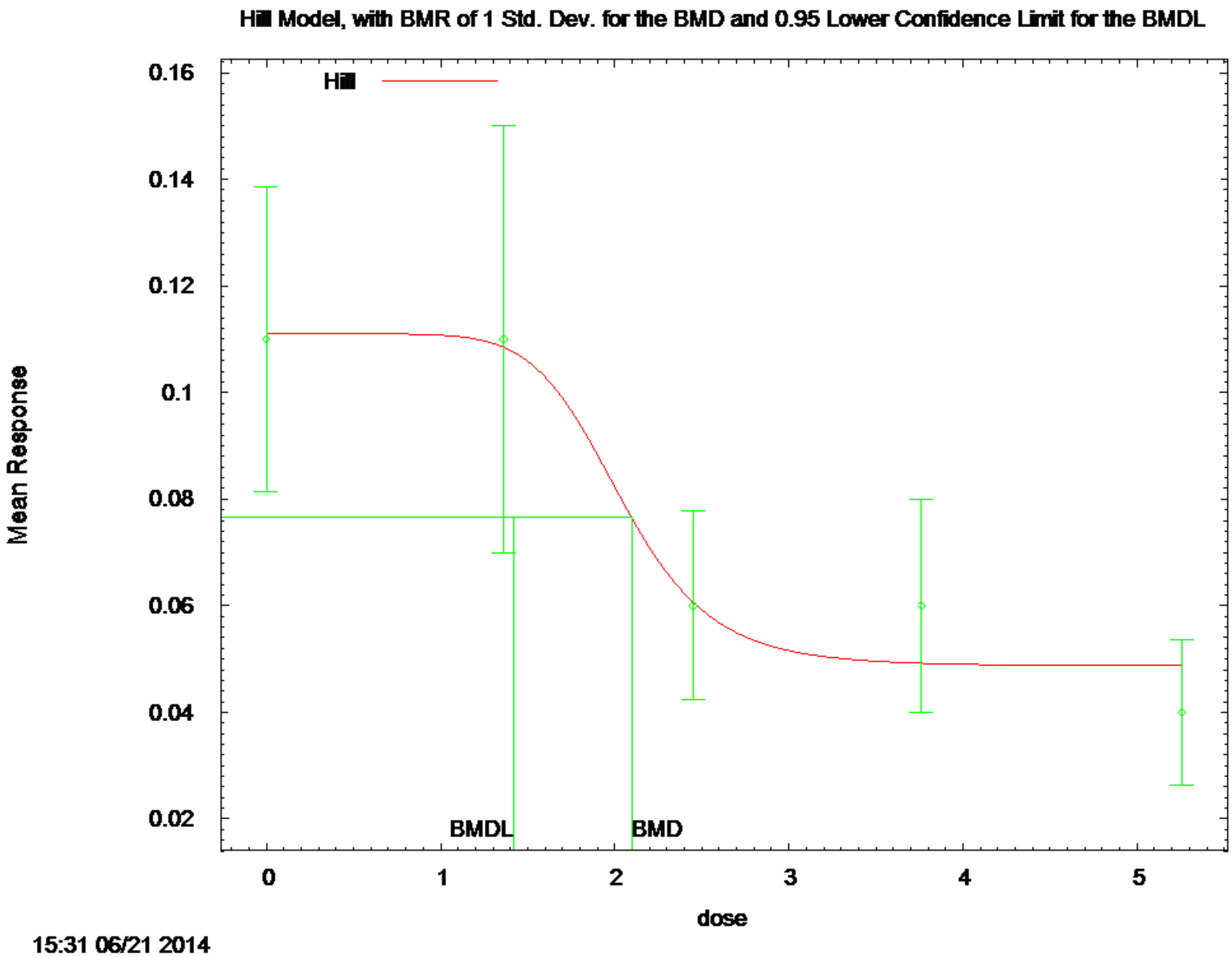
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 170.581

BMDL = 120.78

BMDS Model Results for Large Unstained Cells Count (Log-transformed Doses, Concurrent Controls)


Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Hill
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
HillCV-1SD-5d.plt
                                       Sat Jun 21 15:31:12 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                      intercept =         0.11
                              v =        -0.07
                              n =      16.2187
                              k =        2.124


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	2e-006	-1.5e-006	-2.5e-006	-2.6e-006
intercept	2e-006	1	-0.81	-0.6	-0.57
v	-1.5e-006	-0.81	1	0.67	0.35
n	-2.5e-006	-0.6	0.67	1	0.65
k	-2.6e-006	-0.57	0.35	0.65	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00119497	0.000243923	0.000716893	0.00167305
intercept	0.111175	0.010299	0.0909893	0.131361
v	-0.0623099	0.0149175	-0.0915477	-0.0330721
n	7.84542	11.0062	-13.7263	29.4172
k	2.04202	0.46892	1.12296	2.96109

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.111	0.04	0.0346	-0.107

1.361	10	0.11	0.109	0.056	0.0346
0.119					
2.451	9	0.06	0.0609	0.023	0.0346
-0.076					
3.761	9	0.06	0.0494	0.026	0.0346
0.922					
5.258	10	0.04	0.0489	0.019	0.0346
-0.814					

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	137.511155	5	-265.022309
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test -2*log(Likelihood Ratio) Test df p-value

Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	1.56997	1	0.2102

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

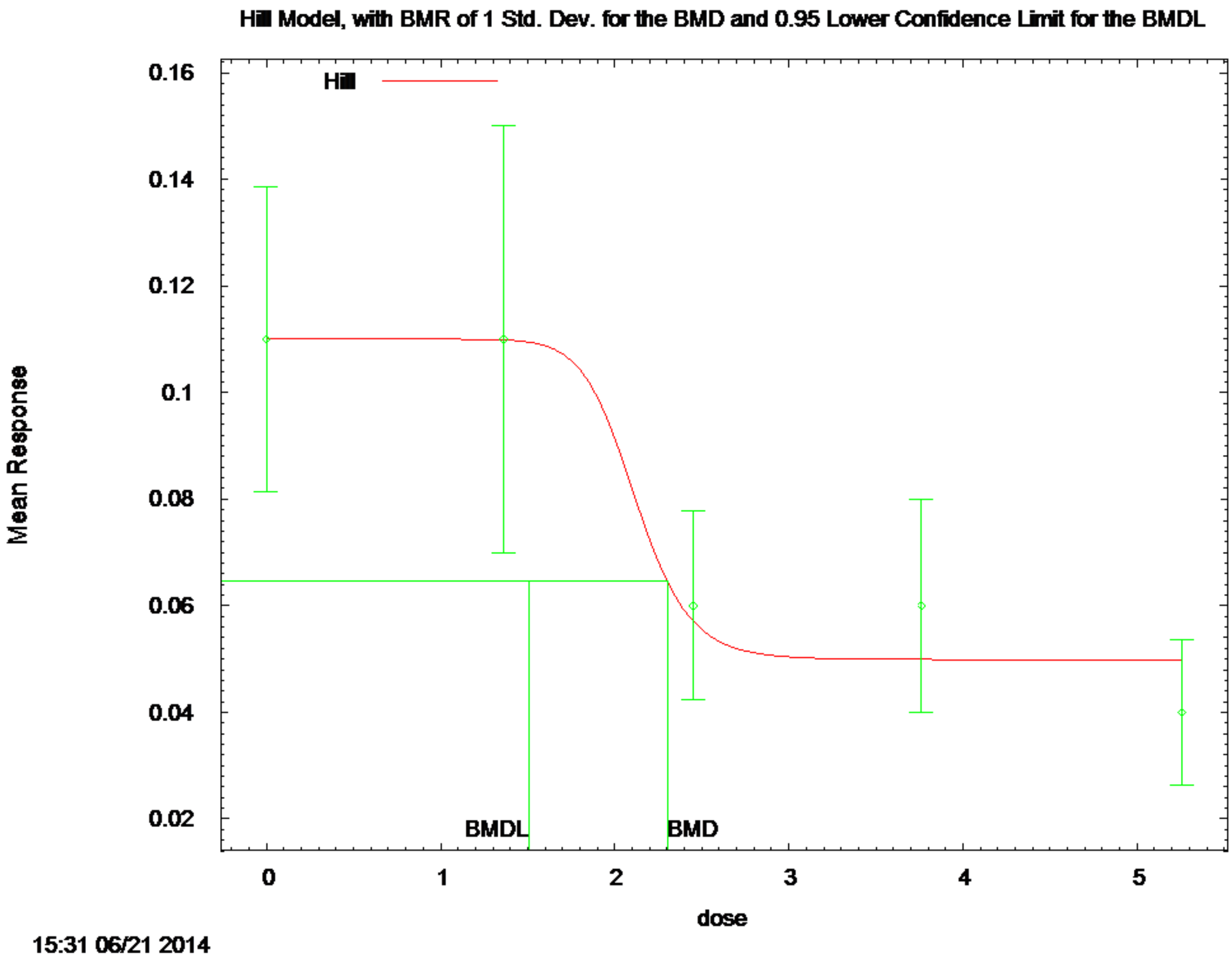
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.1001

BMDL = 1.41795



Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Hill
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
HillNCV-1SD-5d.plt
                                       Sat Jun 21 15:31:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                      intercept =         0.11
                              v =        -0.07
                              n =      16.2187
                              k =        2.124


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

	lalpha	rho	intercept	v	n	k
lalpha	1	0.99	-0.38	0.46	0.027	0.011
rho	0.99	1	-0.34	0.45	0.028	0.012
intercept	-0.38	-0.34	1	-0.9	-0.2	-0.21
v	0.46	0.45	-0.9	1	0.27	0.25
n	0.027	0.028	-0.2	0.27	1	0.98
k	0.011	0.012	-0.21	0.25	0.98	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-2.17641	1.65816	-5.42635	1.07352
rho	1.81184	0.624065	0.588697	3.03499
intercept	0.110395	0.0104058	0.0900003	0.13079
v	-0.060051	0.0119329	-0.0834391	-0.0366628
n	13.7775	54.3009	-92.6503	120.205
k	2.11962	1.16519	-0.164118	4.40336

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.11	0.04	0.0457	-0.0273

1.361	10	0.11	0.11	0.056	0.0457	-0.0181
2.451	9	0.06	0.0575	0.023	0.0253	0.297
3.761	9	0.06	0.0504	0.026	0.0225	1.29
5.258	10	0.04	0.0503	0.019	0.0225	-1.46

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	142.900991	6	-273.801982
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	5.18262	1	0.02281

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

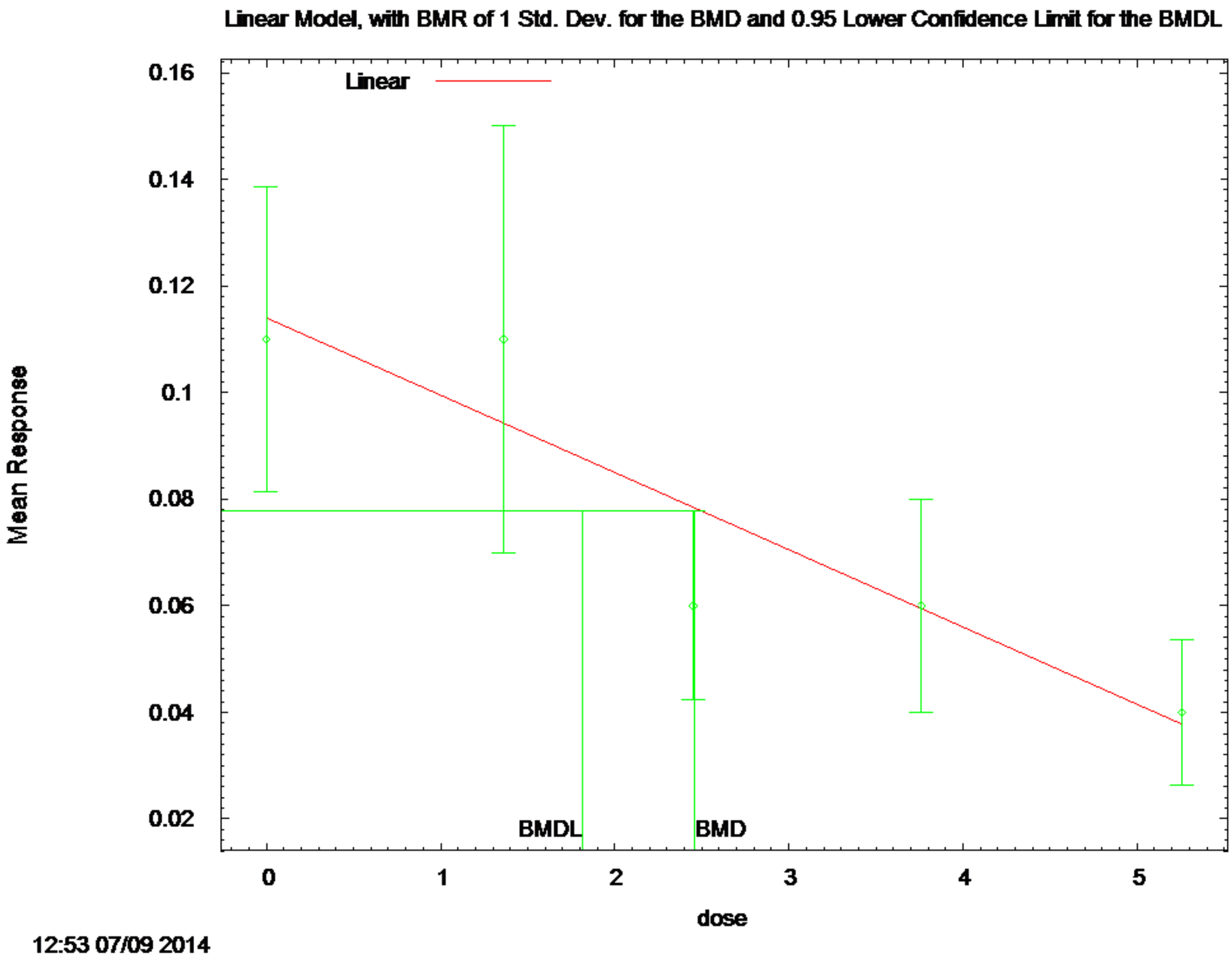
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.30628

BMDL = 1.50553


Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:53:08 2014
=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =     0.113195
                         beta_1 =   -0.0144941


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	7.4e-009	-7.8e-009
beta_0	7.4e-009	1	-0.81
beta_1	-7.8e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00127623	0.000260509	0.000765639	0.00178682
beta_0	0.113585	0.00874069	0.0964537	0.130717
beta_1	-0.0145136	0.00277459	-0.0199517	-0.00907554

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.114	0.04	0.0357	-0.317
1.361	10	0.11	0.0938	0.056	0.0357	1.43
2.451	9	0.06	0.078	0.023	0.0357	-1.51
3.761	9	0.06	0.059	0.026	0.0357	0.084
5.258	10	0.04	0.0373	0.019	0.0357	0.241

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	135.932325	3	-265.864651
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	4.72762	3	0.1929

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a

different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

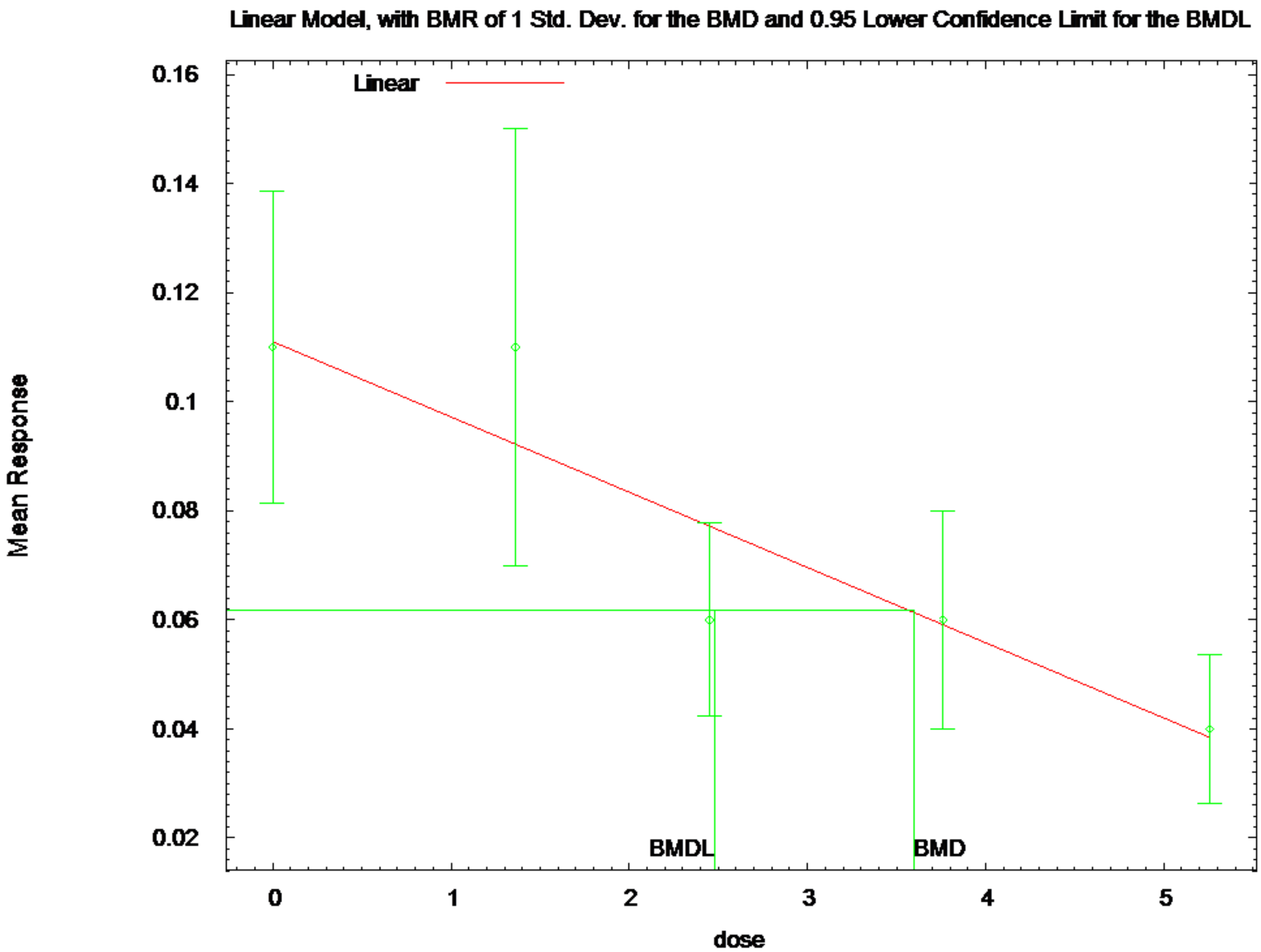
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.46143

BMDL = 1.81322



12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:53:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =     0.113195
                         beta_1 =   -0.0144941


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho        beta_0        beta_1

    lalpha            1         0.99        -0.073         0.086
```

rho	0.99	1	-0.073	0.087
beta_0	-0.073	-0.073	1	-0.92
beta_1	0.086	0.087	-0.92	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-1.68251	1.47799	-4.57931	1.21429
rho	1.97135	0.555285	0.883008	3.05969
beta_0	0.111471	0.0102095	0.0914608	0.131481
beta_1	-0.0137839	0.00240468	-0.018497	-0.00907084

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.111	0.04	0.0496	-0.0938
1.361	10	0.11	0.0927	0.056	0.0414	1.32
2.451	9	0.06	0.0777	0.023	0.0347	-1.53
3.761	9	0.06	0.0596	0.026	0.0268	0.0415
5.258	10	0.04	0.039	0.019	0.0176	0.18

Model Descriptions for likelihoods calculated

```
Model A1:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	141.105082	4	-274.210164
R	125.105720	2	-246.211439

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	8.77444	3	0.03245

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different model

Benchmark Dose Computation

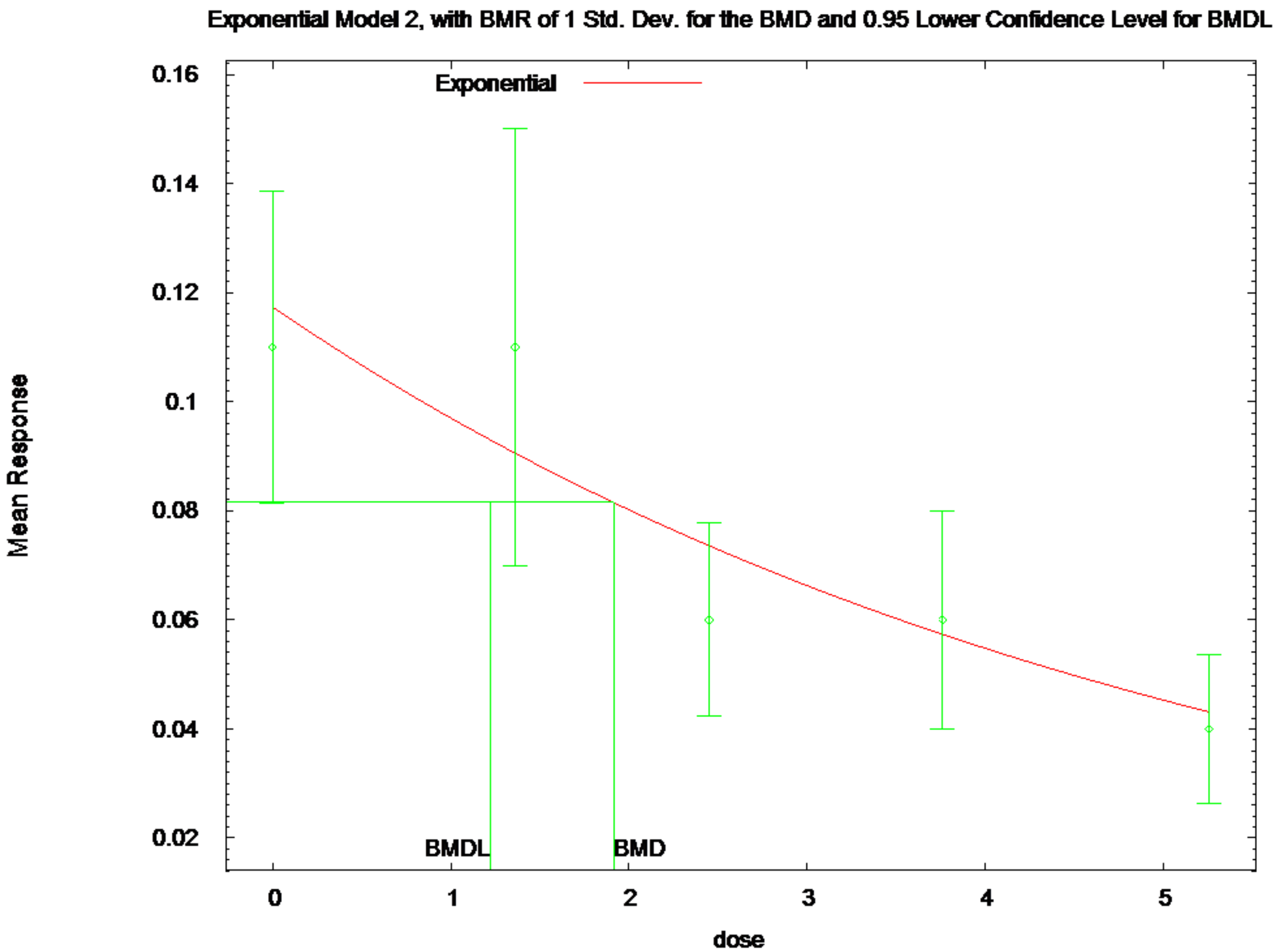
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.59823

BMDL = 2.47874



15:31 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:31:12 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-6.76234
rho(S)	0
a	0.0423932
b	0.202634
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	-6.65741
rho	0
a	0.117357
b	0.190434
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1174	0.03584	-0.6491
1.361	0.09056	0.03584	1.715
2.451	0.07359	0.03584	-1.137
3.761	0.05734	0.03584	0.2227
5.258	0.04312	0.03584	-0.275

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
          Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
2	135.7778	3	-265.5555

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	

< 0.0001
Test 2 15.58 4
0.003646
Test 3 15.58 4
0.003646
Test 4 5.037 3
0.1691

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

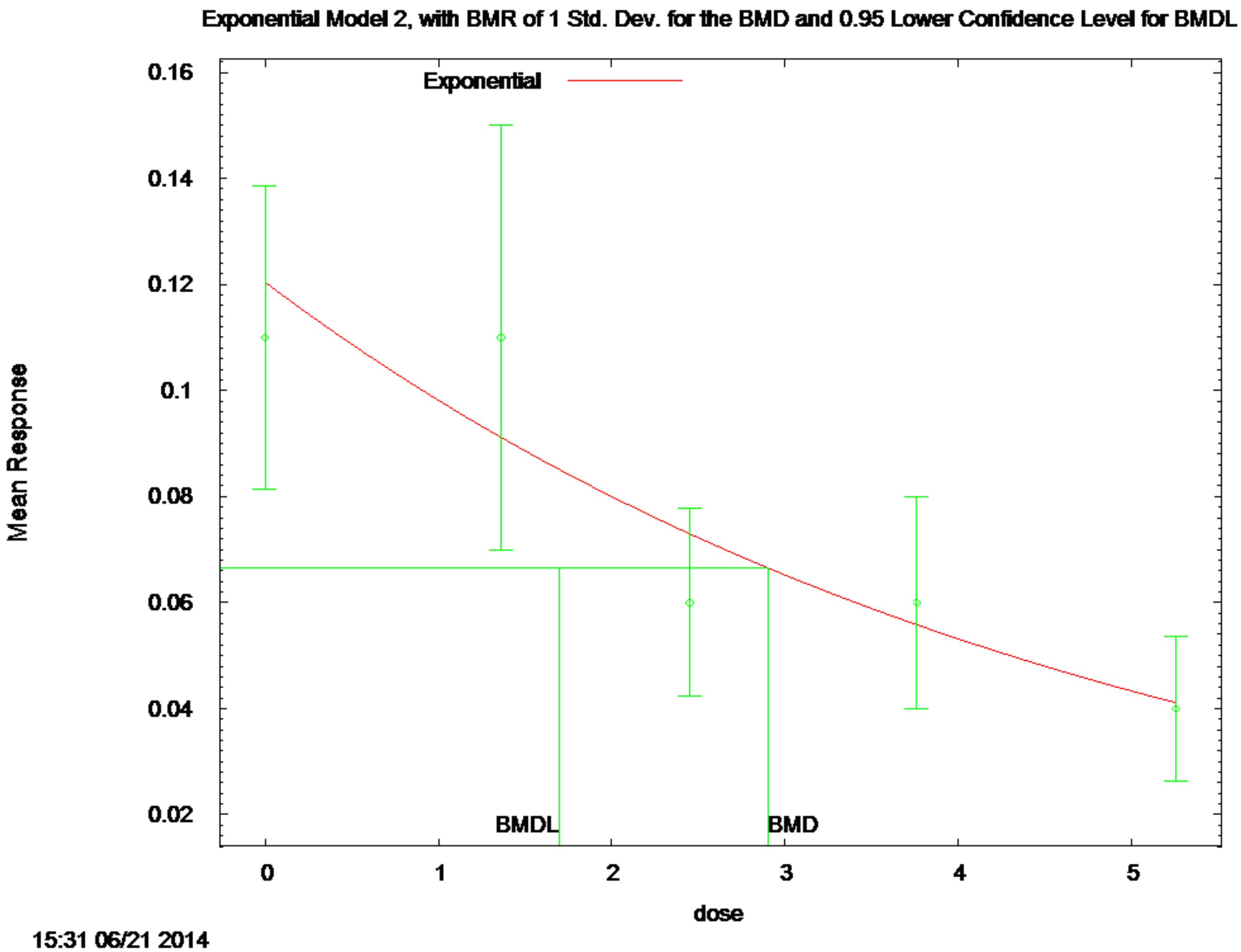
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 1.91354

BMDL = 1.22128



Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                    Sat Jun 21 15:31:13 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-1.95665
rho	1.89965
a	0.0423932
b	0.202634
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-1.63386
rho	1.9875
a	0.12042
b	0.204379
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1204	0.05391	-0.6113
1.361	0.09118	0.04089	1.456
2.451	0.07297	0.03277	-1.187
3.761	0.05583	0.02511	0.4981
5.258	0.04111	0.01853	-0.1902

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
2	140.9803	4	-273.9606

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001
Test 2	15.58	4	

```
0.003646
     Test 3                              1.183          3
0.7571
     Test 4                              9.024          3
0.02897
```

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

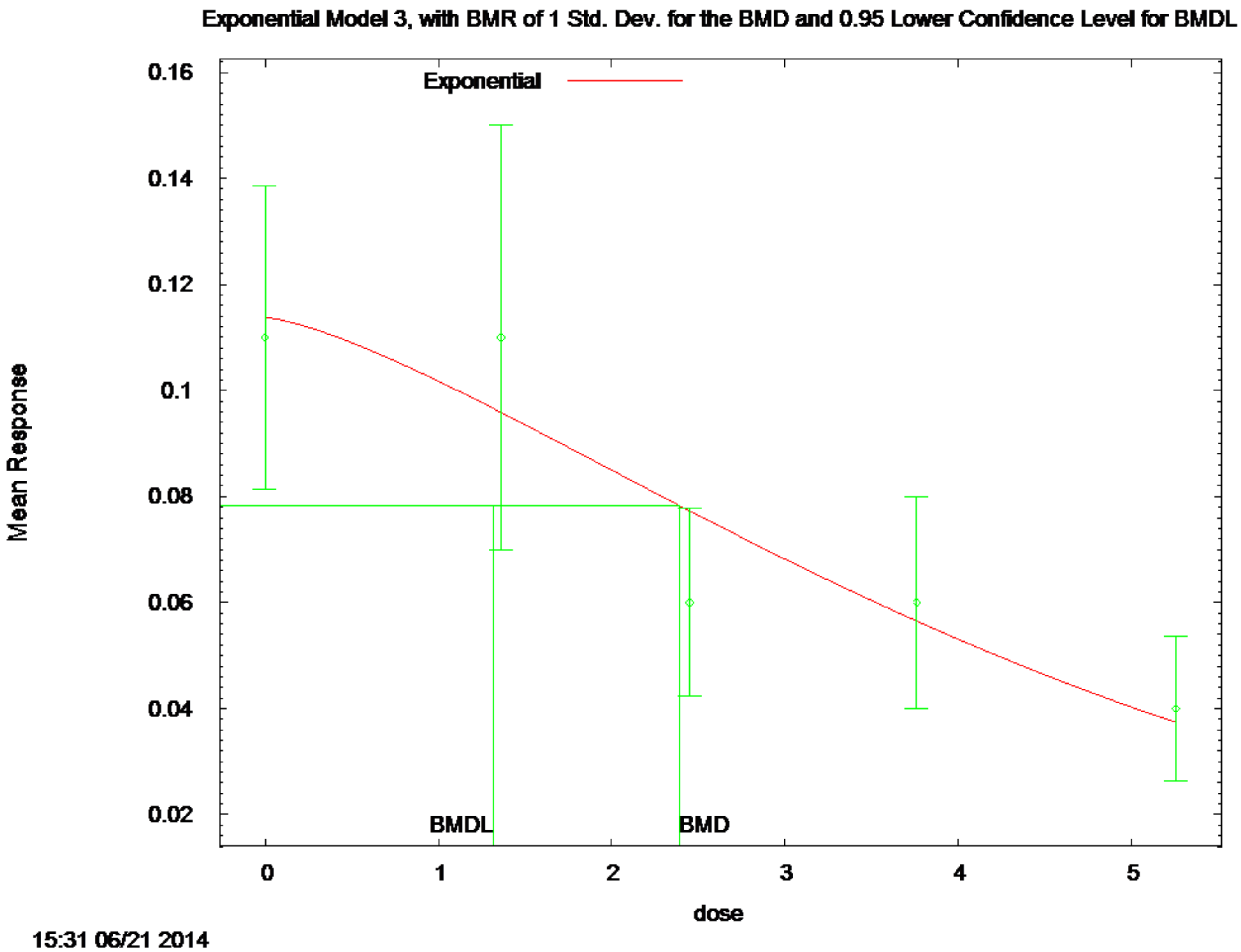
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.90447

BMDL = 1.69873


Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:31:12 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-6.76234
rho(S)	0
a	0.134683
b	0.131222
c	0
d	2

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	-6.676
rho	0
a	0.113757
b	0.205456
c	0
d	1.3856

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1138	0.03551	-0.3346
1.361	0.09587	0.03551	1.258
2.451	0.07729	0.03551	-1.461
3.761	0.05651	0.03551	0.2946
5.258	0.03738	0.03551	0.2334

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
3	136.2241	4	-264.4482

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 5a	4.144	2	0.1259

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

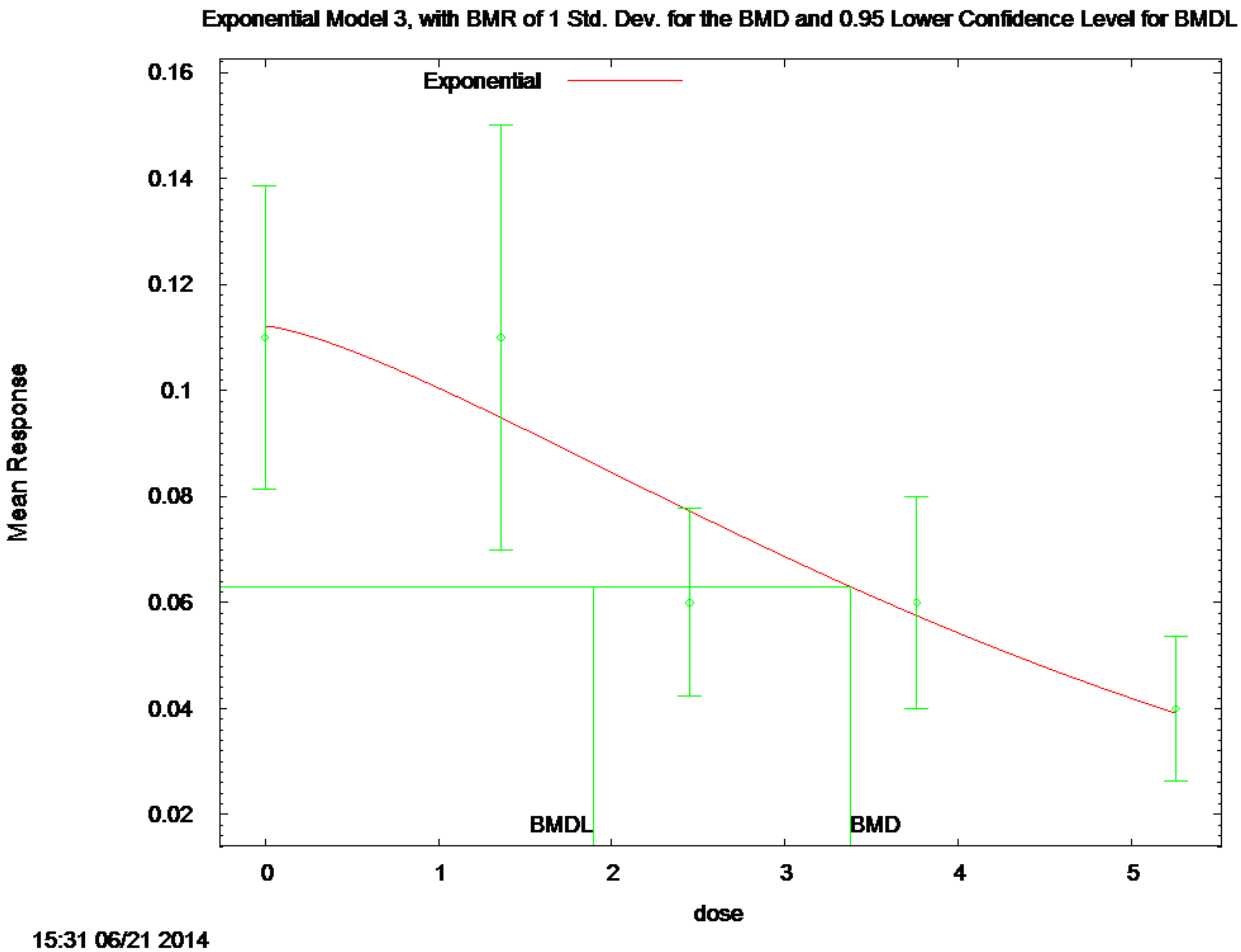
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.3942

BMDL = 1.31419



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:31:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-1.95665
rho	1.89965
a	0.134683
b	0.131222
c	0
d	2

Parameter Estimates

Variable	Model 3
lnalpha	-1.78769
rho	1.93751
a	0.112162
b	0.197578
c	0
d	1.36103

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1122	0.04913	-0.1392
1.361	0.09488	0.04178	1.145
2.451	0.07726	0.03424	-1.513
3.761	0.05754	0.02573	0.2874
5.258	0.03912	0.01771	0.1568

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)

```
                 Var{e(ij)} = Sigma(i)^2

     Model A3:          Yij = Mu(i) + e(ij)
                 Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:          Yij = Mu + e(i)
                 Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
3	141.5335	5	-273.067

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 5a	7.918	2	0.01909

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

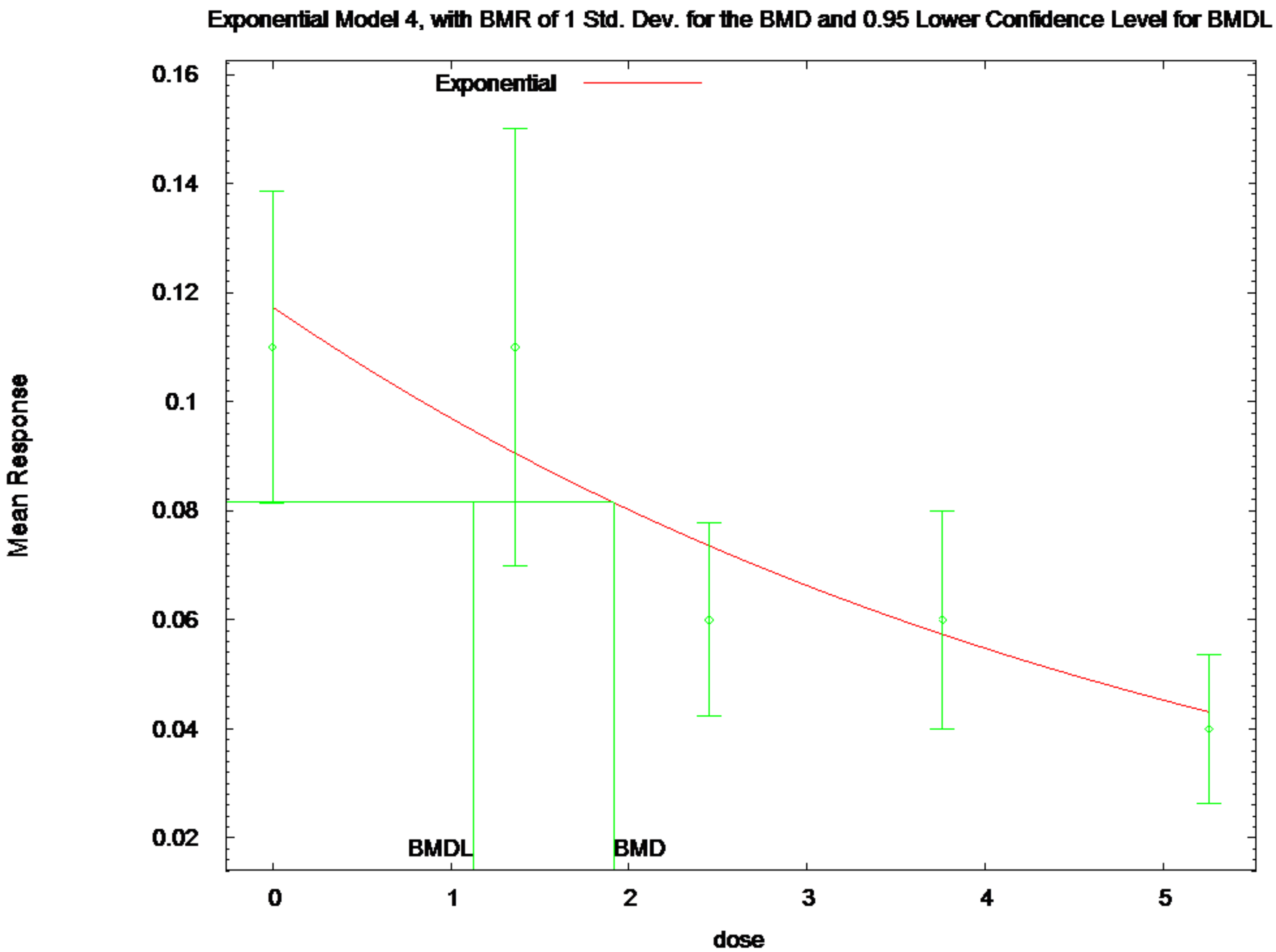
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.37592

BMDL = 1.89841



15:31 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sat Jun 21 15:31:12 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-6.76234
rho(S)	0
a	0.1155
b	0.19568
c	0.00034632
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	-6.65741
rho	0
a	0.117357
b	0.190434
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1174	0.03584	-0.6491
1.361	0.09056	0.03584	1.715
2.451	0.07359	0.03584	-1.137
3.761	0.05734	0.03584	0.2227
5.258	0.04312	0.03584	-0.275

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
4	135.7778	3	-265.5555

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 6a	5.037	3	0.1691

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

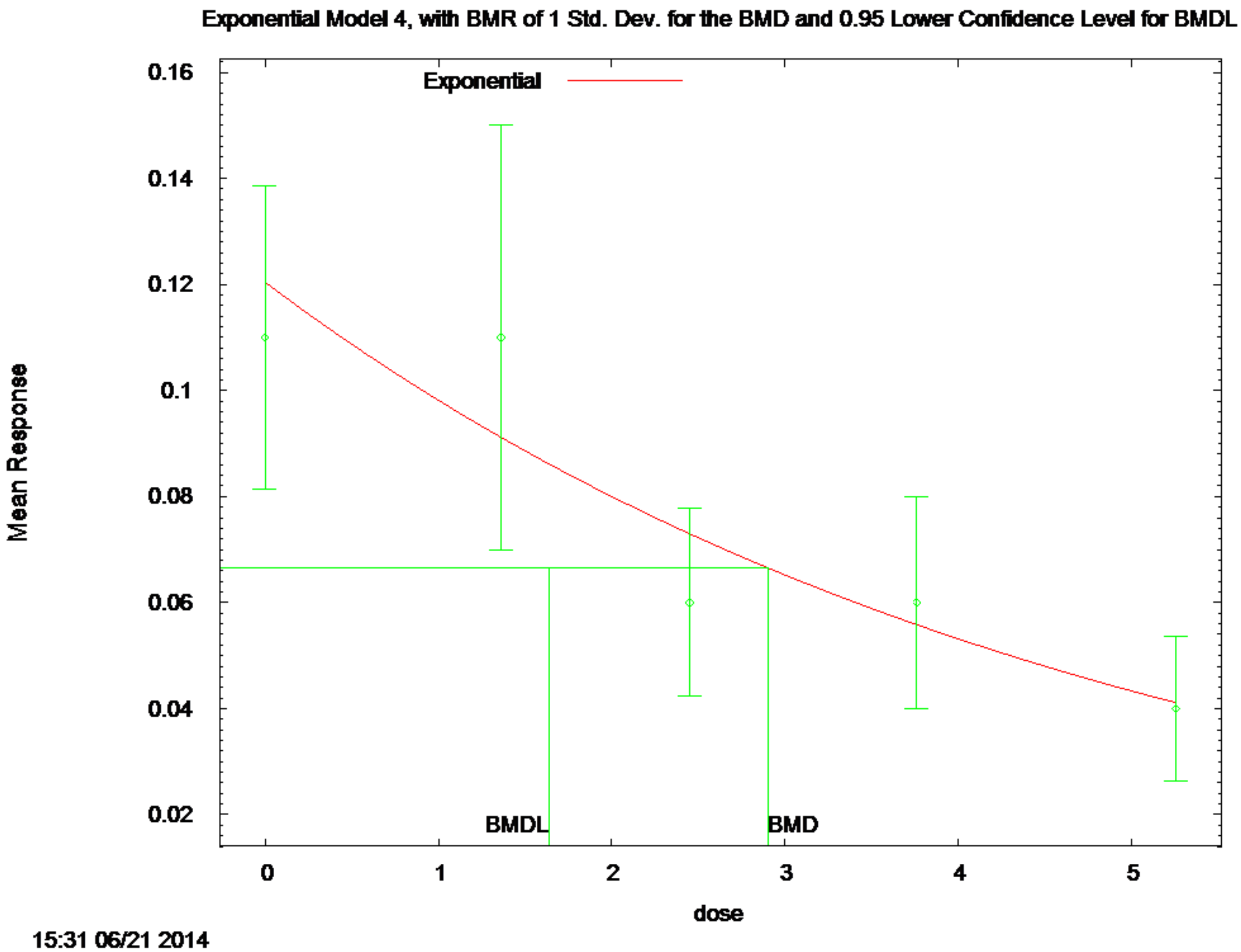
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 1.91354

BMDL = 1.12587



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:31:13 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-1.95665
rho	1.89965
a	0.1155
b	0.19568
c	0.00034632
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-1.63385
rho	1.9875
a	0.12042
b	0.204378
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1204	0.05391	-0.6113
1.361	0.09118	0.04089	1.456
2.451	0.07297	0.03277	-1.187
3.761	0.05583	0.02511	0.4981
5.258	0.04111	0.01853	-0.1902

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
4	140.9803	4	-273.9606

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 6a	9.024	3	0.02897

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

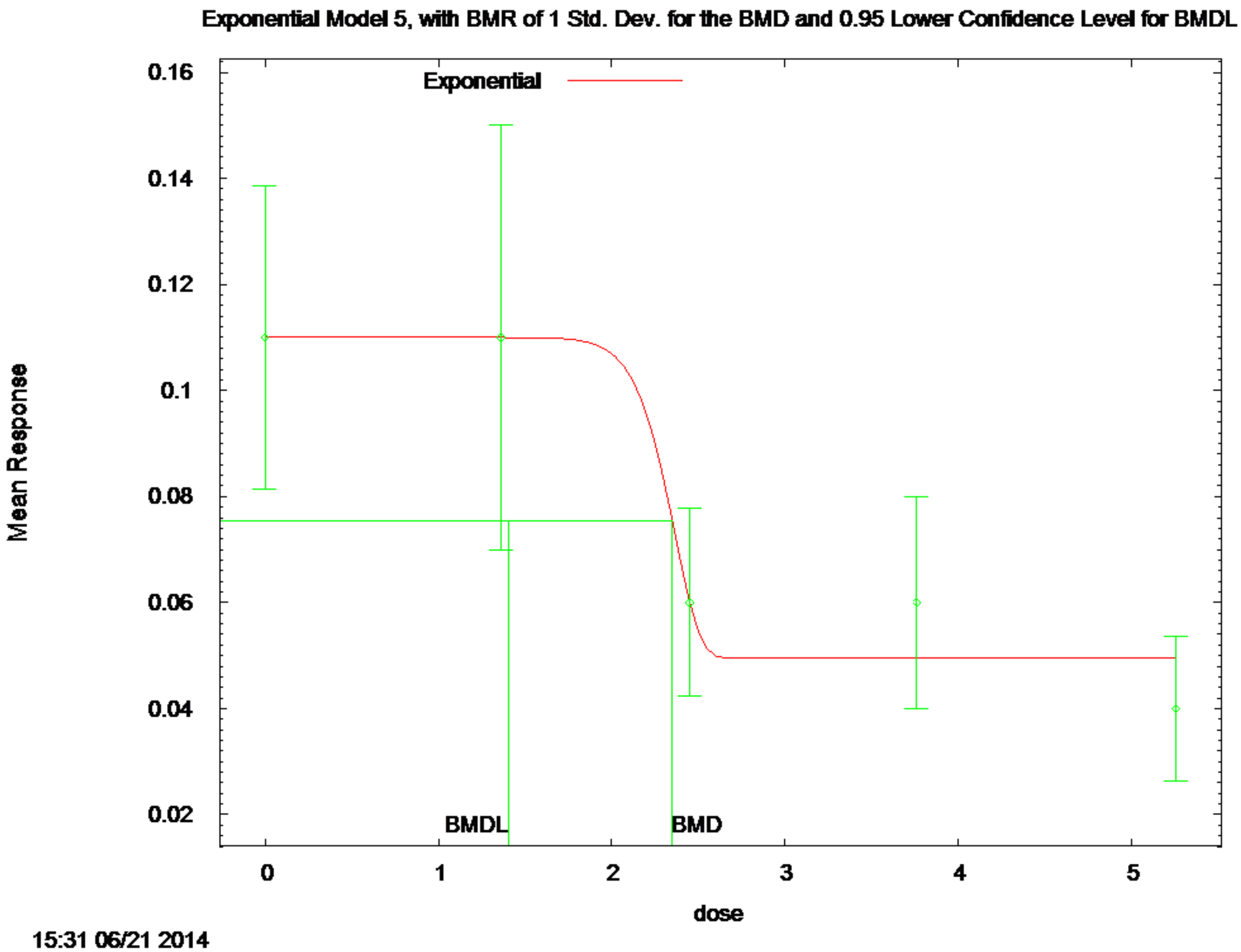
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.90448

BMDL = 1.63628


Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:31:12 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-6.76234
rho(S)	0
a	0.1155
b	0.19568
c	0.00034632
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	-6.72878
rho	0
a	0.110002
b	0.421364
c	0.449753
d	17.3452

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.11	0.03458	-0.0001791
1.361	0.11	0.03458	0.0001794
2.451	0.06	0.03458	-3.466e-008
3.761	0.04947	0.03458	0.9131
5.258	0.04947	0.03458	-0.8663

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	138.2961	6	-264.5923
R	125.1057	2	-246.2114
5	137.4907	5	-264.9813

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	41.96	8	< 0.0001
Test 2	15.58	4	0.003646
Test 3	15.58	4	0.003646
Test 7a	1.611	1	0.2044

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

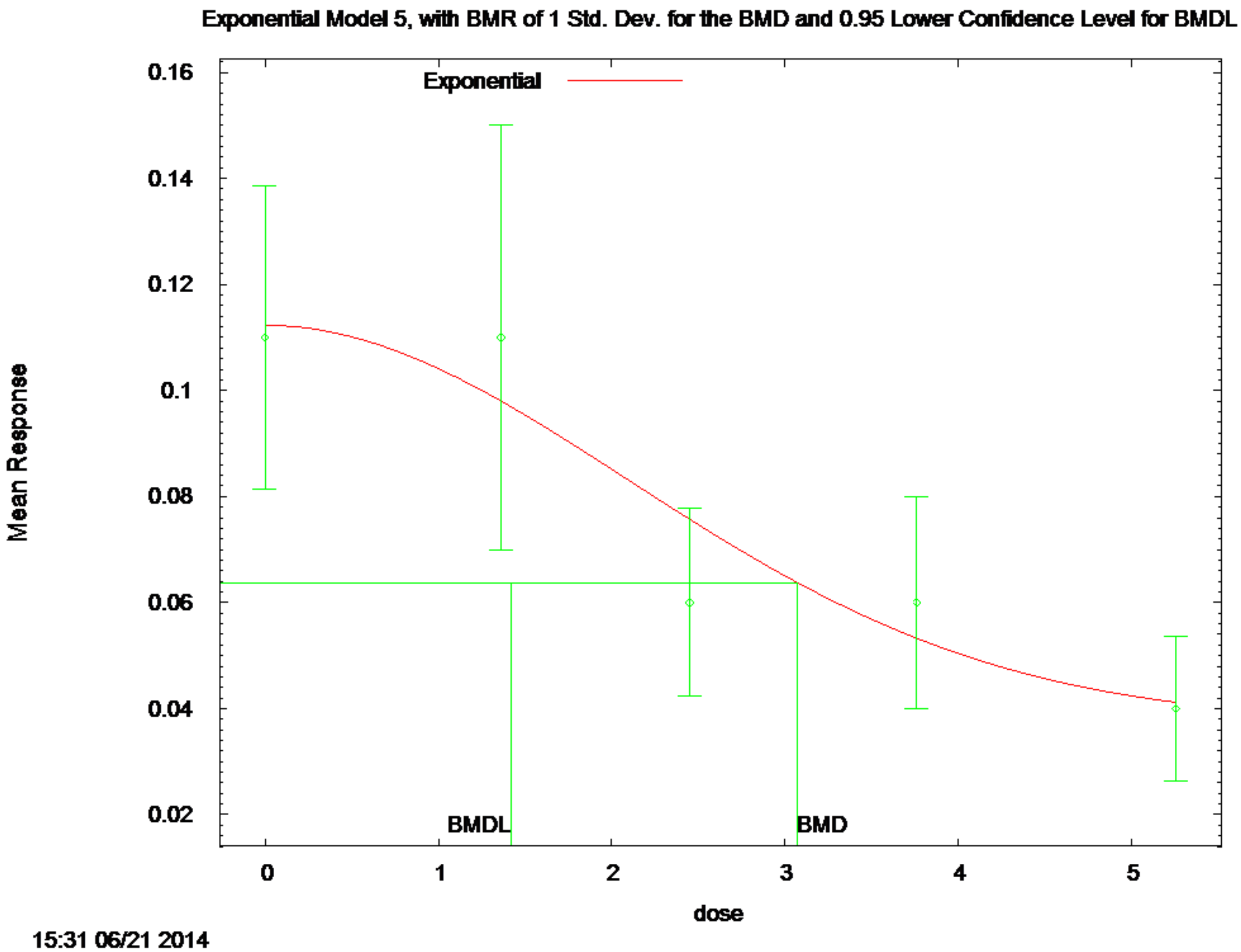
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.35065

BMDL = 1.40406



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
1
2
3
4
5
dose
BMDL
BMD
15:31 06/21 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sat Jun 21 15:31:13 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-1.95665
rho	1.89965
a	0.1155
b	0.19568
c	0.00034632
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-1.86635
rho	1.91354
a	0.112314
b	0.332923
c	0.333365
d	1.95986

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.11	0.04
1.361	10	0.11	0.056
2.451	9	0.06	0.023
3.761	9	0.06	0.026
5.258	10	0.04	0.019

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1123	0.04855	-0.1507
1.361	0.09801	0.04262	0.8893
2.451	0.0757	0.03329	-1.415
3.761	0.05327	0.02378	0.8484
5.258	0.04118	0.01859	-0.2013

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	138.2961	6	-264.5923
A2	146.0837	10	-272.1674
A3	145.4923	7	-276.9846
R	125.1057	2	-246.2114
5	141.9263	6	-271.8527

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	41.96	8	< 0.0001

Test 2	15.58	4	0.003646
Test 3	1.183	3	0.7571
Test 7a	7.132	1	0.007572

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

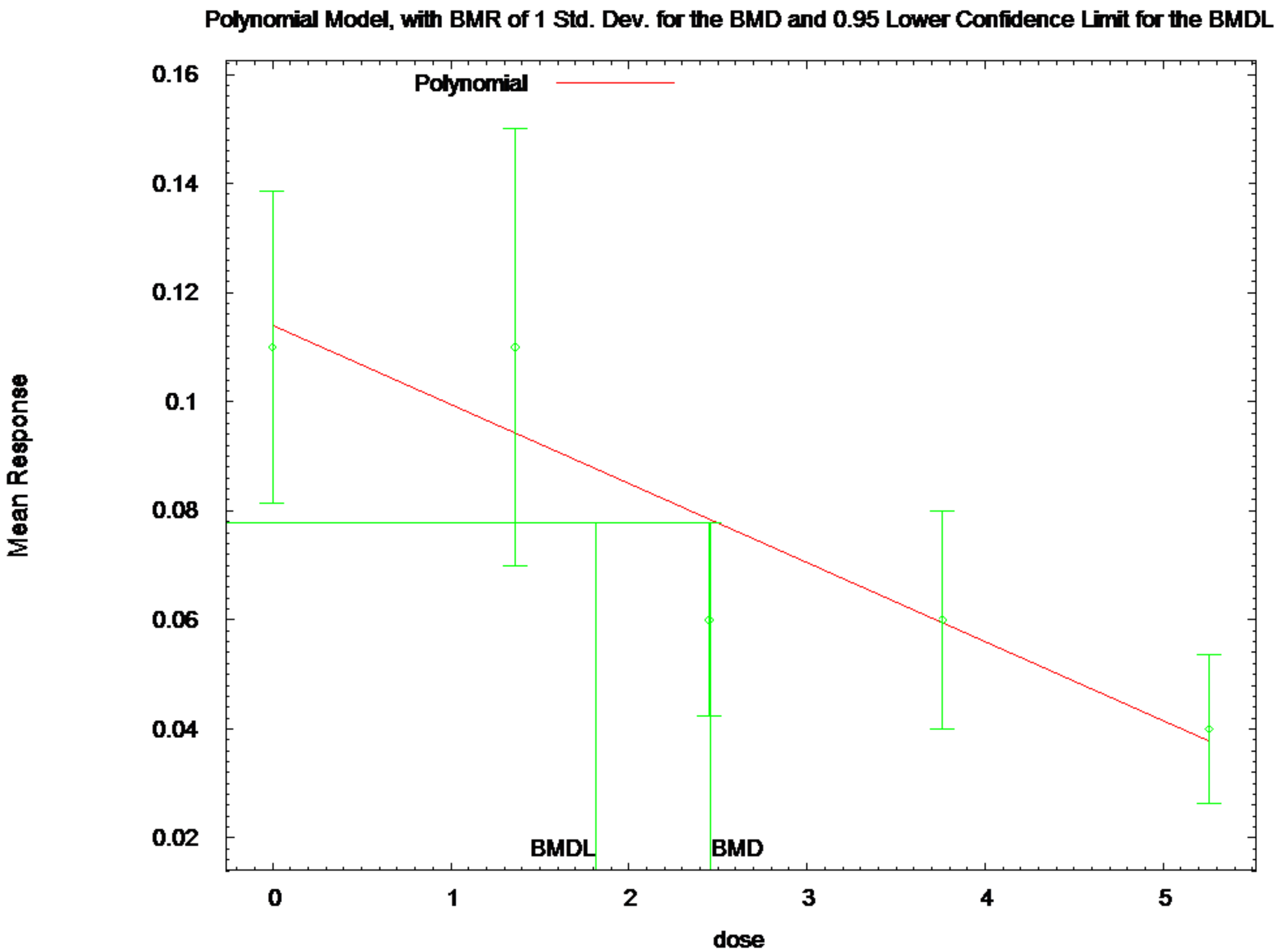
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.07261

BMDL = 1.42137



12:53 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:53:07 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =     0.115396
                         beta_1 =   -0.0176965
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-6.6e-009	2.1e-008
beta_0	-6.6e-009	1	-0.81
beta_1	2.1e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00127623	0.000260509	0.000765639	0.00178682
beta_0	0.113585	0.00874069	0.0964537	0.130717
beta_1	-0.0145136	0.00277459	-0.0199517	-0.00907554
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.114	0.04	0.0357	-0.317
1.361	10	0.11	0.0938	0.056	0.0357	1.43
2.451	9	0.06	0.078	0.023	0.0357	-1.51
3.761	9	0.06	0.059	0.026	0.0357	0.084
5.258	10	0.04	0.0373	0.019	0.0357	0.241

```
Model Descriptions for likelihoods calculated


Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	135.932325	3	-265.864651
R	125.105720	2	-246.211439

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	4.72762	3	0.1929

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

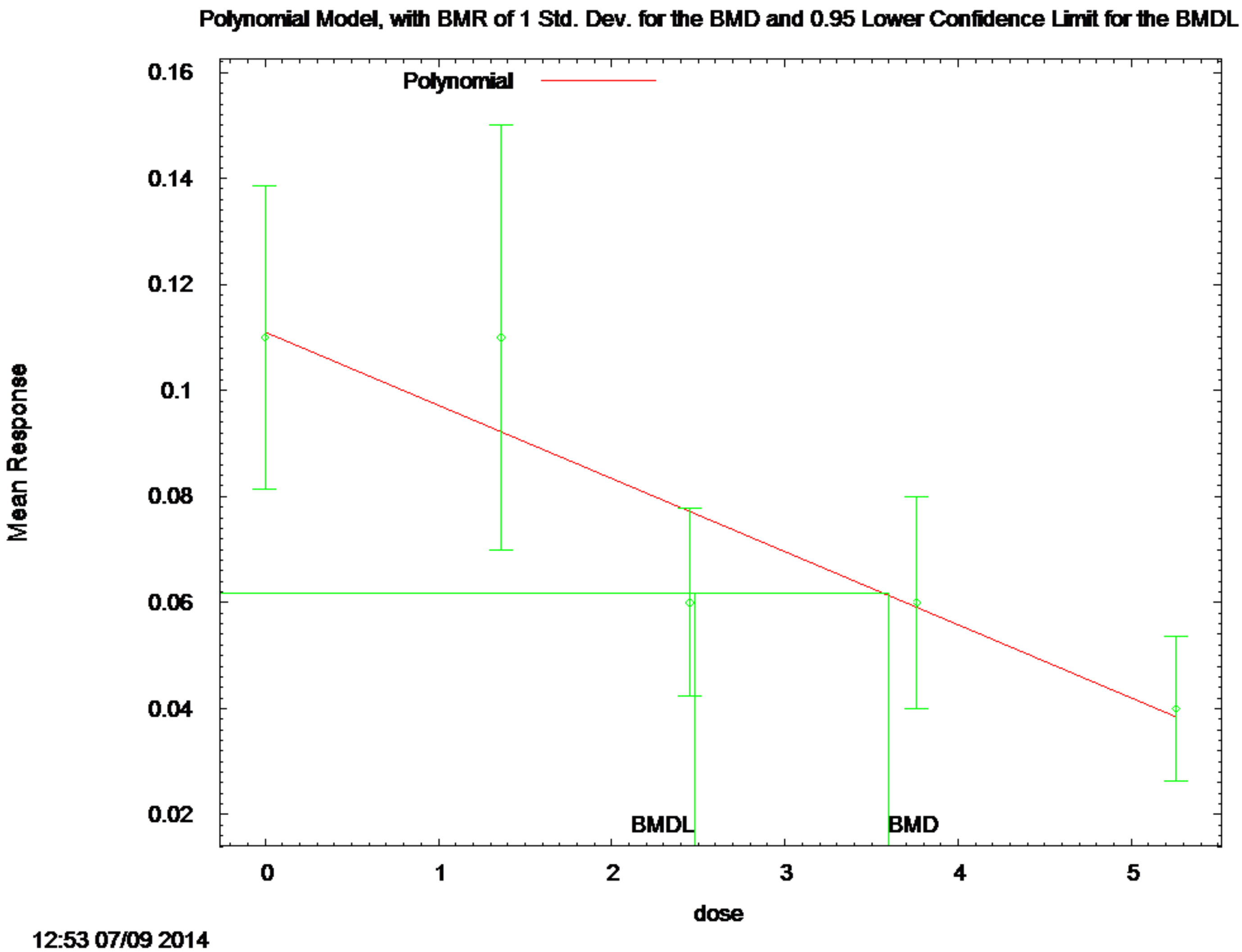
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.46143

BMDL = 1.81322


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:53:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =     0.115396
                         beta_1 =   -0.0176965
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.073	0.086
rho	0.99	1	-0.073	0.087
beta_0	-0.073	-0.073	1	-0.92
beta_1	0.086	0.087	-0.92	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-1.68251	1.47799	-4.57931	1.21429
rho	1.97135	0.555285	0.883008	3.05969
beta_0	0.111471	0.0102095	0.0914608	0.131481
beta_1	-0.0137839	0.00240468	-0.018497	-0.00907084
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.111	0.04	0.0496	-0.0938
1.361	10	0.11	0.0927	0.056	0.0414	1.32
2.451	9	0.06	0.0777	0.023	0.0347	-1.53
3.761	9	0.06	0.0596	0.026	0.0268	0.0415

5.258	10	0.04	0.039	0.019	0.0176

0.18

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	141.105082	4	-274.210164
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	8.77444	3	0.03245

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

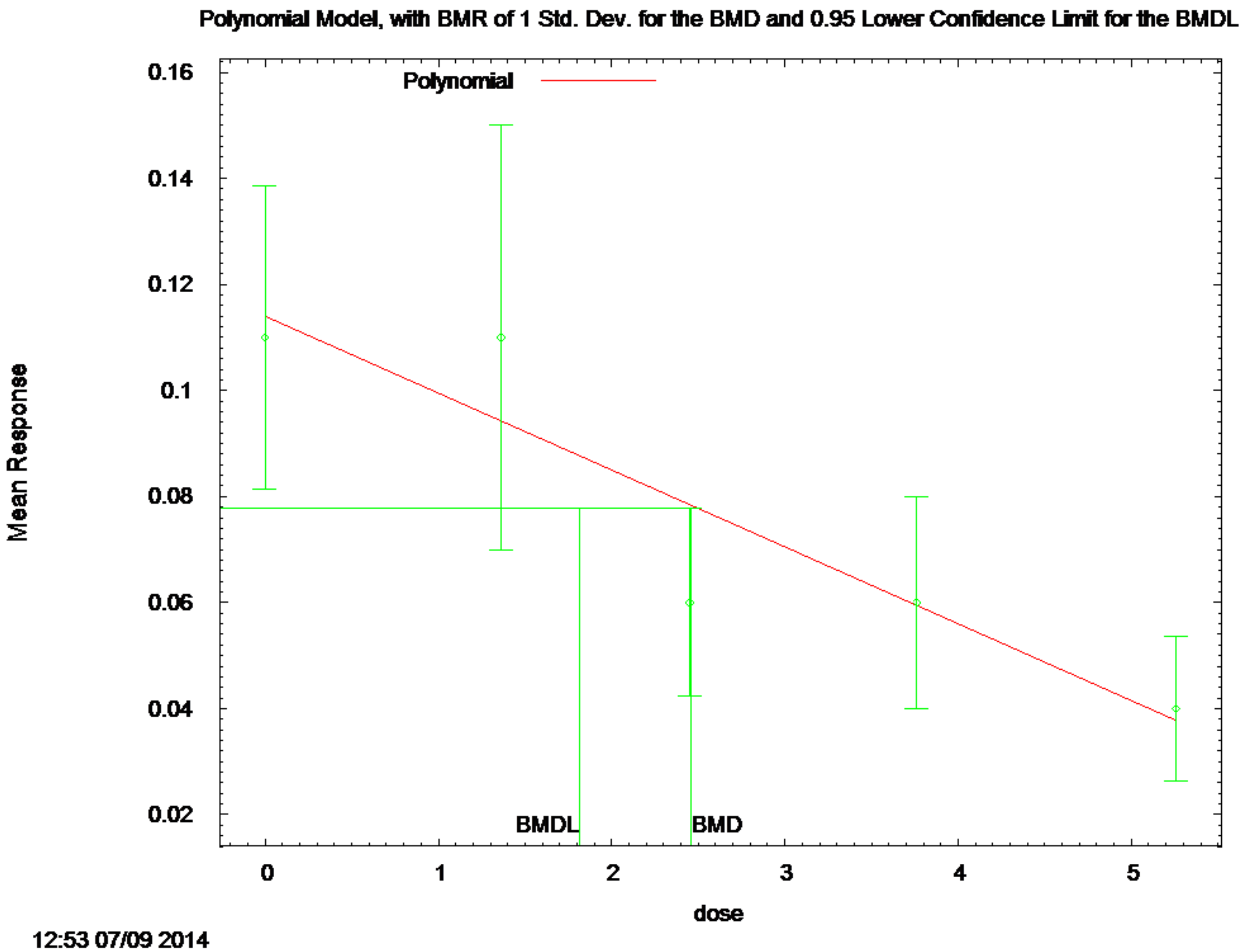
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.59823

BMDL = 2.47874



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:53:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =     0.112441
                         beta_1 =   -0.0010106
                         beta_2 =  -0.00840676
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

```
beta_3
                 have been estimated at a boundary point, or have
been specified by the user,
                 and do not appear in the correlation matrix )

                  alpha       beta_0       beta_1

     alpha            1     3.3e-012    -8.2e-014

    beta_0     3.3e-012            1        -0.81

    beta_1    -8.2e-014        -0.81            1



                                 Parameter Estimates

                                                          95.0%
Wald Confidence Interval
       Variable         Estimate        Std. Err.     Lower Conf.
Limit   Upper Conf. Limit
          alpha       0.00127623      0.000260509
0.000765639          0.00178682
         beta_0         0.113585       0.00874069
0.0964537            0.130717
         beta_1       -0.0145136       0.00277459            -
0.0199517         -0.00907554
         beta_2    -1.86999e-027               NA
         beta_3                0               NA

NA - Indicates that this parameter has hit a bound
     implied by some inequality constraint and thus
     has no standard error.



     Table of Data and Estimated Values of Interest

 Dose       N    Obs Mean     Est Mean   Obs Std Dev  Est Std Dev
Scaled Res.
------     ---   --------     --------   -----------  -----------
----------

    0    10       0.11        0.114         0.04       0.0357
-0.317
1.361    10       0.11       0.0938        0.056       0.0357
1.43
2.451     9       0.06        0.078        0.023       0.0357
-1.51
3.761     9       0.06        0.059        0.026       0.0357
0.084
5.258    10       0.04       0.0373        0.019       0.0357
```

0.241

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	135.932325	3	-265.864651
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	4.72762	3	0.1929

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

Specified effect = 1

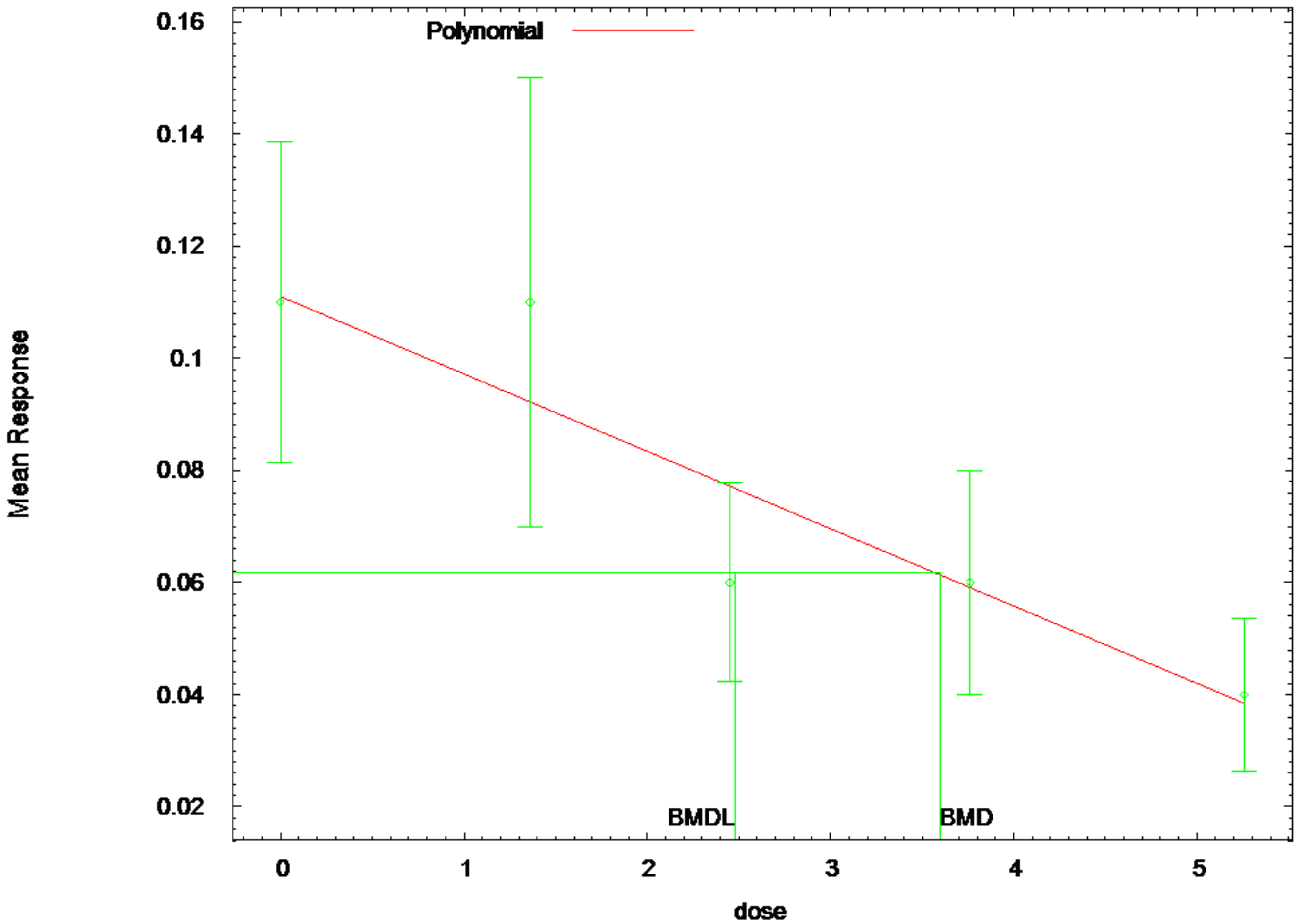
Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.46143

BMDL = 1.81322

Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly3NCV-1SD-5d.plt
                                      Wed Jul 09 12:53:09 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =     0.112441
                         beta_1 =   -0.0010106
                         beta_2 =  -0.00840676
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.073	0.086
rho	0.99	1	-0.073	0.087
beta_0	-0.073	-0.073	1	-0.92
beta_1	0.086	0.087	-0.92	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-1.68252	1.47799	-4.57932	1.21429
rho	1.97134	0.555285	0.883005	3.05968
beta_0	0.111471	0.0102095	0.0914608	0.131481
beta_1	-0.0137839	0.00240468	-0.018497	-0.00907085
beta_2	-9.34995e-028	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.111	0.04	0.0496	-0.0938
1.361	10	0.11	0.0927	0.056	0.0414	1.32
2.451	9	0.06	0.0777	0.023	0.0347	-1.53

```
3.761     9       0.06       0.0596        0.026       0.0268
0.0415
5.258    10       0.04        0.039        0.019       0.0176
0.18
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	141.105082	4	-274.210164
R	125.105720	2	-246.211439

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571

Test 4	8.77444	3	0.03245

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

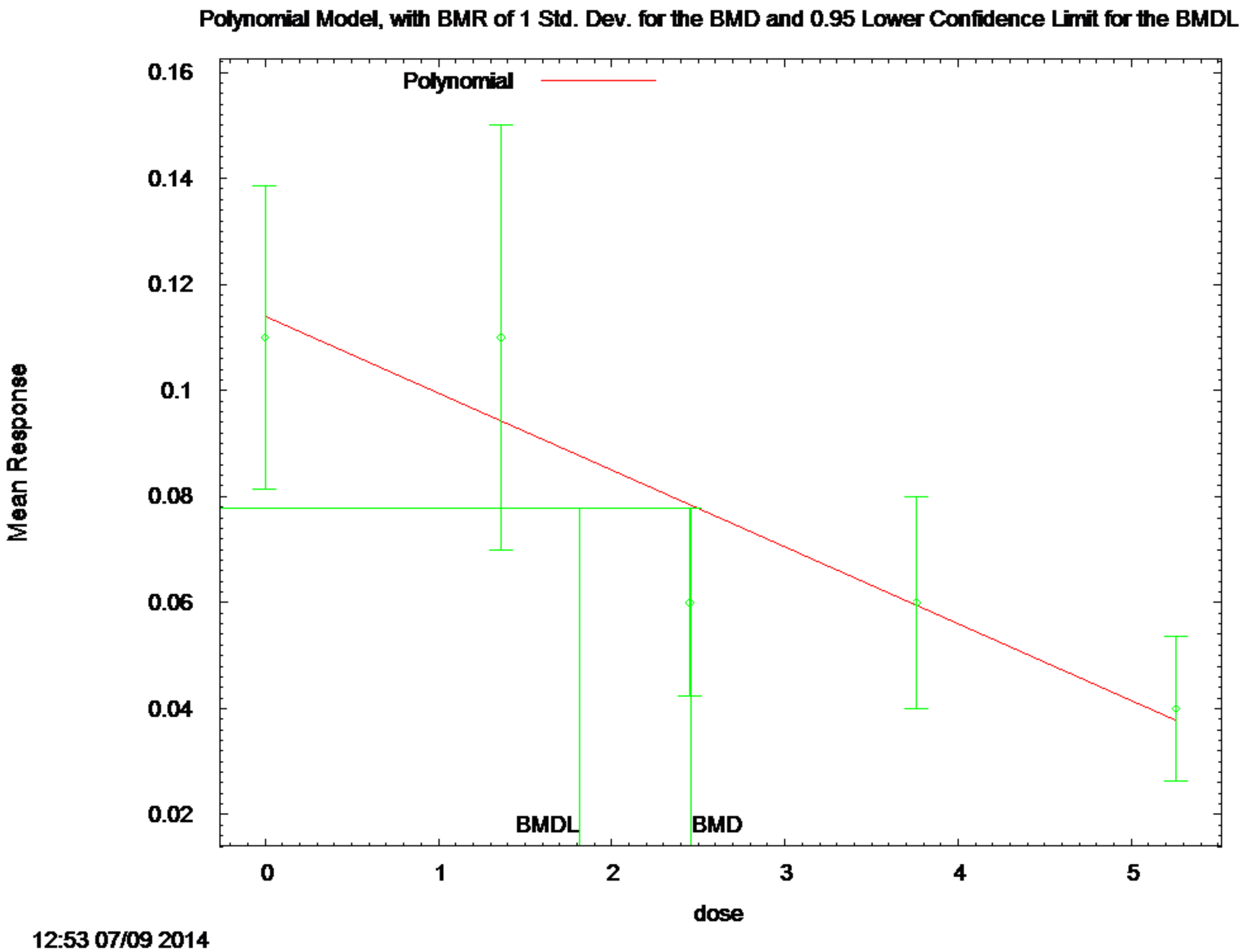
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.59822

BMDL = 2.47874


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:53:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                         beta_0 =         0.11
                         beta_1 =            0
                         beta_2 =    -0.111453
                         beta_3 =            0
                         beta_4 =  -0.00307798


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.2e-008	-6.8e-009
beta_0	1.2e-008	1	-0.81
beta_1	-6.8e-009	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00127623	0.000260509	0.000765639	0.00178682
beta_0	0.113585	0.00874069	0.0964537	0.130717
beta_1	-0.0145136	0.00277459	-0.0199517	-0.00907554
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.114	0.04	0.0357	-0.317
1.361	10	0.11	0.0938	0.056	0.0357	1.43
2.451	9	0.06	0.078	0.023	0.0357	-1.51
3.761	9	0.06	0.059	0.026	0.0357	

0.084
5.258 10 0.04 0.0373 0.019 0.0357
0.241

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	135.932325	3	-265.864651
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	4.72762	3	0.1929

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

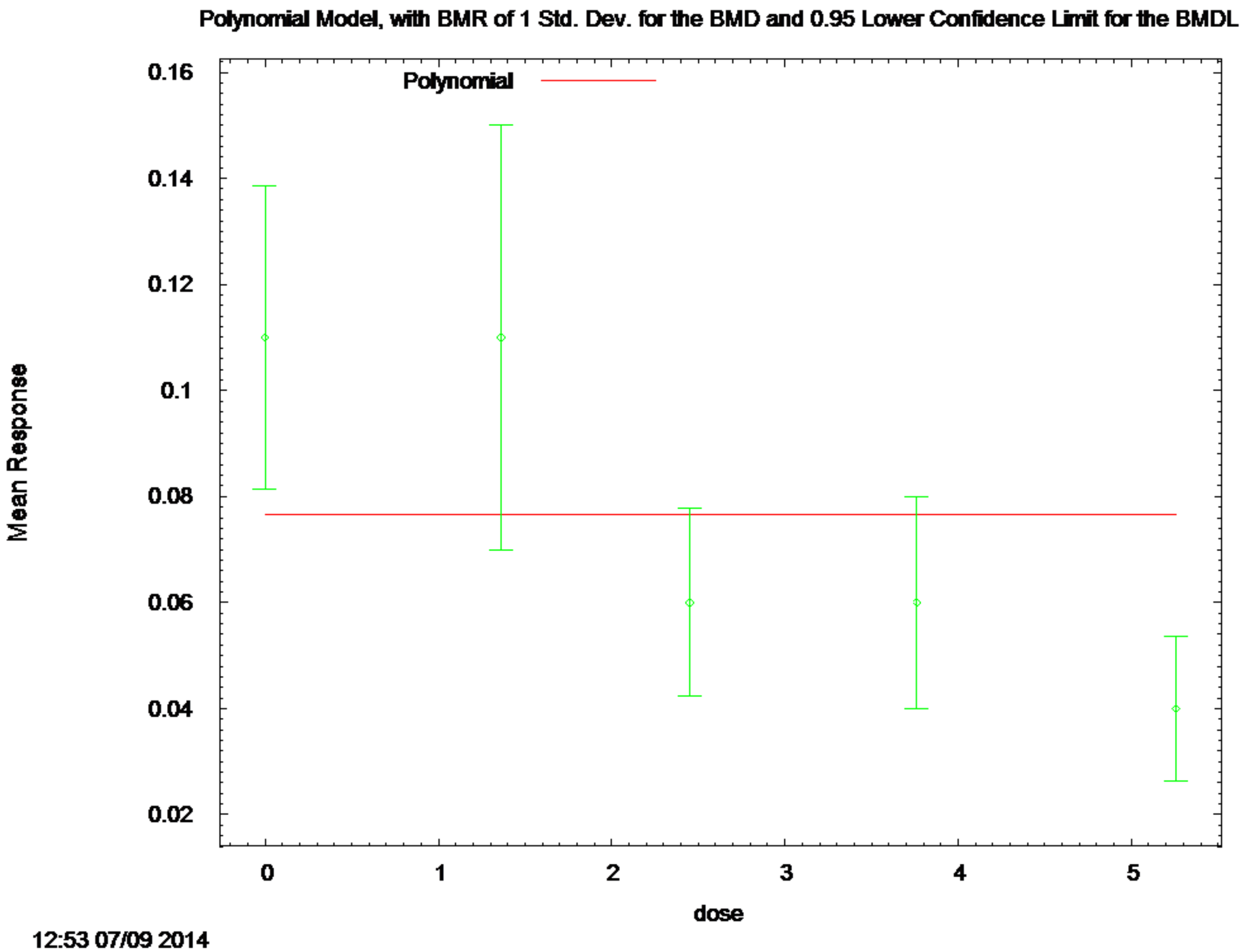
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.46143

BMDL = 1.81322


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
1
2
3
4
5
dose
12:53 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_LUC_Concurren_Ln/LUC_concurrent-
HLS 2001-LUC count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:53:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                         beta_0 =         0.11
                         beta_1 =            0
                         beta_2 =    -0.111453
                         beta_3 =            0
                         beta_4 =  -0.00307798


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_1 -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0
lalpha	NA	NA	NA
rho	NA	NA	NA
beta_0	NA	NA	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-244.198	NA	NA	NA
rho	-92.6629	NA	NA	NA
beta_0	0.0766667	NA	NA	NA
beta_1	0	NA		
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

At least some variance estimates are negative.
THIS USUALLY MEANS THE MODEL HAS NOT CONVERGED!
Try again from another starting point.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.0767	0.04	0.0448	2.35
1.361	10	0.11	0.0767	0.056	0.0448	2.35
2.451	9	0.06	0.0767	0.023	0.0448	-1.12

```
3.761     9       0.06       0.0767        0.026       0.0448
-1.12
5.258    10       0.04       0.0767        0.019       0.0448
-2.59
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	125.105720	3	-244.211439
R	125.105720	2	-246.211439

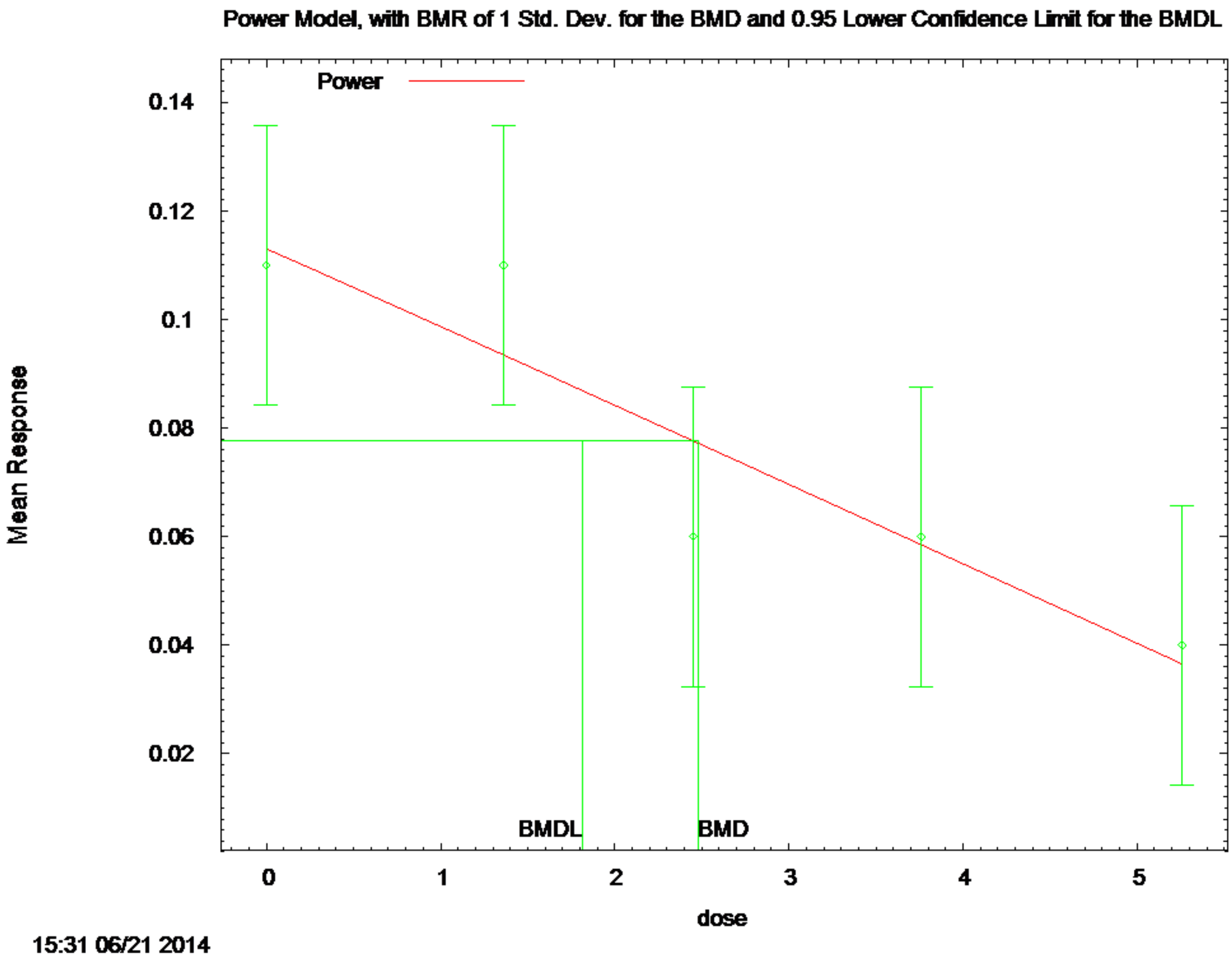
Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571

```
   Test 4              40.7732          4          <.0001

The p-value for Test 1 is less than .05.  There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1.  A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1.  The modeled variance
appears
 to be appropriate here

The p-value for Test 4 is less than .1.  You may want to try a
different
model

BMD computation failed for BMR =      0.0319035
Setting BMD = 100*(maximum dose)

             Benchmark Dose Computation

Specified effect =             1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =          0.95

             BMD =          -9999


BMDL computation failed.
```



Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
0.14
0.12
0.1
0.08
0.06
0.04
0.02
Mean Response
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
====================================================================
===
        Power Model. (Version: 2.18;  Date: 05/19/2014)
        Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
PowerCV-1SD-5d.(d)
        Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
PowerCV-1SD-5d.plt
                                        Sat Jun 21 15:31:12 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =     0.001291
                            rho =            0   Specified
                        control =         0.11
                          slope =    -0.592187
                          power =     -1.28654


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope	power
alpha	1	3.7e-007	-5.2e-007	-5.1e-007
control	3.7e-007	1	-0.73	-0.56
slope	-5.2e-007	-0.73	1	0.96
power	-5.1e-007	-0.56	0.96	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00127621	0.000260506	0.000765631	0.0017868
control	0.113451	0.0105385	0.092796	0.134106
slope	-0.0143078	0.0094404	-0.0328106	0.00419509
power	1.00832	0.367697	0.287652	1.729

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.113	0.04	0.0357	-0.305
1.361	10	0.11	0.0939	0.056	0.0357	1.42
2.451	9	0.06	0.0781	0.023	0.0357	-1.52
3.761	9	0.06	0.059	0.026	0.0357	0.0804
5.258	10	0.04	0.0372	0.019	0.0357	0.25

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	138.296137	6	-264.592275
fitted	135.932584	4	-263.865168
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	15.5751	4	0.003646
Test 4	4.72711	2	0.09409

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

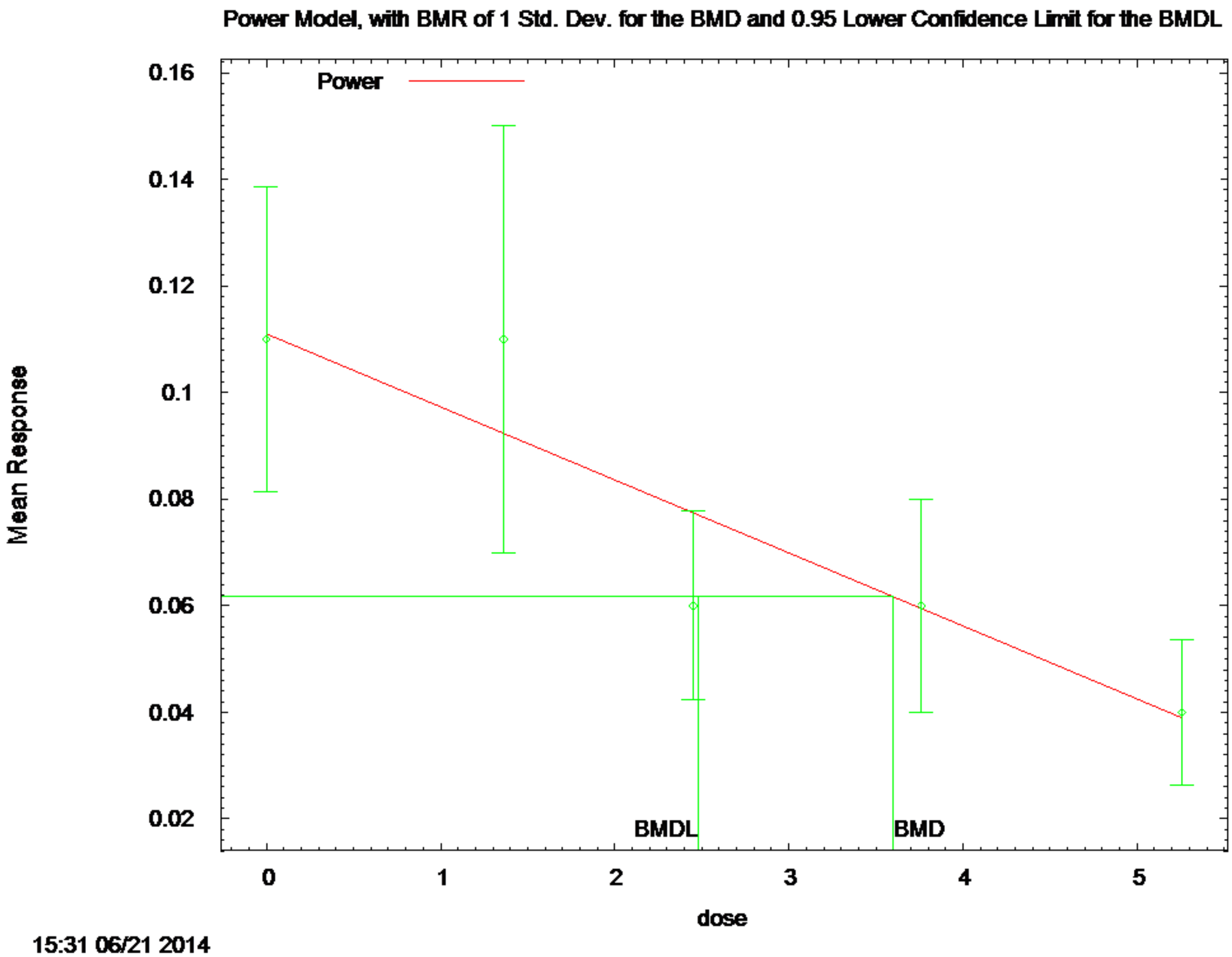
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.47805

BMDL = 1.81327


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
BMDL
BMD
0
1
2
3
4
5
dose
15:31 06/21 2014

```
==================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Ln/LUC_concurrent-HLS 2001-LUC count-
PowerNCV-1SD-5d.plt
                                      Sat Jun 21 15:31:13 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -6.65234
                            rho =            0
                        control =         0.11
                          slope =    -0.592187
                          power =     -1.28654


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho      control        slope
power
```

lalpha	1	0.99	-0.39	0.19	0.058
rho	0.99	1	-0.35	0.19	0.06
control	-0.39	-0.35	1	-0.82	-0.67
slope	0.19	0.19	-0.82	1	0.97
power	0.058	0.06	-0.67	0.97	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-1.68197	1.81421	-5.23774	1.87381
rho	1.97156	0.68144	0.635958	3.30715
control	0.111423	0.0137997	0.0843765	0.13847
slope	-0.0137341	0.00995796	-0.0332514	0.0057831
power	1.00182	0.353281	0.309397	1.69423

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.11	0.111	0.04	0.0496	-0.0908
1.361	10	0.11	0.0927	0.056	0.0414	1.32
2.451	9	0.06	0.0777	0.023	0.0348	-1.53
3.761	9	0.06	0.0596	0.026	0.0268	0.0398

5.258   10   0.04   0.039   0.019   0.0176
0.181

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
Model A3 uses any fixed variance parameters that were specified by the user

Model R: Yi = Mu + e(i)
Var{e(i)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	138.296137	6	-264.592275
A2	146.083690	10	-272.167381
A3	145.492300	7	-276.984600
fitted	141.105095	5	-272.210190
R	125.105720	2	-246.211439

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	41.9559	8	<.0001
Test 2	15.5751	4	0.003646
Test 3	1.18278	3	0.7571
Test 4	8.77441	2	0.01244

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

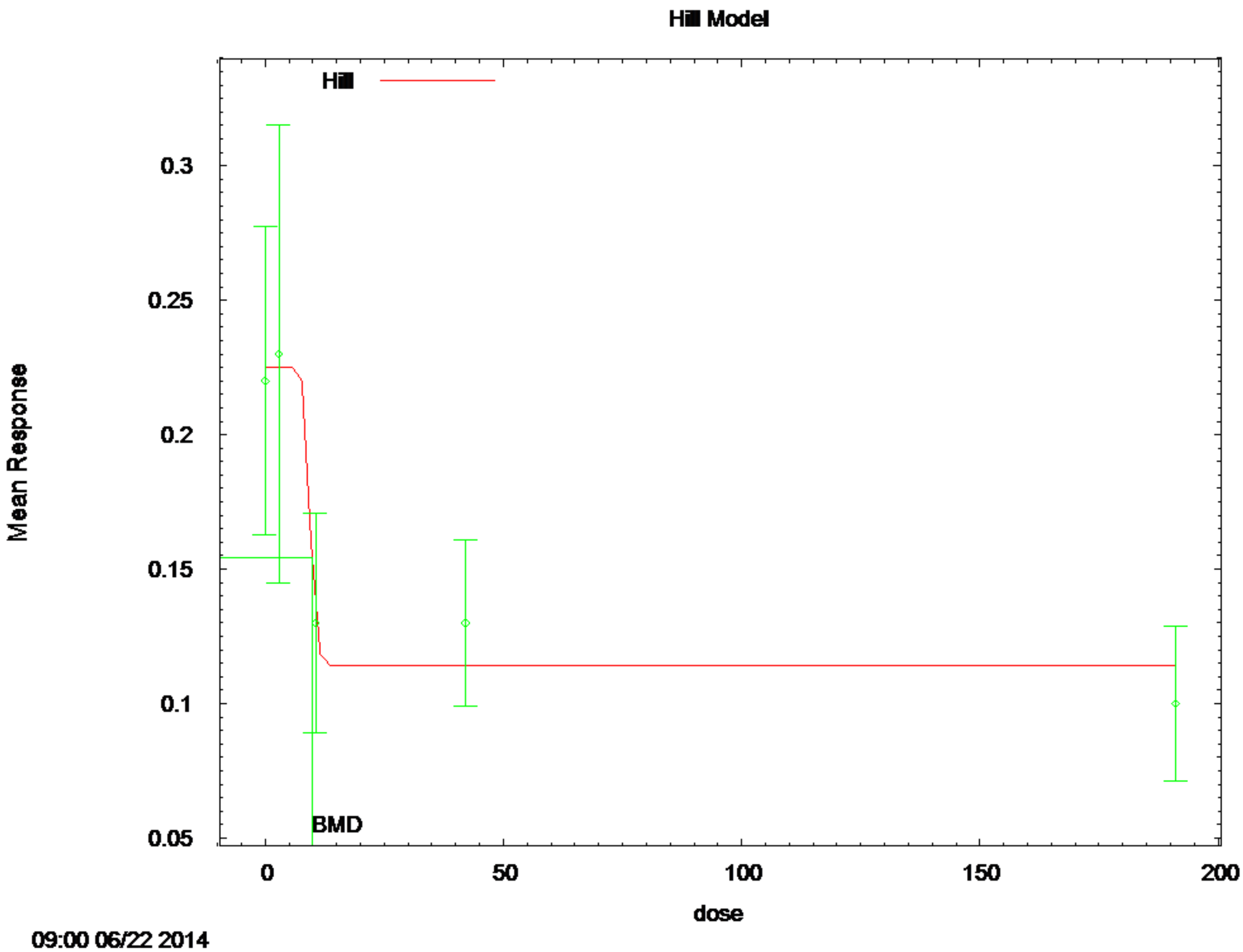
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 3.6015

BMDL = 2.47875

BMDS Model Results for Monocyte Count (Untransformed Doses, Concurrent Controls)



Hill Model
Hill
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-HillCV-1SD-5d.plt
                                        Sun Jun 22 09:00:28 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                      intercept =         0.22
                              v =        -0.12
                              n =      2.57326
                              k =         8.29


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	-2.2e-008	2.7e-008	-2.6e-005	-2.6e-005
intercept	-2.2e-008	1	-0.7	-0.00038	-0.00059
v	2.7e-008	-0.7	1	0.00031	-0.00048
n	-2.6e-005	-0.00038	0.00031	1	1
k	-2.6e-005	-0.00059	-0.00048	1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00498925	0.00101843	0.00299317	0.00698533
intercept	0.225	0.0157944	0.194044	0.255956
v	-0.110789	0.0226286	-0.155141	-0.0664382
n	15.3673	6667.32	-13052.3	13083.1
k	9.43171	477.861	-927.159	946.023

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.225	0.08	0.0706	-0.224

```
  2.9    10       0.23        0.225        0.119       0.0706
0.224
 10.6     9       0.13         0.13        0.053       0.0706
2.12e-007
   42     9       0.13        0.114         0.04       0.0706
0.671
191.1    10        0.1        0.114         0.04       0.0706
-0.636



 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          103.693409            6    -195.386818
             A2          112.779870           10    -205.559741
             A3          103.693409            6    -195.386818
         fitted          103.211257            5    -196.422513
              R           92.681036            2    -181.362073


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	0.964305	1	0.3261

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

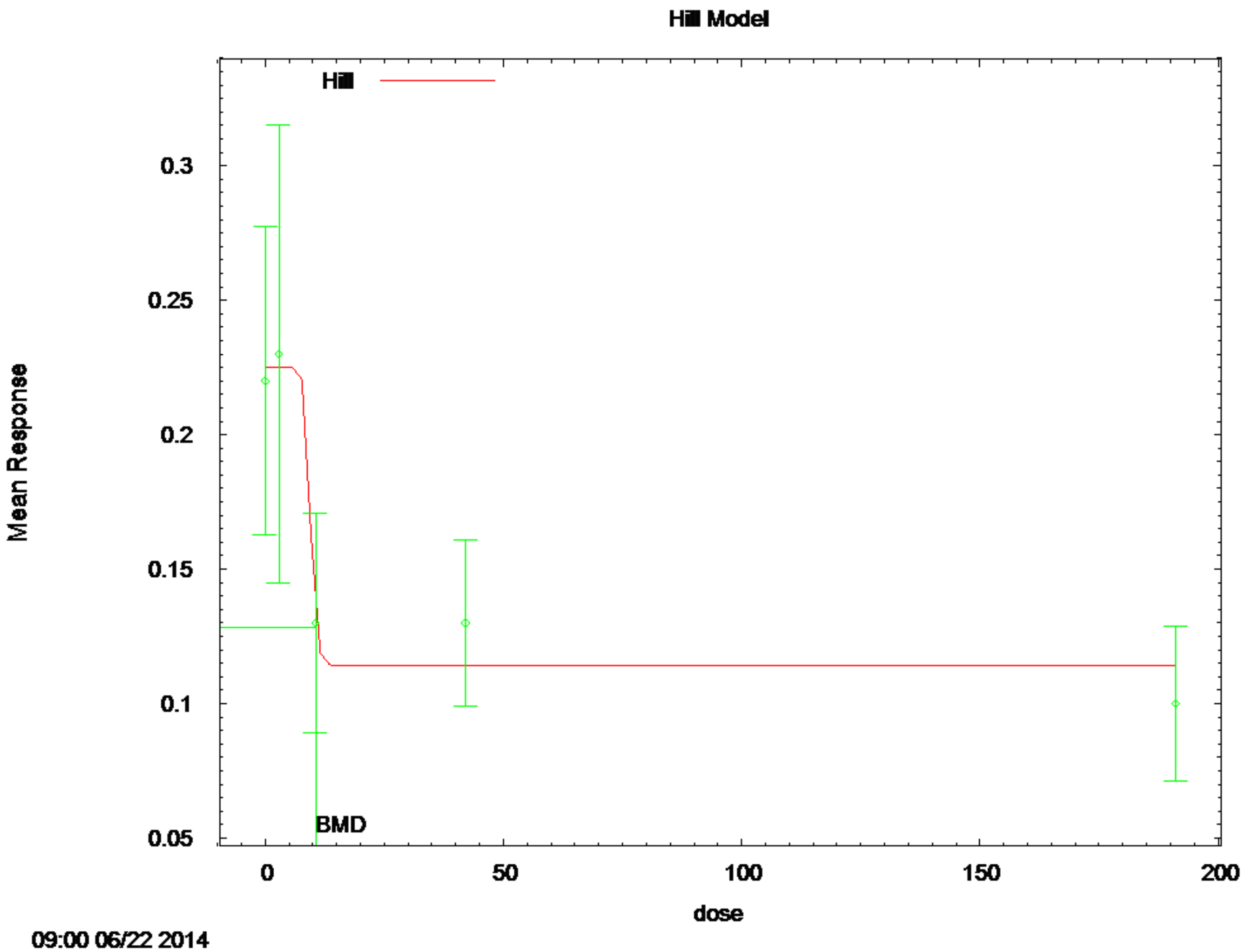
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 9.78479

BMDL computation failed.



Hill Model
Hill
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
=================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-HillNCV-1SD-5d.plt
                                        Sun Jun 22 09:00:29 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                      intercept =         0.22
                              v =        -0.12
                              n =      2.57326
                              k =         8.29


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	0.99	-0.53	0.59	-2.8e-005	0.00016
rho	0.99	1	-0.47	0.56	-2.4e-005	0.00016
intercept	-0.53	-0.47	1	-0.92	-0.00011	-0.00052
v	0.59	0.56	-0.92	1	0.00014	0.0002
n	-2.8e-005	-2.4e-005	-0.00011	0.00014	1	1
k	0.00016	0.00016	-0.00052	0.0002	1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.920071	1.51601	-3.89139	2.05125
rho	2.51647	0.795521	0.957276	4.07566
intercept	0.22479	0.0215475	0.182558	0.267022
v	-0.110884	0.0235358	-0.157013	-0.0647546
n	15.4349	4108.6	-8037.27	8068.14
k	9.49312	278.689	-536.728	555.714

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.225	0.08	0.0965	-0.157

2.9	10	0.23	0.225	0.119	0.0965	0.171
10.6	9	0.13	0.131	0.053	0.0489	-0.0614
42	9	0.13	0.114	0.04	0.041	1.18
191.1	10	0.1	0.114	0.04	0.041	-1.07

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	110.593061	6	-209.186122
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	2.79513	1	0.09455

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

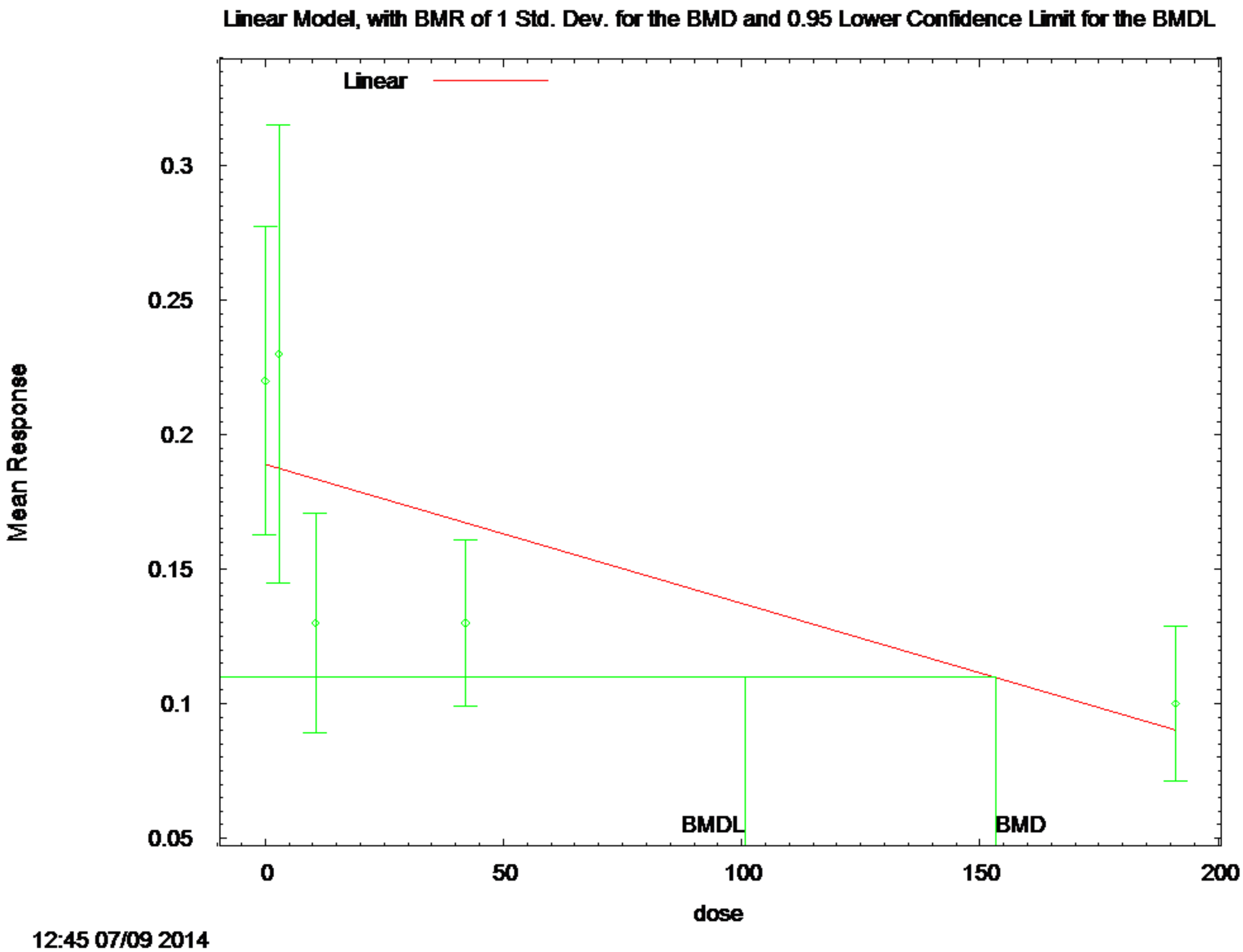
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 10.7399

BMDL computation failed.



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-LinearCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-LinearCV-1SD-5d.plt
                                      Wed Jul 09 12:45:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =     0.187061
                         beta_1 = -0.000508131


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
been specified by the user,
```

and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.6e-008	-3.5e-008
beta_0	1.6e-008	1	-0.56
beta_1	-3.5e-008	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00628416	0.00128275	0.00377002	0.0087983
beta_0	0.189334	0.0138502	0.162188	0.21648
beta_1	-0.000517126	0.000155222	-0.000821356	-0.000212897

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.189	0.08	0.0793	1.22
2.9	10	0.23	0.188	0.119	0.0793	1.68
10.6	9	0.13	0.184	0.053	0.0793	-2.04
42	9	0.13	0.168	0.04	0.0793	-1.42
191.1	10	0.1	0.0905	0.04	0.0793	0.379

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
Model A2:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:          Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	97.673375	3	-189.346749
R	92.681036	2	-181.362073

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	12.0401	3	0.007247

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a

different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

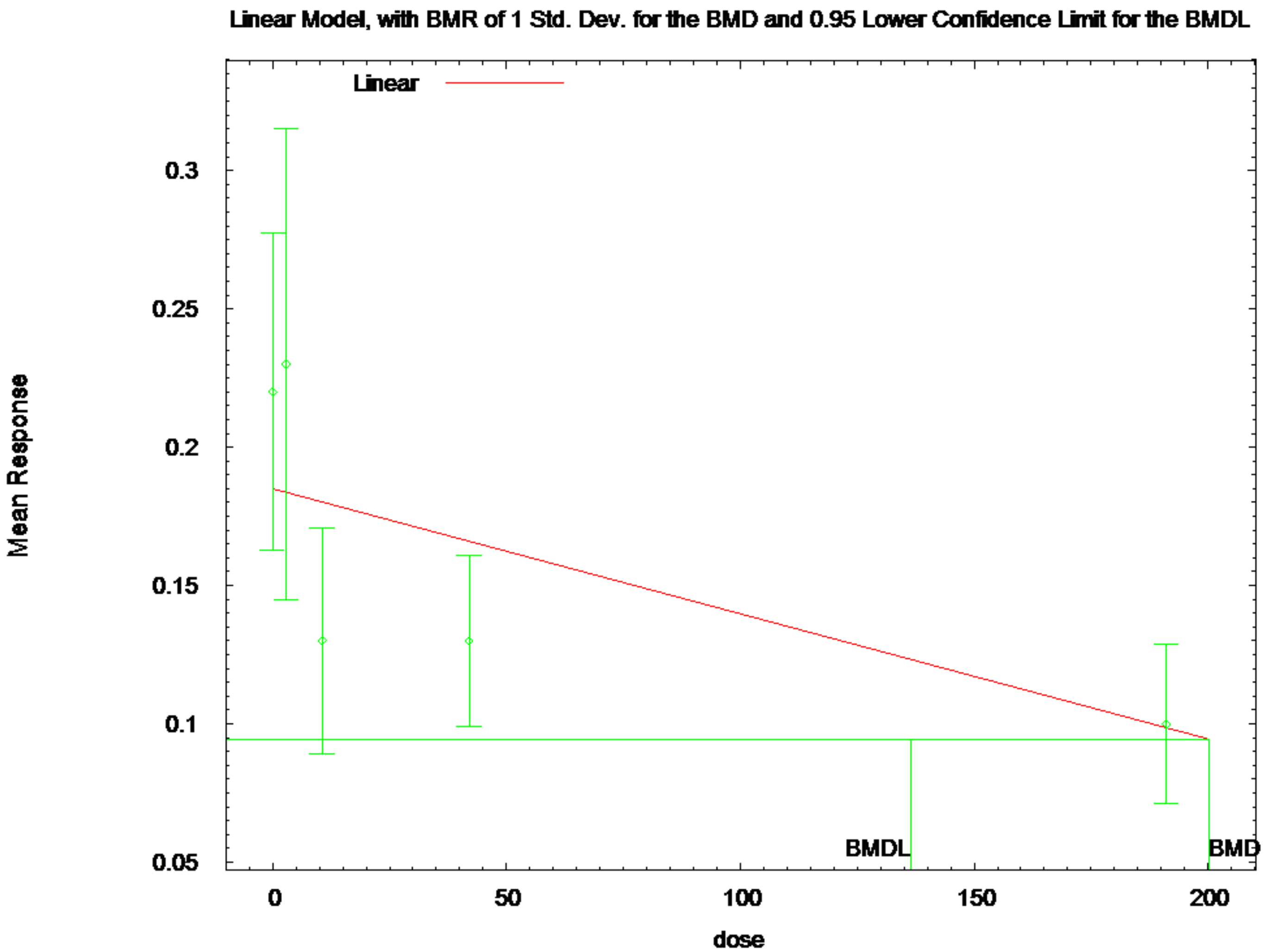
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 153.295

BMDL = 100.721



12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-LinearNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-LinearNCV-1SD-5d.plt
                                      Wed Jul 09 12:45:48 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =     0.187061
                         beta_1 = -0.000508131


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1

    lalpha            1         0.99       -0.037        0.035
```

rho	0.99	1	-0.036	0.033
beta_0	-0.037	-0.036	1	-0.81
beta_1	0.035	0.033	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	0.0784577	1.48211	-2.82642	2.98334
rho	2.89289	0.795215	1.3343	4.45148
beta_0	0.184882	0.015175	0.15514	0.214625
beta_1	-0.000451919	0.000103729	-0.000655225	-0.000248614

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.185	0.08	0.0905	1.23
2.9	10	0.23	0.184	0.119	0.0896	1.64
10.6	9	0.13	0.18	0.053	0.0871	-1.72
42	9	0.13	0.166	0.04	0.0774	-1.39
191.1	10	0.1	0.0985	0.04	0.0364	0.128

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	102.275742	4	-196.551485
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	19.4298	3	0.0002228

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous
variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance
appears

to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

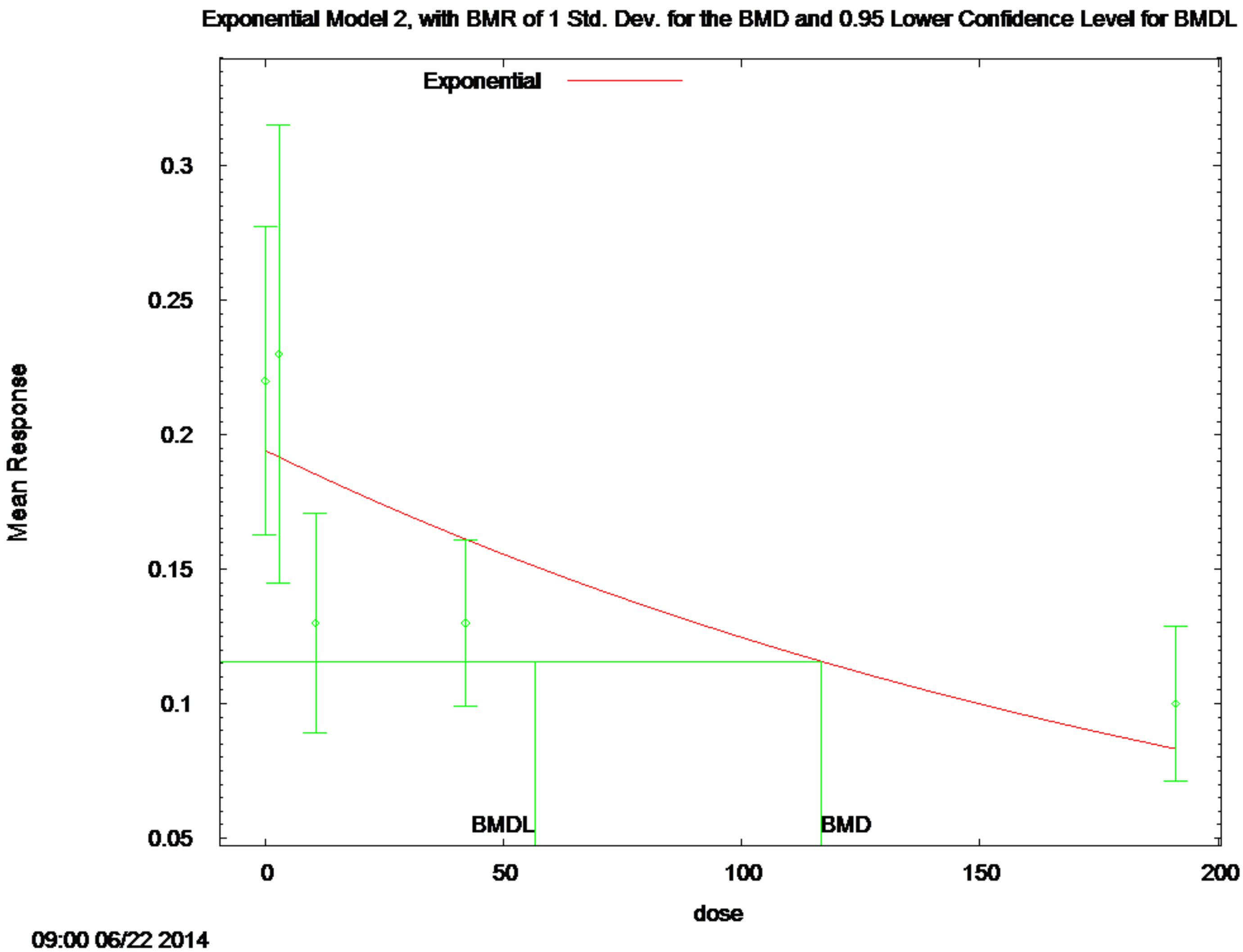
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.254

BMDL = 136.469


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                    Sun Jun 22 09:00:28 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-5.32056
rho(S)	0
a	0.129933
b	0.00346714
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	-5.09159
rho	0
a	0.194195
b	0.00443287
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1942	0.07841	1.041
2.9	0.1917	0.07841	1.544
10.6	0.1853	0.07841	-2.115
42	0.1612	0.07841	-1.194
191.1	0.08324	0.07841	0.6759

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
2	98.19822	3	-190.3964

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	

< 0.0001
Test 2 18.17 4
0.001142
Test 3 18.17 4
0.001142
Test 4 10.99 3
0.01178

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running
a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to
consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

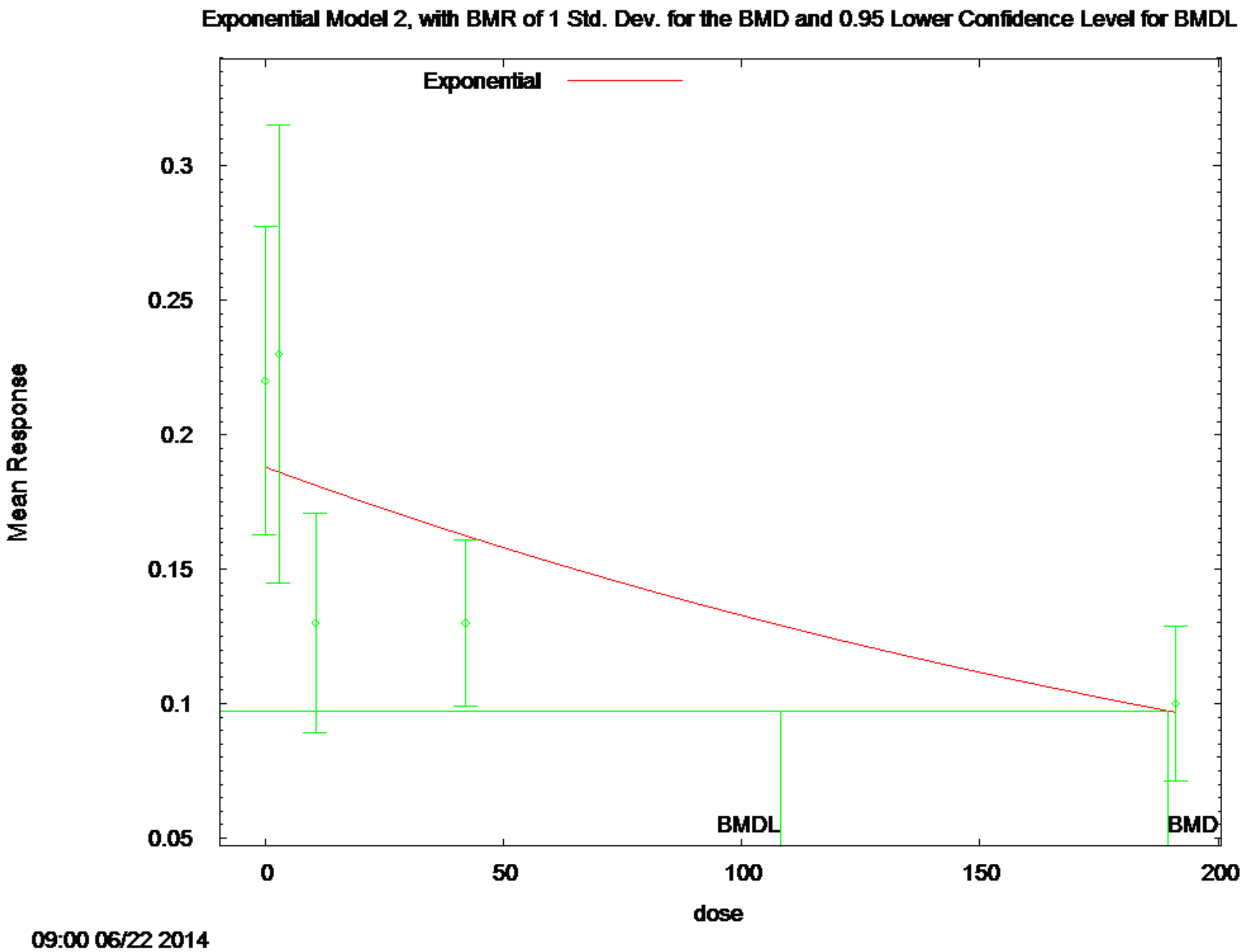
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 116.658

BMDL = 56.7657


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
0
50
100
150
200
dose
BMDL
BMD
09:00 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:00:29 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-1.08858
rho	2.4145
a	0.129933
b	0.00346714
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-0.168436
rho	2.77209
a	0.188
b	0.00347346
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.188	0.09065	1.116
2.9	0.1861	0.08939	1.552
10.6	0.1812	0.08614	-1.783
42	0.1625	0.07406	-1.316
191.1	0.0968	0.03613	0.28

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
2	102.8544	4	-197.7087

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001
Test 2	18.17	4	

0.001142
Test 3 1.578 3
0.6643
Test 4 18.27 3
0.0003864

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous
variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled
variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately
describe the data; you may want to consider another model.

Benchmark Dose Computations:

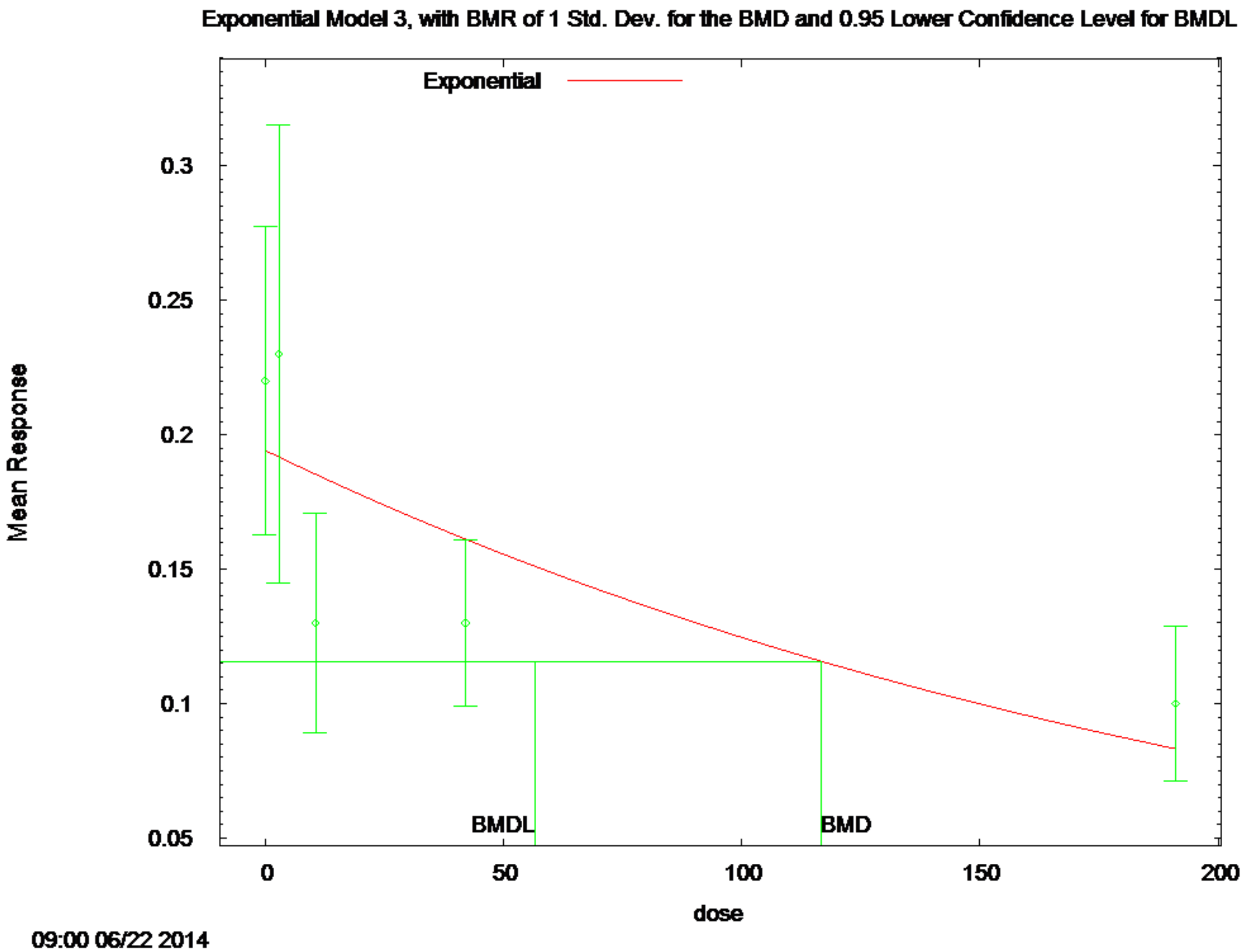
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 189.478

BMDL = 108.159



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:00:28 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-5.32056
rho(S)	0
a	0.129933
b	0.00346714
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	-5.09159
rho	0
a	0.194195
b	0.00443287
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.1942	0.07841	1.041
2.9	0.1917	0.07841	1.544
10.6	0.1853	0.07841	-2.115
42	0.1612	0.07841	-1.194
191.1	0.08324	0.07841	0.6759

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
3	98.19822	3	-190.3964

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 5a	10.99	3	0.01178

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

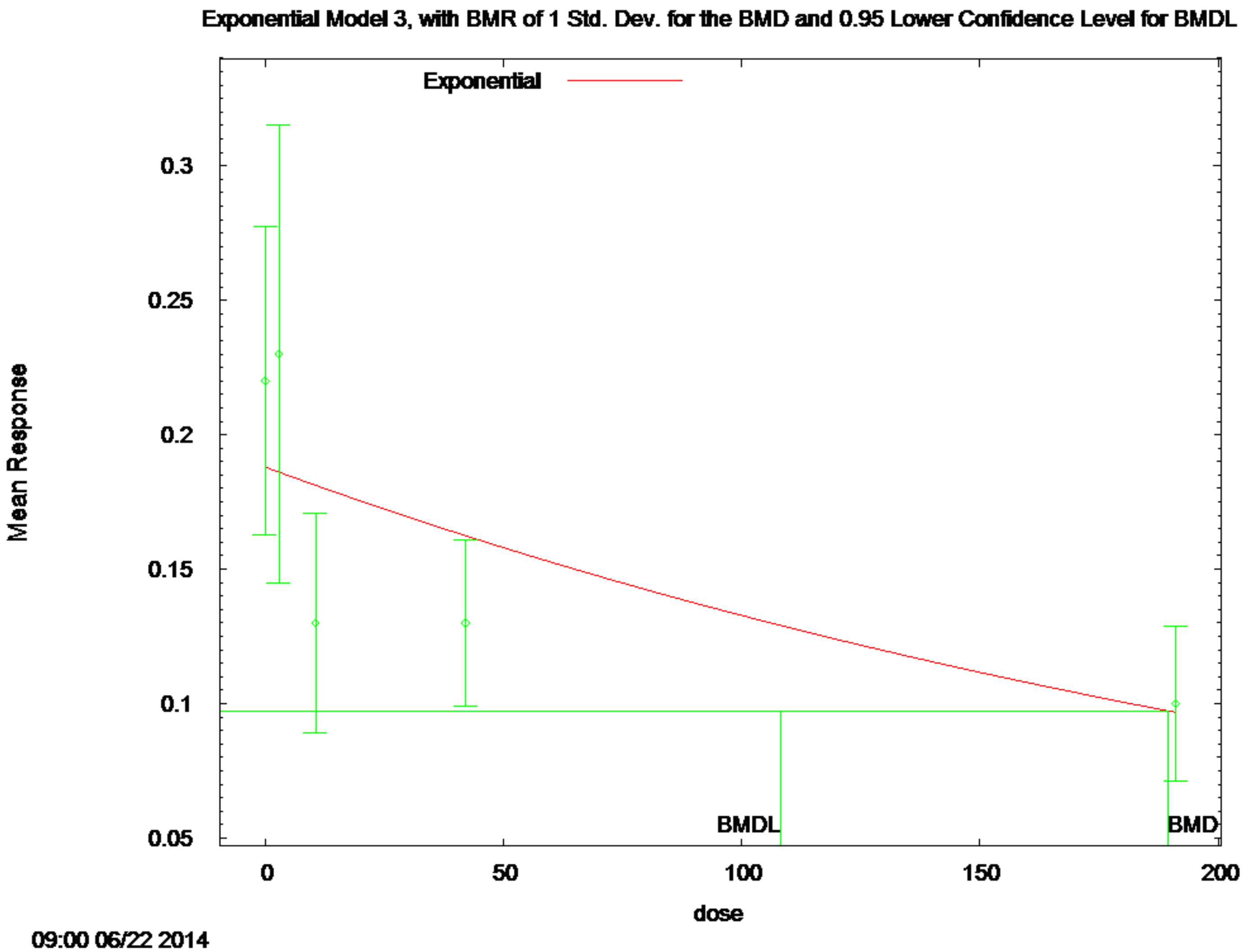
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 116.658

BMDL = 56.7657



Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:00:29 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-1.08858
rho	2.4145
a	0.32003
b	4.68914e-005
c	0
d	2

Parameter Estimates

Variable	Model 3
lnalpha	-0.168453
rho	2.77208
a	0.188
b	0.00347346
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.188	0.09065	1.116
2.9	0.1861	0.08939	1.552
10.6	0.1812	0.08614	-1.783
42	0.1625	0.07406	-1.316
191.1	0.0968	0.03613	0.28

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
3	102.8544	4	-197.7087

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 5a	18.27	3	0.0003864

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

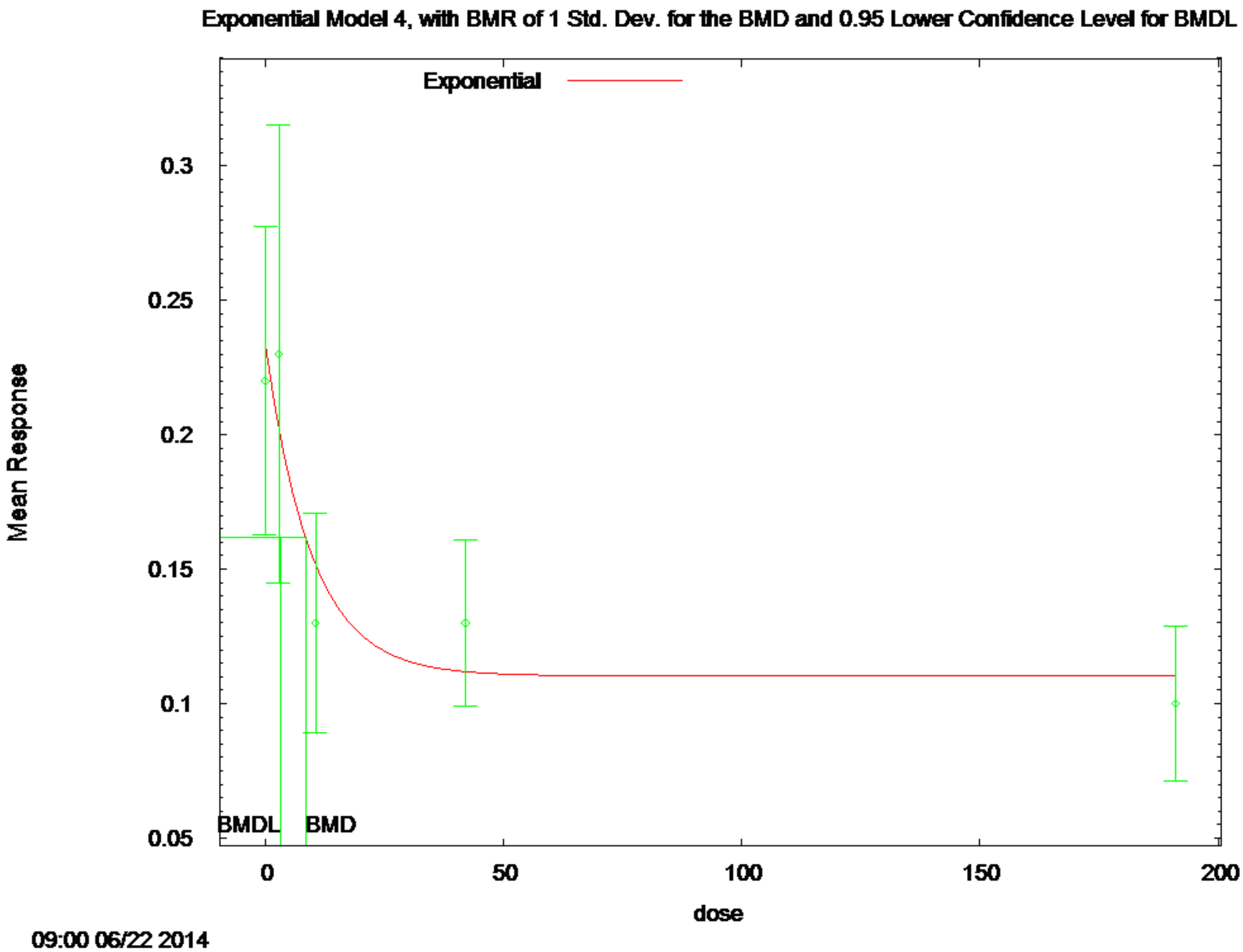
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 189.477

BMDL = 108.159


Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                    Sun Jun 22 09:00:28 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-5.32056
rho(S)	0
a	0.2415
b	0.0190159
c	0.394361
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	-5.24649
rho	0
a	0.23437
b	0.103831
c	0.470786
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2344	0.07257	-0.6262
2.9	0.2021	0.07257	1.215
10.6	0.1516	0.07257	-0.893
42	0.1119	0.07257	0.7474
191.1	0.1103	0.07257	-0.4505

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
4	101.9157	4	-195.8314

Additive constant for all log-likelihoods =   -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 6a	3.555	2	0.169

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

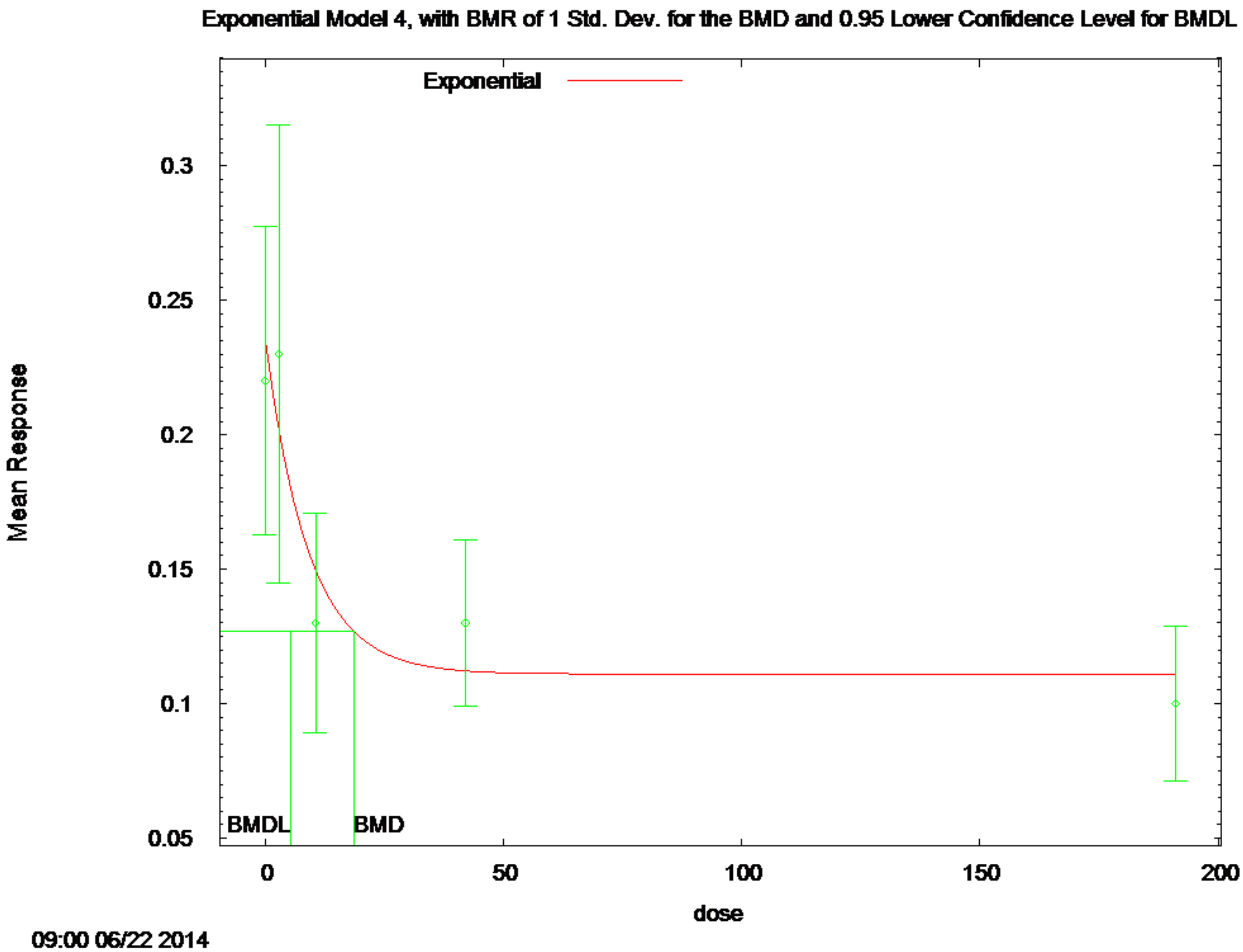
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 8.47184

BMDL = 3.37129



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:00:29 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-1.08858
rho	2.4145
a	0.2415
b	0.0190159
c	0.394361
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-0.648692
rho	2.61787
a	0.235853
b	0.110756
c	0.470676
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2359	0.1091	-0.4593
2.9	0.2016	0.08885	1.012
10.6	0.1496	0.06014	-0.9778
42	0.1122	0.04127	1.294
191.1	0.111	0.0407	-0.8555

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
                Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
                Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
                Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
4	108.3631	5	-206.7262

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 6a	7.255	2	0.02658

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

Specified Effect = 1.000000

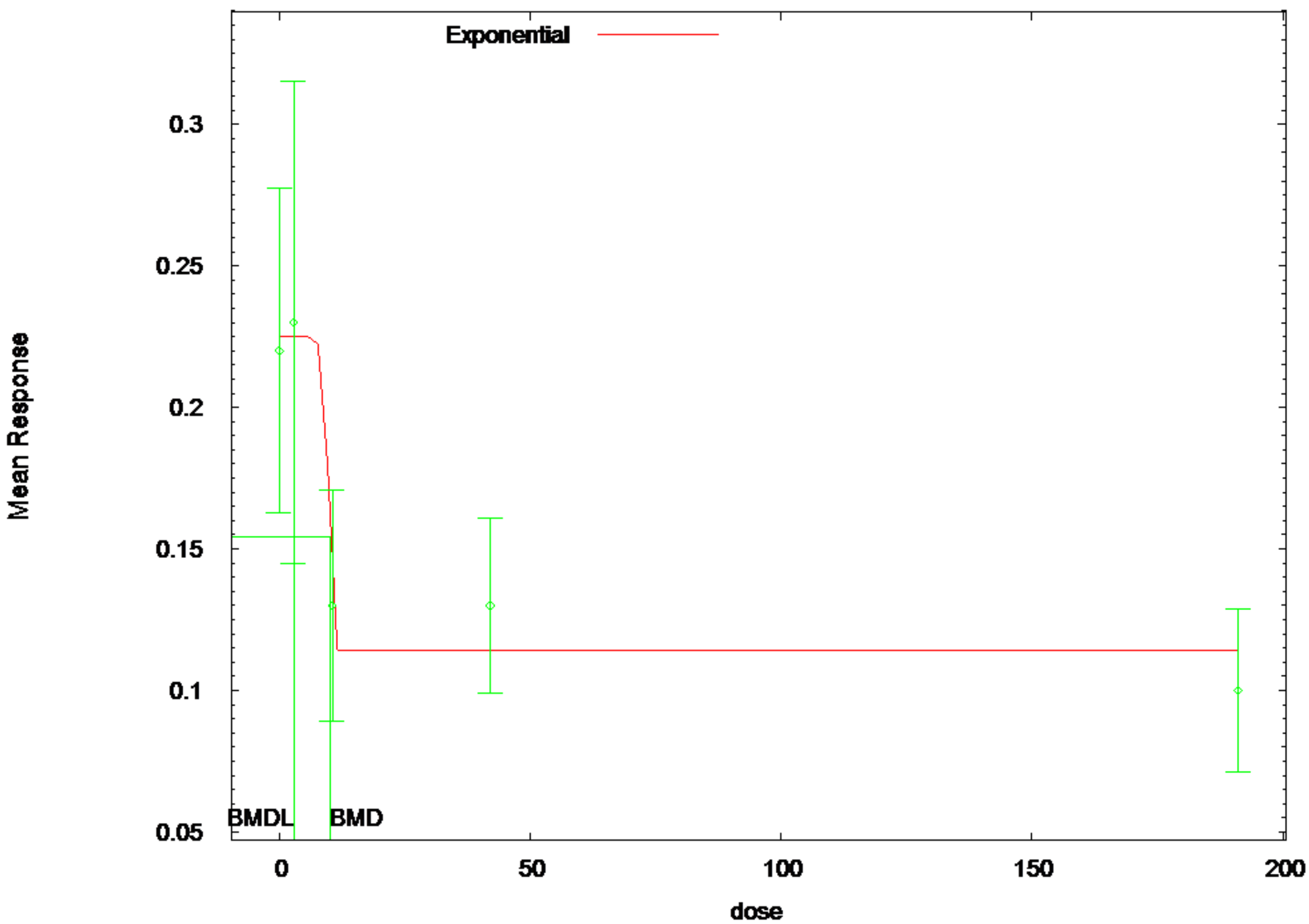
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 18.7165

BMDL = 5.48116

Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:00 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                    Sun Jun 22 09:00:28 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-5.32056
rho(S)	0
a	0.2415
b	0.0190159
c	0.394361
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	-5.30047
rho	0
a	0.225
b	0.0989556
c	0.507602
d	13.9617

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.225	0.07063	-0.2238
2.9	0.225	0.07063	0.2238
10.6	0.13	0.07063	3.526e-007
42	0.1142	0.07063	0.6706
191.1	0.1142	0.07063	-0.6362

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

```
     Model A2:         Yij = Mu(i) + e(ij)
              Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
              Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
              Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
5	103.2113	5	-196.4225

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 7a	0.9643	1	0.3261

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

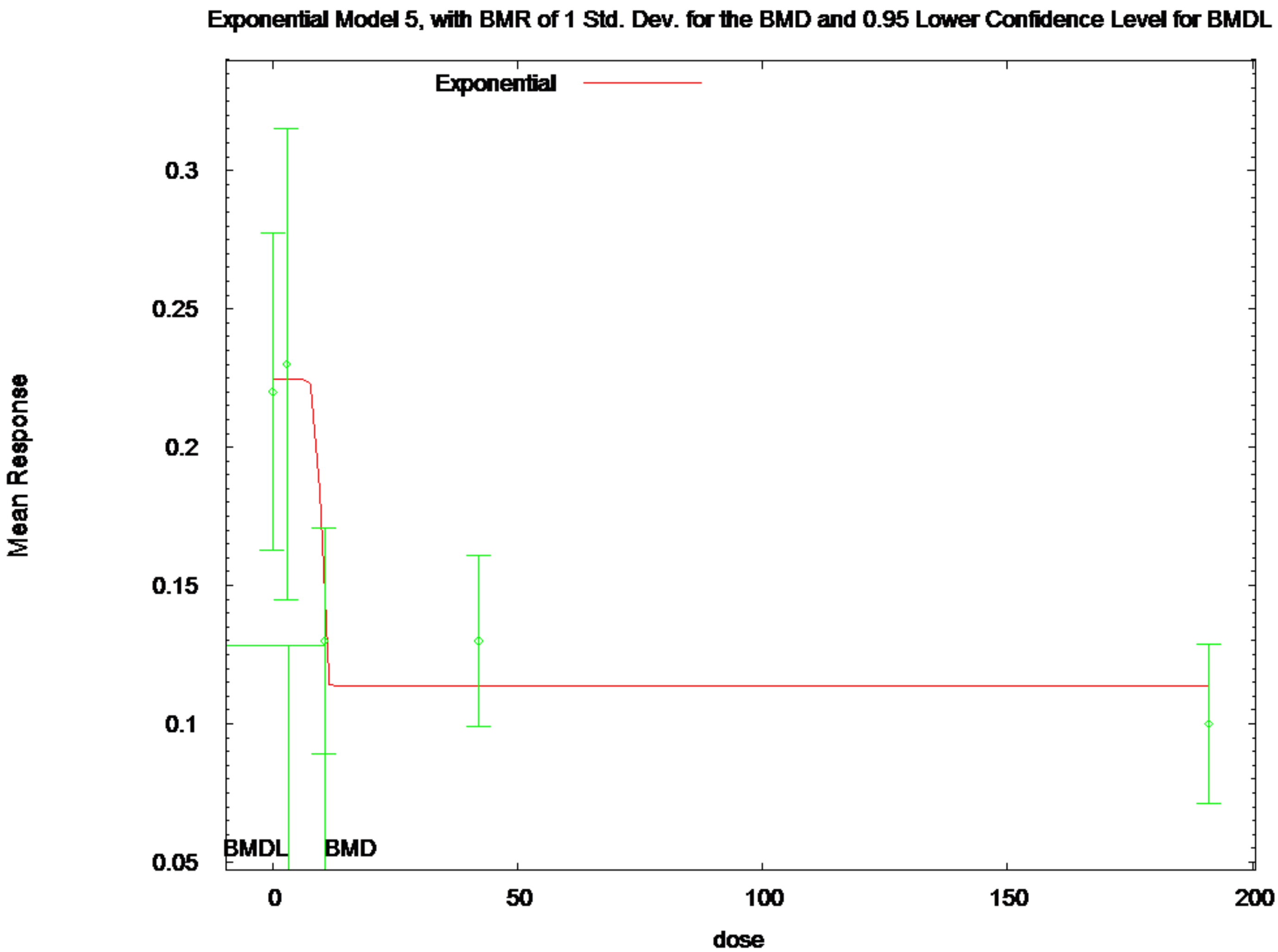
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 10.1162

BMDL = 3.02618



09:00 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:00:29 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-1.08858
rho	2.4145
a	0.2415
b	0.0190159
c	0.394361
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-0.920072
rho	2.51647
a	0.22479
b	0.0983632
c	0.506722
d	14.9831

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
2.9	10	0.23	0.119
10.6	9	0.13	0.053
42	9	0.13	0.04
191.1	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2248	0.09651	-0.1569
2.9	0.2248	0.09651	0.1707
10.6	0.131	0.04893	-0.06137
42	0.1139	0.04103	1.177
191.1	0.1139	0.04103	-1.072

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
5	110.5931	6	-209.1861

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 7a	2.795	1	0.09455

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

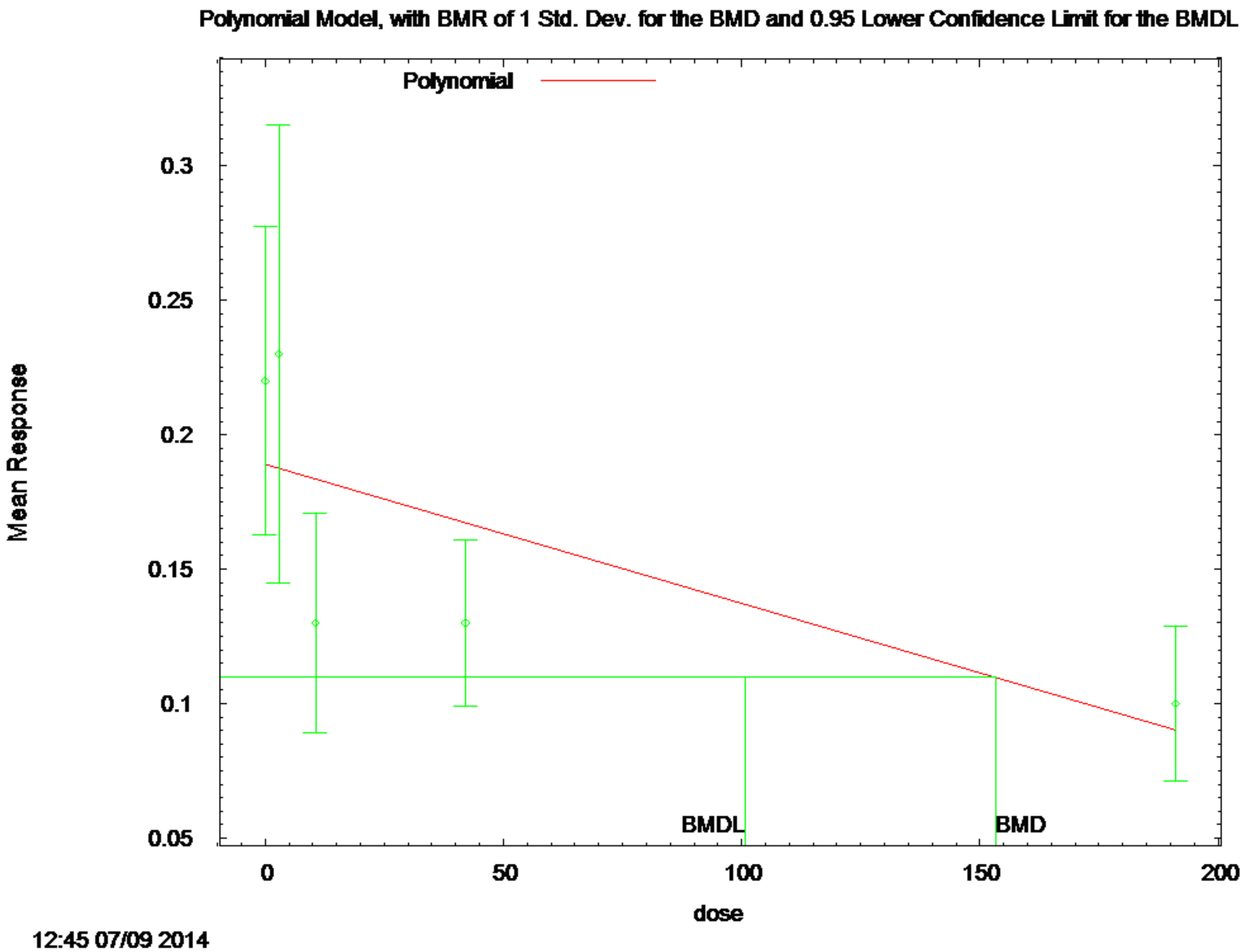
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 10.663

BMDL = 3.27746



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly2CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly2CV-1SD-5d.plt
                                      Wed Jul 09 12:45:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =      0.20922
                         beta_1 =  -0.00266808
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	4.2e-008	5.1e-009
beta_0	4.2e-008	1	-0.56
beta_1	5.1e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00628415	0.00128275	0.00377002	0.00879829
beta_0	0.189334	0.0138502	0.162188	0.21648
beta_1	-0.000517126	0.000155222	-0.000821356	-0.000212897
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.189	0.08	0.0793	1.22
2.9	10	0.23	0.188	0.119	0.0793	1.68
10.6	9	0.13	0.184	0.053	0.0793	-2.04
42	9	0.13	0.168	0.04	0.0793	-1.42
191.1	10	0.1	0.0905	0.04	0.0793	0.379

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	97.673375	3	-189.346749
R	92.681036	2	-181.362073

Explanation of Tests

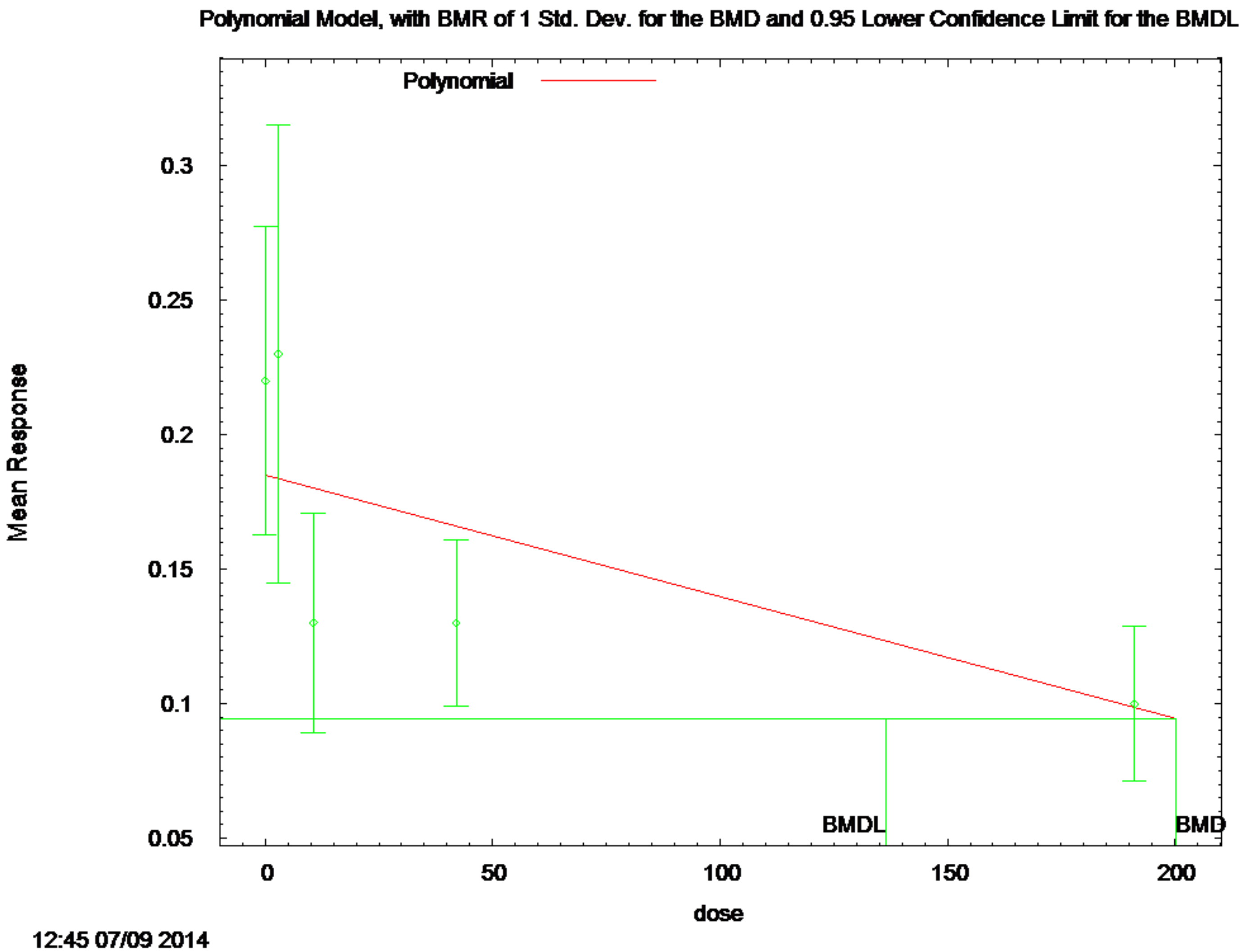
Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	12.0401	3	0.007247

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

```
The p-value for Test 2 is less than .1.  Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1.  You may want to consider
a
different variance model

The p-value for Test 4 is less than .1.  You may want to try a
different
model


             Benchmark Dose Computation

Specified effect =             1

Risk Type        =     Estimated standard deviations from the
control mean

Confidence level =          0.95

             BMD =        153.295


            BMDL =        100.721
```


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
0.3
0.25
0.2
0.15
0.1
0.05
Mean Response
BMDL
BMD
0
50
100
150
200
dose
12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly2NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly2NCV-1SD-5d.plt
                                      Wed Jul 09 12:45:48 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =      0.20922
                         beta_1 =  -0.00266808
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.037	0.035
rho	0.99	1	-0.036	0.033
beta_0	-0.037	-0.036	1	-0.81
beta_1	0.035	0.033	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	0.0784563	1.48211	-2.82642	2.98333
rho	2.89289	0.795215	1.3343	4.45148
beta_0	0.184882	0.015175	0.15514	0.214625
beta_1	-0.000451919	0.000103729	-0.000655225	-0.000248614
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.185	0.08	0.0905	1.23
2.9	10	0.23	0.184	0.119	0.0896	1.64
10.6	9	0.13	0.18	0.053	0.0871	-1.72
42	9	0.13	0.166	0.04	0.0774	-1.39

191.1   10   0.1   0.0985   0.04   0.0364
0.128

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	102.275742	4	-196.551485
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	19.4298	3	0.0002228

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

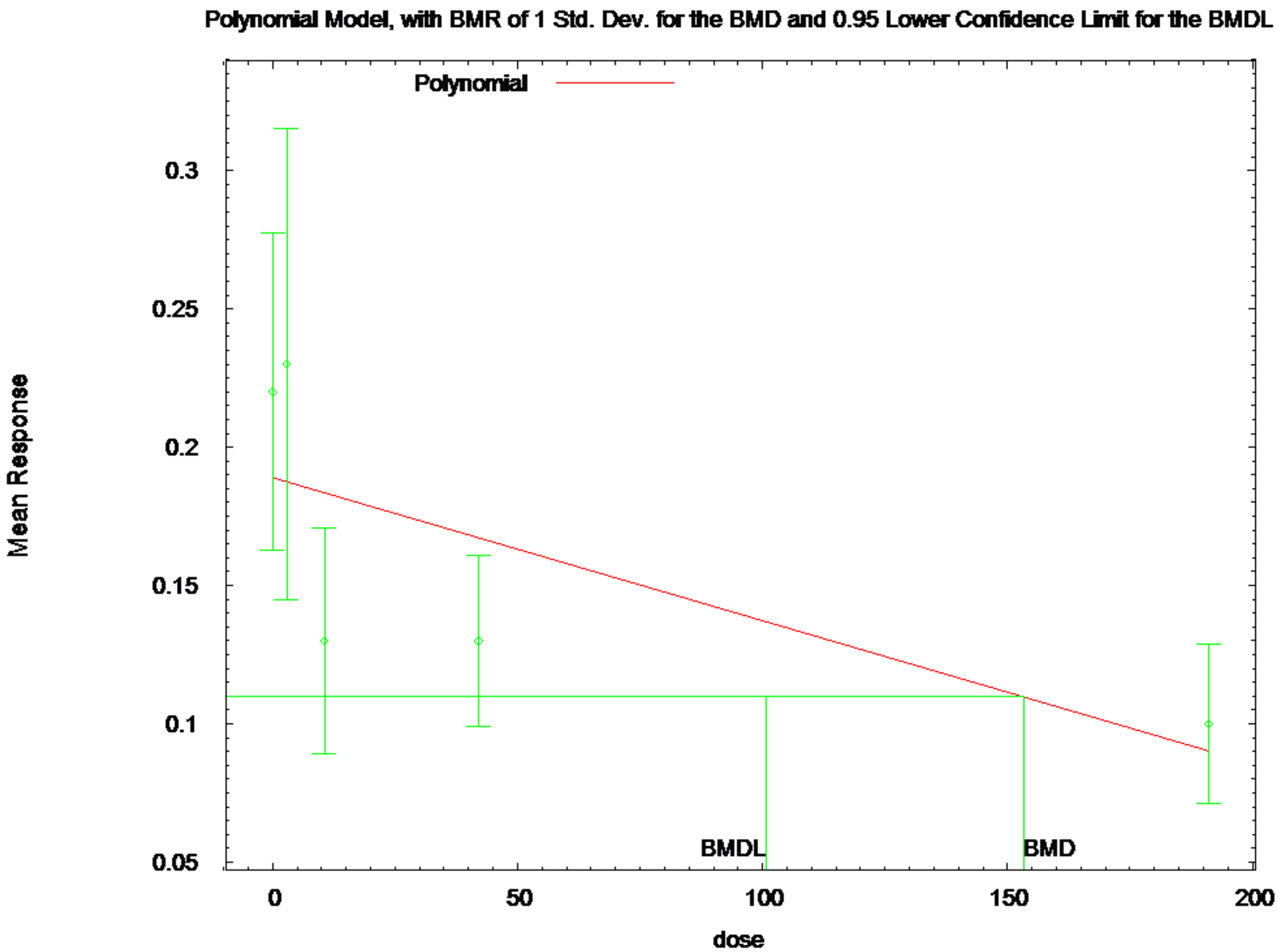
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.254

BMDL = 136.469



12:45 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly3CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly3CV-1SD-5d.plt
                                      Wed Jul 09 12:45:45 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =     0.236994
                         beta_1 =   -0.0119872
                         beta_2 =            0
                         beta_3 = -1.10979e-006


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -beta_2    -
```

beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.4e-009	-1.8e-010
beta_0	-1.4e-009	1	-0.56
beta_1	-1.8e-010	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00628415	0.00128275	0.00377002	0.00879829
beta_0	0.189334	0.0138502	0.162188	0.21648
beta_1	-0.000517126	0.000155222	-0.000821356	-0.000212897
beta_2	-0	NA		
beta_3	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.189	0.08	0.0793	1.22
2.9	10	0.23	0.188	0.119	0.0793	1.68
10.6	9	0.13	0.184	0.053	0.0793	-2.04
42	9	0.13	0.168	0.04	0.0793	-1.42
191.1	10	0.1	0.0905	0.04	0.0793	

0.379

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	97.673375	3	-189.346749
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	12.0401	3	0.007247

The p-value for Test 1 is less than .05. There appears to be a

difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

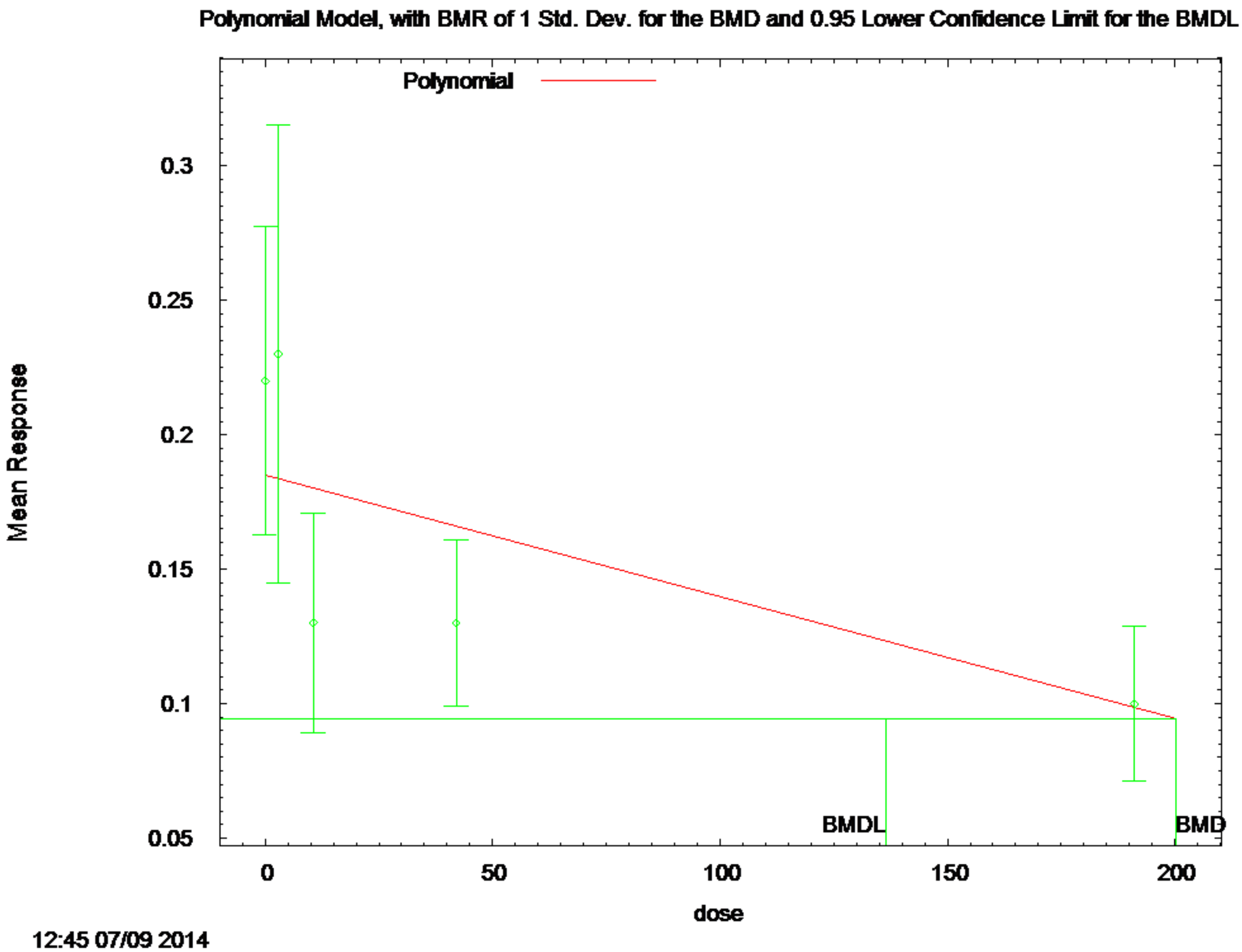
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 153.295

BMDL = 100.721


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
12:45 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly3NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly3NCV-1SD-5d.plt
                                       Wed Jul 09 12:45:47 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =     0.236994
                         beta_1 =   -0.0119872
                         beta_2 =            0
                         beta_3 = -1.10979e-006


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -beta_2    -beta_3
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.037	0.035
rho	0.99	1	-0.036	0.033
beta_0	-0.037	-0.036	1	-0.81
beta_1	0.035	0.033	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	0.0784582	1.48211	-2.82642	2.98333
rho	2.89289	0.795215	1.3343	4.45148
beta_0	0.184882	0.015175	0.15514	0.214625
beta_1	-0.000451919	0.000103729	-0.000655224	-0.000248614
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.185	0.08	0.0905	1.23
2.9	10	0.23	0.184	0.119	0.0896	1.64
10.6	9	0.13	0.18	0.053	0.0871	-1.72

```
  42     9       0.13        0.166         0.04       0.0774
-1.39
191.1    10        0.1       0.0985         0.04       0.0364
0.128
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	102.275742	4	-196.551485
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643

Test 4	19.4298	3	0.0002228

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

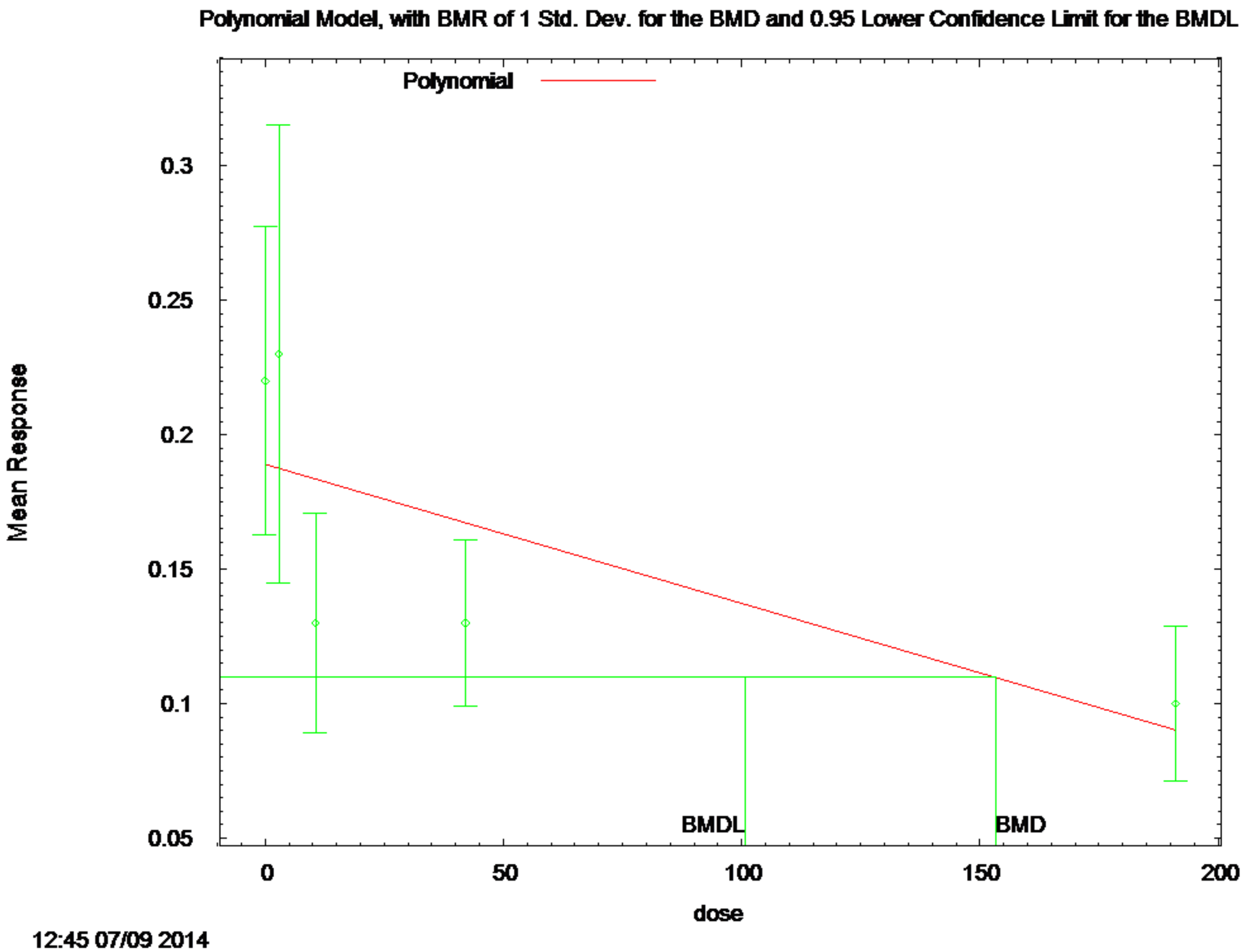
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.254

BMDL = 136.469


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly4CV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly4CV-1SD-5d.plt
                                      Wed Jul 09 12:45:45 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         alpha =   0.00545863
                           rho =            0   Specified
                        beta_0 =         0.22
                        beta_1 =            0
                        beta_2 =  -0.00230138
                        beta_3 =            0
                        beta_4 = -2.43829e-007


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.9e-010	-2.1e-010
beta_0	-1.9e-010	1	-0.56
beta_1	-2.1e-010	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00628415	0.00128275	0.00377002	0.00879829
beta_0	0.189334	0.0138502	0.162188	0.21648
beta_1	-0.000517126	0.000155222	-0.000821356	-0.000212897
beta_2	0	NA		
beta_3	-0	NA		
beta_4	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.189	0.08	0.0793	1.22
2.9	10	0.23	0.188	0.119	0.0793	1.68
10.6	9	0.13	0.184	0.053	0.0793	-2.04
42	9	0.13	0.168	0.04	0.0793	

-1.42
191.1   10   0.1   0.0905   0.04   0.0793
0.379

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	97.673375	3	-189.346749
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	12.0401	3	0.007247

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

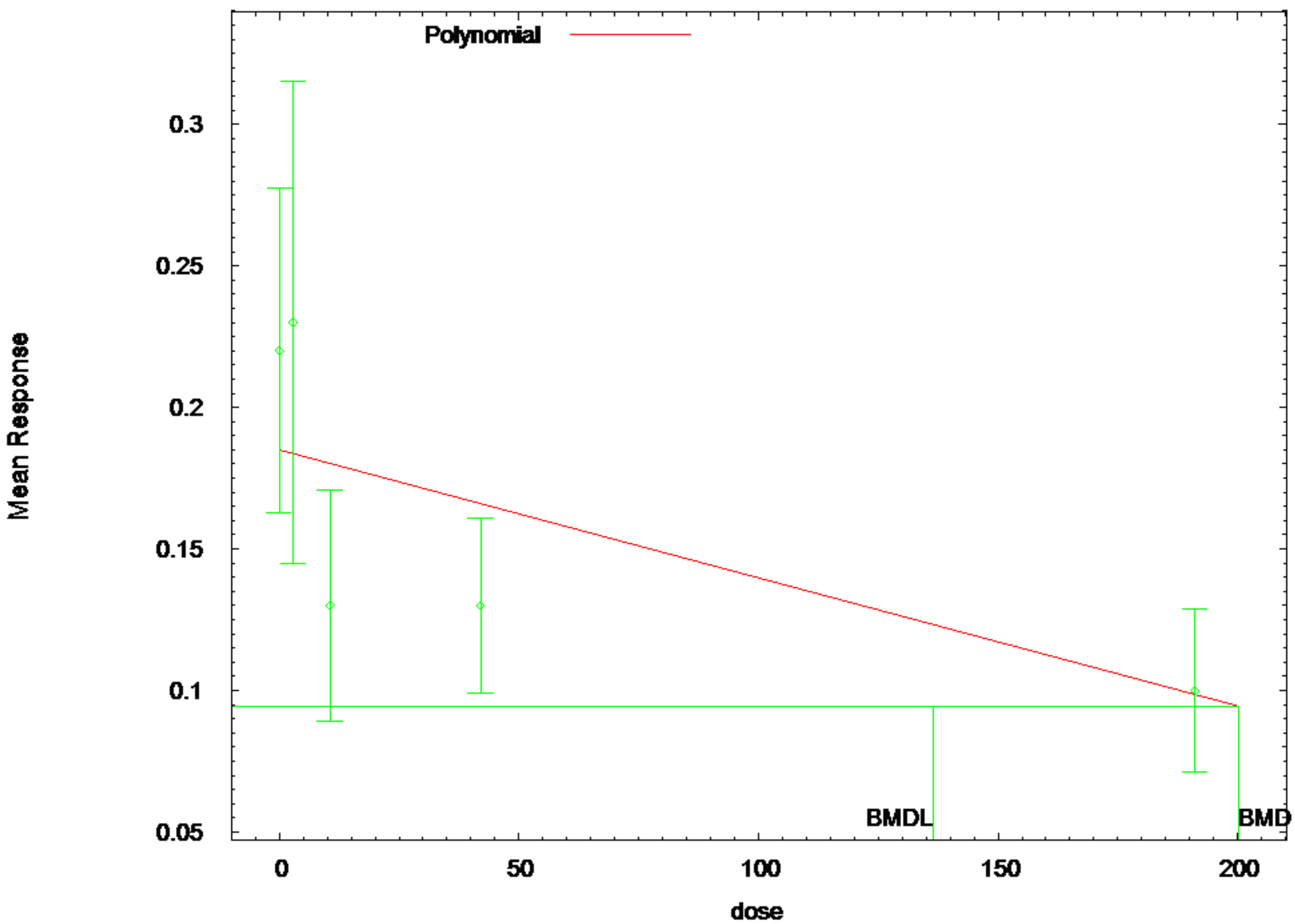
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 153.295

BMDL = 100.721

Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL



12:45 07/09 2014

```
=================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly4NCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent/Monocyte_Concu
rrent_Normal-HLS 2001-Monocyte Count-Poly4NCV-1SD-5d.plt
                                      Wed Jul 09 12:45:47 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =         0.22
                         beta_1 =            0
                         beta_2 =  -0.00230138
                         beta_3 =            0
                         beta_4 = -2.43829e-007


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.037	0.035
rho	0.99	1	-0.036	0.033
beta_0	-0.037	-0.036	1	-0.81
beta_1	0.035	0.033	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	0.0784574	1.48211	-2.82642	2.98333
rho	2.89289	0.795214	1.3343	4.45148
beta_0	0.184883	0.015175	0.15514	0.214625
beta_1	-0.00045192	0.000103729	-0.000655225	-0.000248615
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.185	0.08	0.0905	1.23
2.9	10	0.23	0.184	0.119	0.0896	

```
1.64
 10.6     9       0.13          0.18         0.053       0.0871
-1.72
   42     9       0.13         0.166          0.04       0.0774
-1.39
191.1    10        0.1        0.0985          0.04       0.0364
0.128
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	102.275742	4	-196.551485
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

```
   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	19.4298	3	0.0002228

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

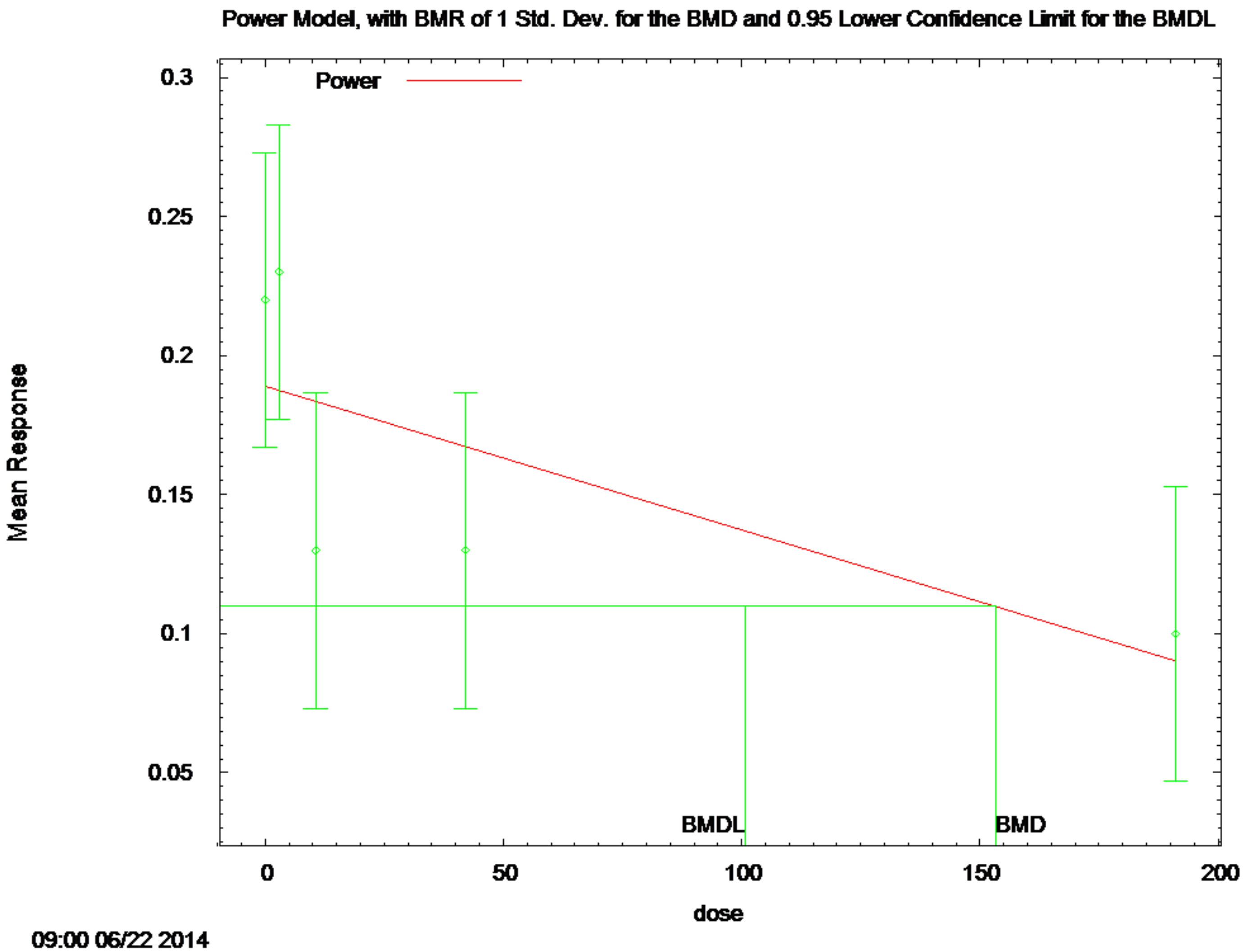
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.254

BMDL = 136.469



Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
50
100
150
200
dose
09:00 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-PowerCV-1SD-5d.plt
                                      Sun Jun 22 09:00:28 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                        control =          0.1
                          slope =     0.178802
                          power =    -0.542898


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho    -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope
alpha	1	8.1e-009	-8.6e-009
control	8.1e-009	1	-0.56
slope	-8.6e-009	-0.56	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00628415	0.00128275	0.00377002	0.00879829
control	0.189334	0.0138502	0.162188	0.21648
slope	-0.000517126	0.000155222	-0.000821356	-0.000212897
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.189	0.08	0.0793	1.22
2.9	10	0.23	0.188	0.119	0.0793	1.68
10.6	9	0.13	0.184	0.053	0.0793	-2.04
42	9	0.13	0.168	0.04	0.0793	-1.42
191.1	10	0.1	0.0905	0.04	0.0793	0.379

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	97.673375	3	-189.346749
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	12.0401	3	0.007247

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

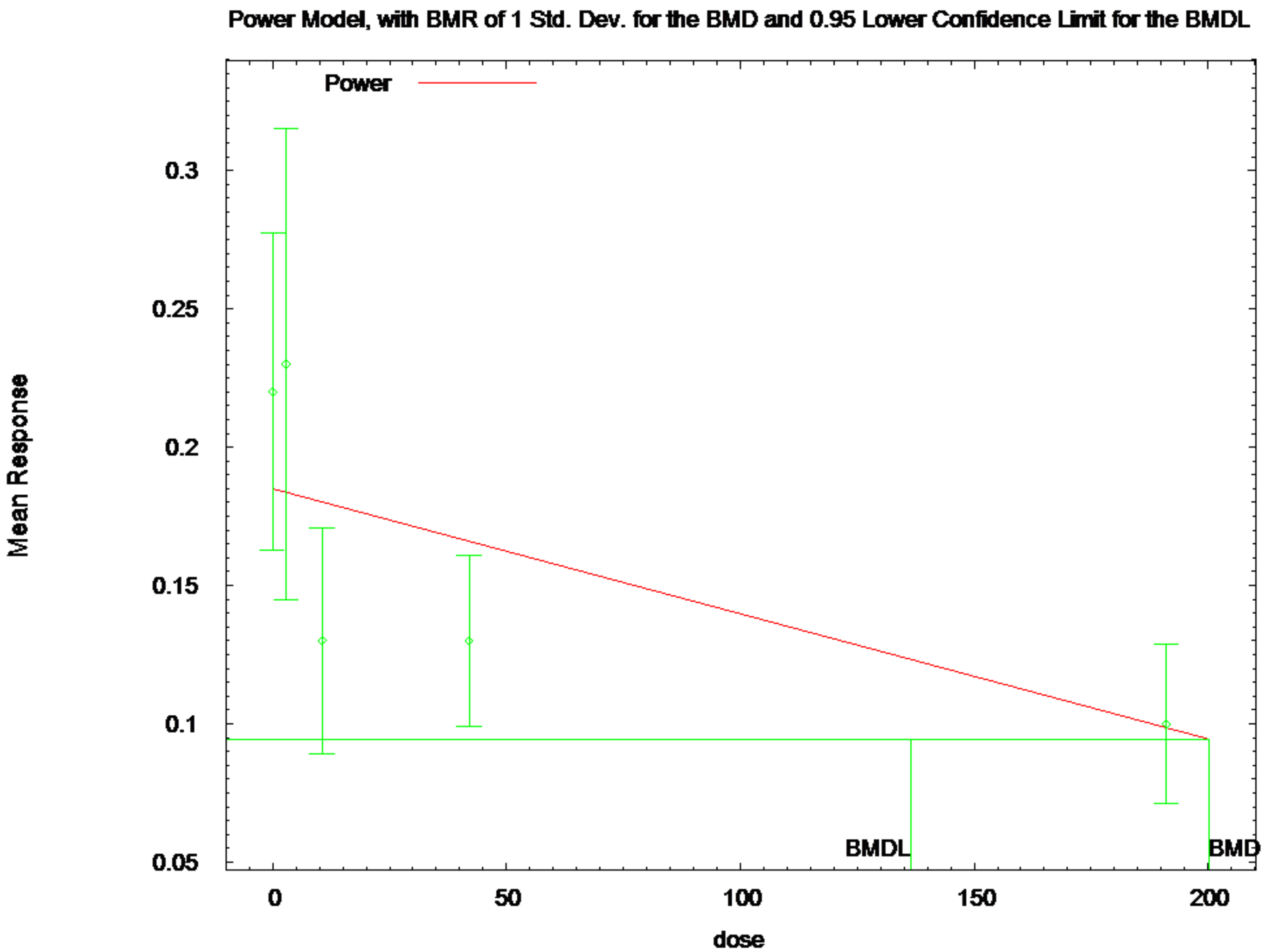
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 153.295

BMDL = 100.721



09:00 06/22 2014

```
====================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Normal-HLS
2001-Monocyte Count-PowerNCV-1SD-5d.plt
                                       Sun Jun 22 09:00:31 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                        control =          0.1
                          slope =     0.178802
                          power =    -0.542898


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -power
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	control	slope
lalpha	1	0.99	-0.52	0.7
rho	0.99	1	-0.44	0.67
control	-0.52	-0.44	1	-0.82
slope	0.7	0.67	-0.82	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	0.0784485	2.09108	-4.01999	4.17689
rho	2.89289	1.10377	0.729543	5.05623
control	0.184882	0.0153067	0.154882	0.214883
slope	-0.00045192	0.000103701	-0.00065517	-0.000248669
power	1	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.185	0.08	0.0905	1.23
2.9	10	0.23	0.184	0.119	0.0896	1.64
10.6	9	0.13	0.18	0.053	0.0871	-1.72
42	9	0.13	0.166	0.04	0.0774	-1.39

191.1   10   0.1   0.0985   0.04   0.0364
0.128

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	102.275742	4	-196.551485
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	19.4298	3	0.0002228

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

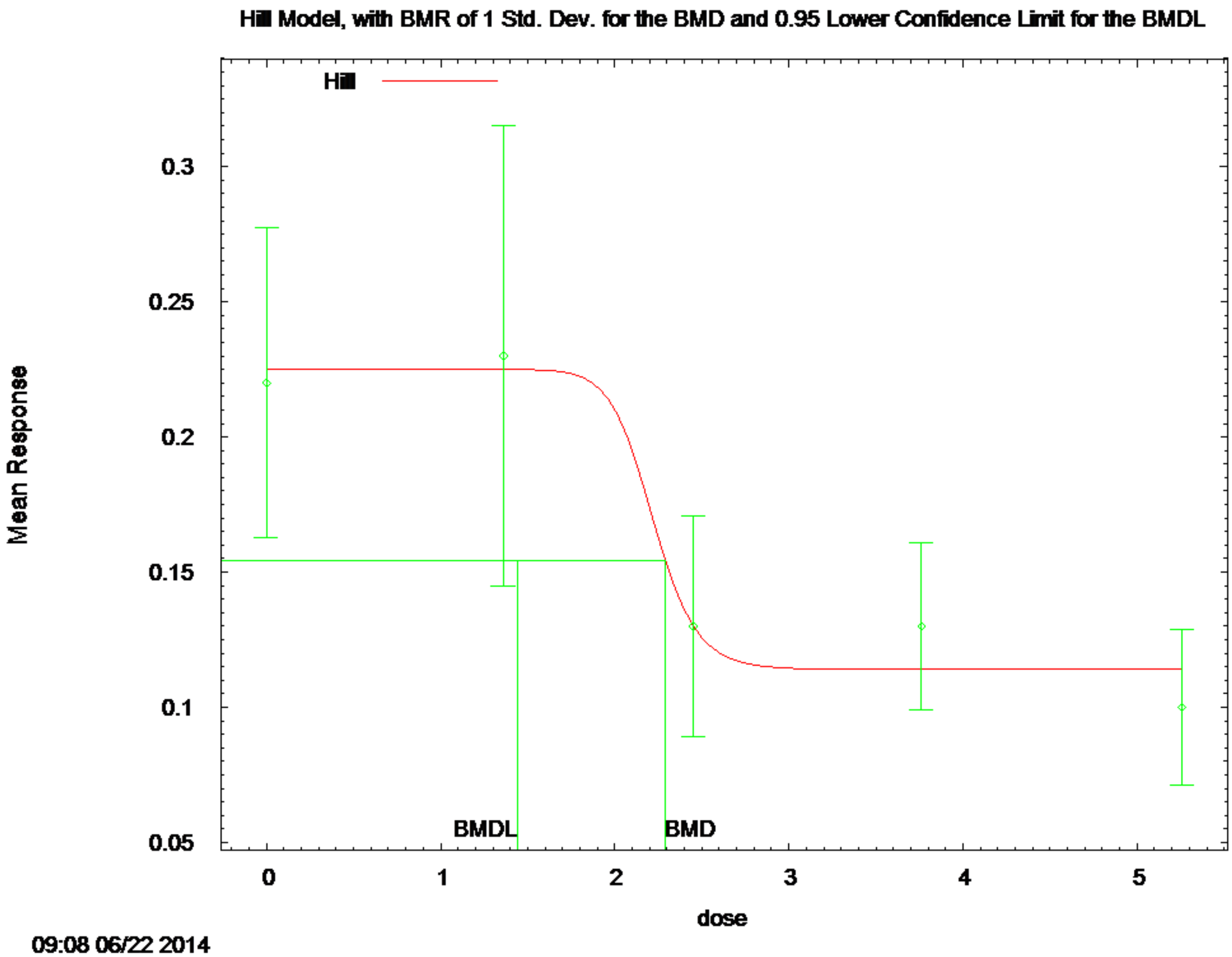
Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 200.254

BMDL = 136.469

BMDS Model Results for Monocyte Count
(Log-transformed Doses, Concurrent Controls)



Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Hill
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
====================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-HillCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-HillCV-1SD-5d.plt
                                       Sun Jun 22 09:08:08 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Power parameter restricted to be greater than 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                      intercept =         0.22
                              v =        -0.12
                              n =      4.79743
                              k =        2.124


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	intercept	v	n	k
alpha	1	1.6e-007	-2.1e-007	-1.5e-006	-1.5e-006
intercept	1.6e-007	1	-0.7	-0.072	-0.079
v	-2.1e-007	-0.7	1	0.11	0.081
n	-1.5e-006	-0.072	0.11	1	1
k	-1.5e-006	-0.079	0.081	1	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00498924	0.00101842	0.00299316	0.00698531
intercept	0.225008	0.0158381	0.193966	0.25605
v	-0.110809	0.0227564	-0.15541	-0.0662072
n	17.8909	242.727	-457.845	493.627
k	2.21732	2.99697	-3.65663	8.09127

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.225	0.08	0.0706	-0.224

```
1.361    10       0.23        0.225        0.119       0.0706
0.224
2.451     9       0.13         0.13        0.053       0.0706
-0.00074
3.761     9       0.13        0.114         0.04       0.0706
0.671
5.258    10        0.1        0.114         0.04       0.0706
-0.636


 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          103.693409            6    -195.386818
             A2          112.779870           10    -205.559741
             A3          103.693409            6    -195.386818
         fitted          103.211324            5    -196.422647
              R           92.681036            2    -181.362073


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest

   Test    -2*log(Likelihood Ratio)  Test df        p-value
```

Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	0.964171	1	0.3261

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a different variance model

The p-value for Test 4 is greater than .1. The model chosen seems to adequately describe the data

Benchmark Dose Computation

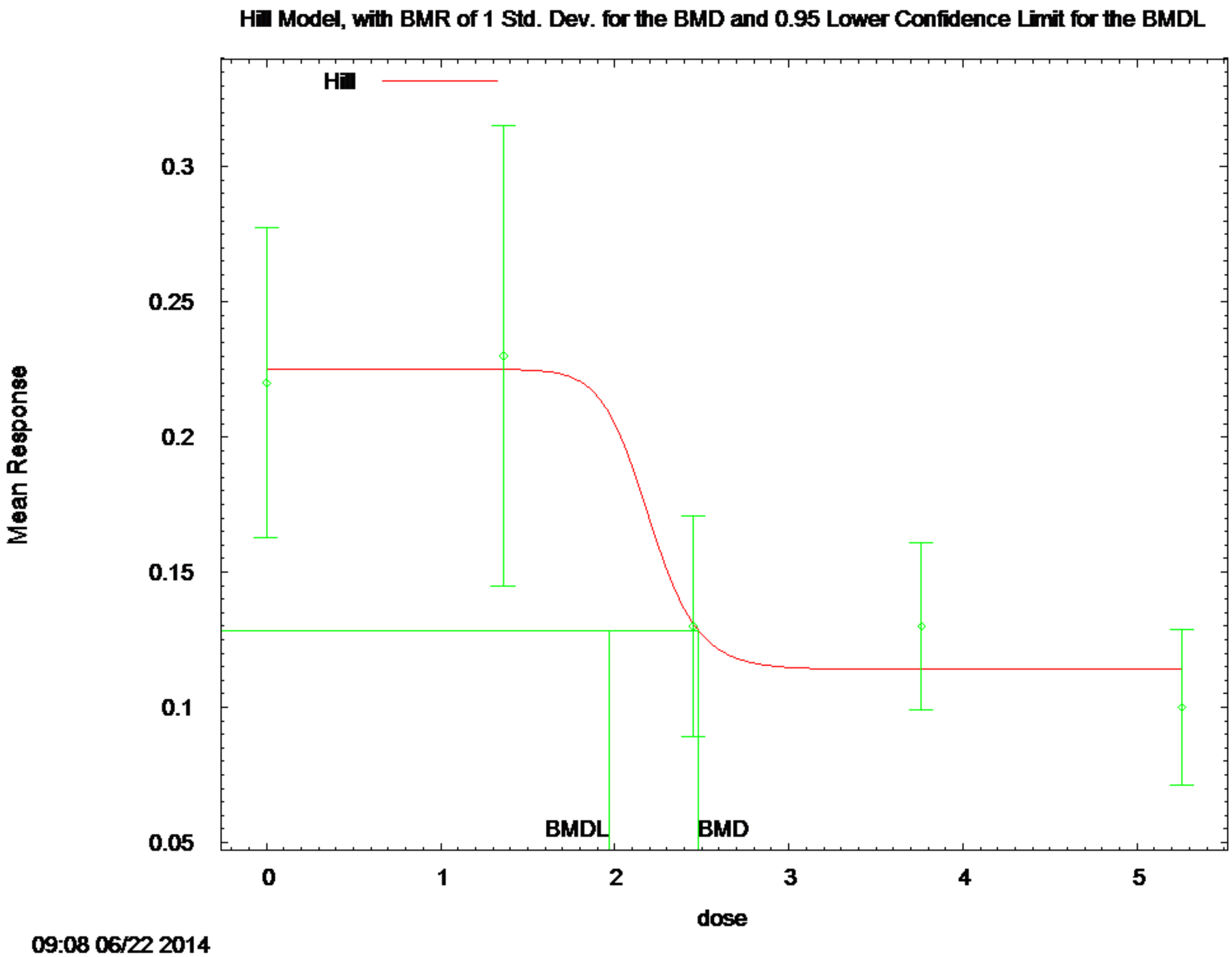
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.28837

BMDL = 1.43897



Hill Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Hill
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
==================================================================
===
       Hill Model. (Version: 2.17;  Date: 01/28/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-HillNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-HillNCV-1SD-5d.plt
                                       Sun Jun 22 09:08:09 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = intercept + v*dose^n/(k^n + dose^n)


   Dependent variable = MeanResponse
   Independent variable = Dose
   Power parameter restricted to be greater than 1
   The variance is to be modeled as Var(i) = exp(lalpha  + rho *
ln(mean(i)))

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                      intercept =         0.22
                              v =        -0.12
                              n =      4.79743
                              k =        2.124


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho    intercept            v
```

					n	k
lalpha	1	0.99	-0.53	0.58	-0.011	-0.0022
rho	0.99	1	-0.47	0.56	-0.011	-0.0021
intercept	-0.53	-0.47	1	-0.92	-0.053	-0.073
v	0.58	0.56	-0.92	1	0.095	0.097
n	-0.011	-0.011	-0.053	0.095	1	0.99
k	-0.0022	-0.0021	-0.073	0.097	0.99	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.919707	1.51609	-3.8912	2.05178
rho	2.51667	0.79556	0.957403	4.07594
intercept	0.224812	0.0215878	0.182501	0.267124
v	-0.110934	0.0236505	-0.157288	-0.06458
n	15.8793	87.1614	-154.954	186.713
k	2.20245	1.27621	-0.298865	4.70378

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.225	0.08	0.0965	-0.158

1.361	10	0.23	0.225	0.119	0.0965	0.172
2.451	9	0.13	0.131	0.053	0.0489	-0.064
3.761	9	0.13	0.114	0.04	0.041	1.18
5.258	10	0.1	0.114	0.04	0.041	-1.07

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	110.593587	6	-209.187174
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value

Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	2.79407	1	0.09461

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

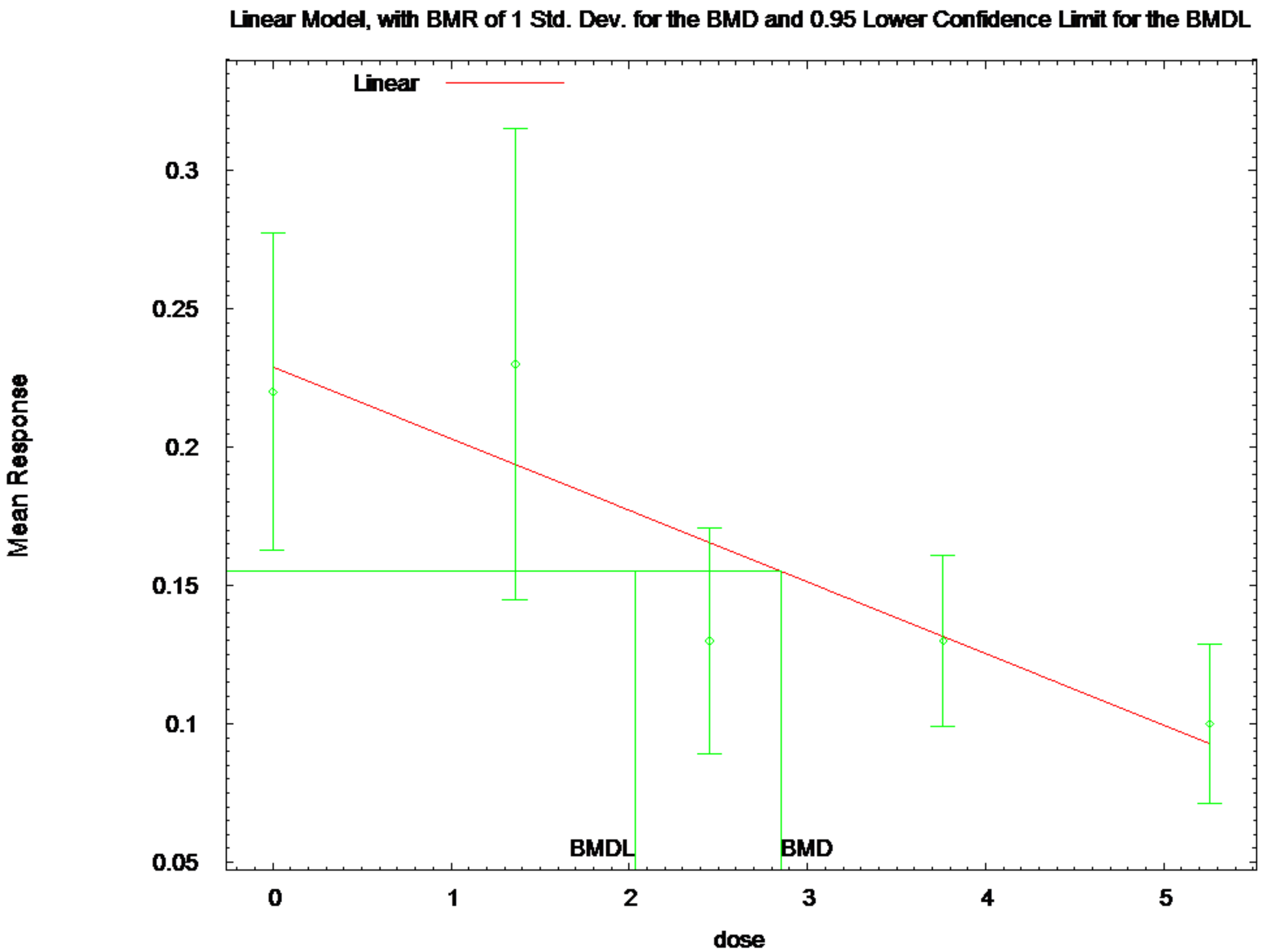
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.48276

BMDL = 1.96659



12:49 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-LinearCV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-LinearCV-1SD-
5d.plt
                                      Wed Jul 09 12:49:38 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   Signs of the polynomial coefficients are not restricted
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =     0.228322
                         beta_1 =   -0.0258442


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
```

have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-2.7e-008	3.1e-008
beta_0	-2.7e-008	1	-0.81
beta_1	3.1e-008	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00542838	0.00110806	0.00325661	0.00760014
beta_0	0.229102	0.0180267	0.193771	0.264434
beta_1	-0.0258556	0.00572228	-0.037071	-0.0146401

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.229	0.08	0.0737	-0.391
1.361	10	0.23	0.194	0.119	0.0737	1.55
2.451	9	0.13	0.166	0.053	0.0737	-1.45
3.761	9	0.13	0.132	0.04	0.0737	-0.0757
5.258	10	0.1	0.0932	0.04	0.0737	0.294

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	101.186766	3	-196.373532
R	92.681036	2	-181.362073

Explanation of Tests

```
Test 1:  Do responses and/or variances differ among Dose levels?
         (A2 vs. R)
Test 2:  Are Variances Homogeneous? (A1 vs A2)
Test 3:  Are variances adequately modeled? (A2 vs. A3)
Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
(Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	5.01329	3	0.1708

The p-value for Test 1 is less than .05. There appears to be a
difference between response and/or variances among the dose
levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

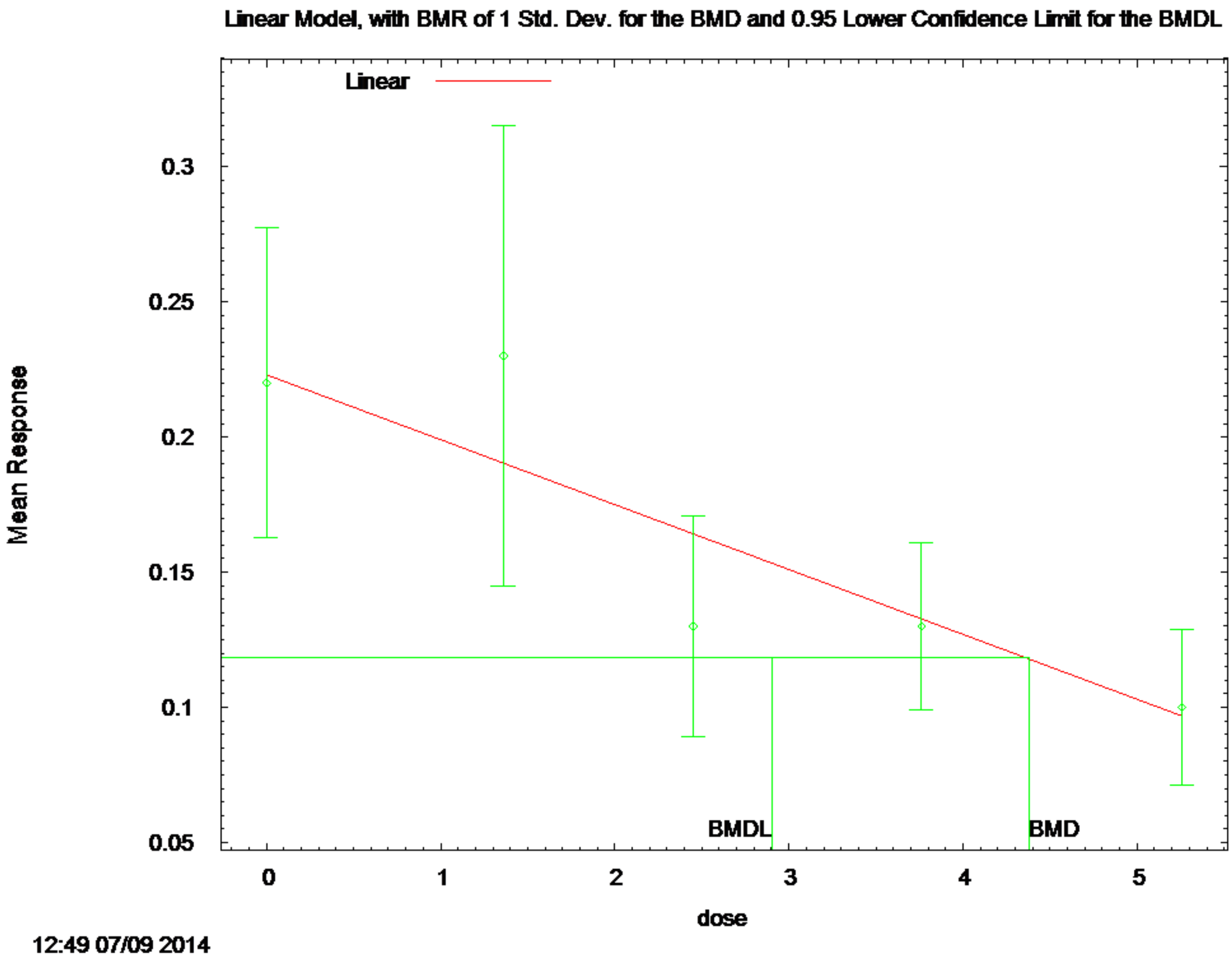
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.84958

BMDL = 2.03295



Linear Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Linear
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
12:49 07/09 2014

```
==================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-LinearNCV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-LinearNCV-1SD-
5d.plt
                                      Wed Jul 09 12:49:39 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   Signs of the polynomial coefficients are not restricted
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =     0.228322
                         beta_1 =   -0.0258442


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho       beta_0       beta_1
```

lalpha	1	0.99	-0.076	0.083
rho	0.99	1	-0.076	0.083
beta_0	-0.076	-0.076	1	-0.92
beta_1	0.083	0.083	-0.92	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.557382	1.30166	-3.1086	1.99383
rho	2.63613	0.691385	1.28104	3.99122
beta_0	0.22329	0.0212241	0.181691	0.264888
beta_1	-0.0239544	0.00497926	-0.0337136	-0.0141953

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.223	0.08	0.105	-0.0992
1.361	10	0.23	0.191	0.119	0.0852	1.46
2.451	9	0.13	0.165	0.053	0.0702	-1.48
3.761	9	0.13	0.133	0.04	0.0531	-0.181
5.258	10	0.1	0.0973	0.04	0.0351	0.24

Model Descriptions for likelihoods calculated

Model A1: Yij = Mu(i) + e(ij)

```
          Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	107.004496	4	-206.008991
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	9.97226	3	0.0188

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

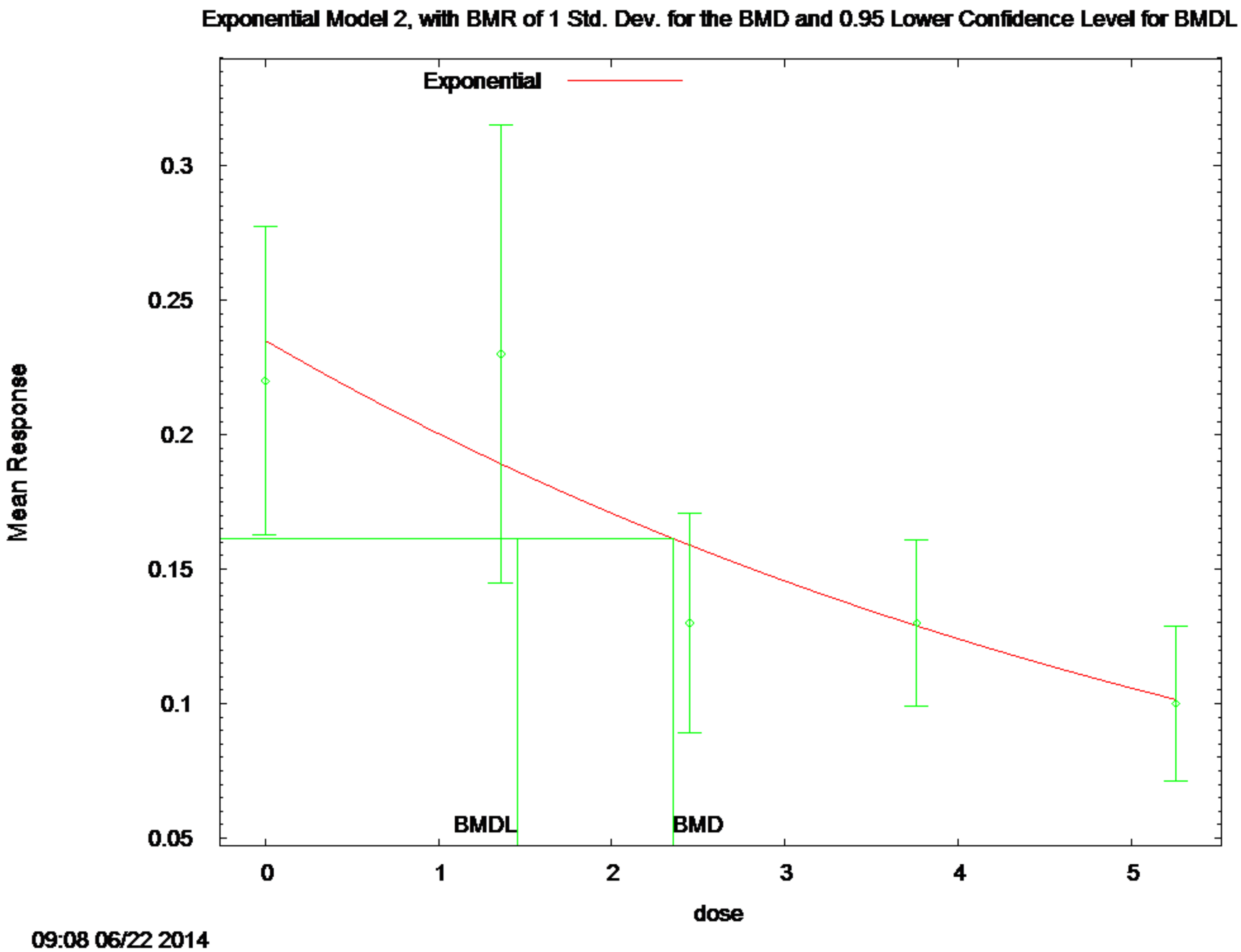
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.37872

BMDL = 2.90647


Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                        Sun Jun 22 09:08:07 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-5.32056
rho(S)	0
a	0.101819
b	0.164384
c	0
d	1

(S) = Specified

Parameter Estimates

Variable	Model 2
lnalpha	-5.21349
rho	0
a	0.235092
b	0.159679
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2351	0.07377	-0.6469
1.361	0.1892	0.07377	1.75
2.451	0.159	0.07377	-1.177
3.761	0.129	0.07377	0.0427
5.258	0.1015	0.07377	-0.06572

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
2	101.1239	3	-196.2477

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	

< 0.0001
Test 2 18.17 4
0.001142
Test 3 18.17 4
0.001142
Test 4 5.139 3
0.1619

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

Benchmark Dose Computations:

Specified Effect = 1.000000

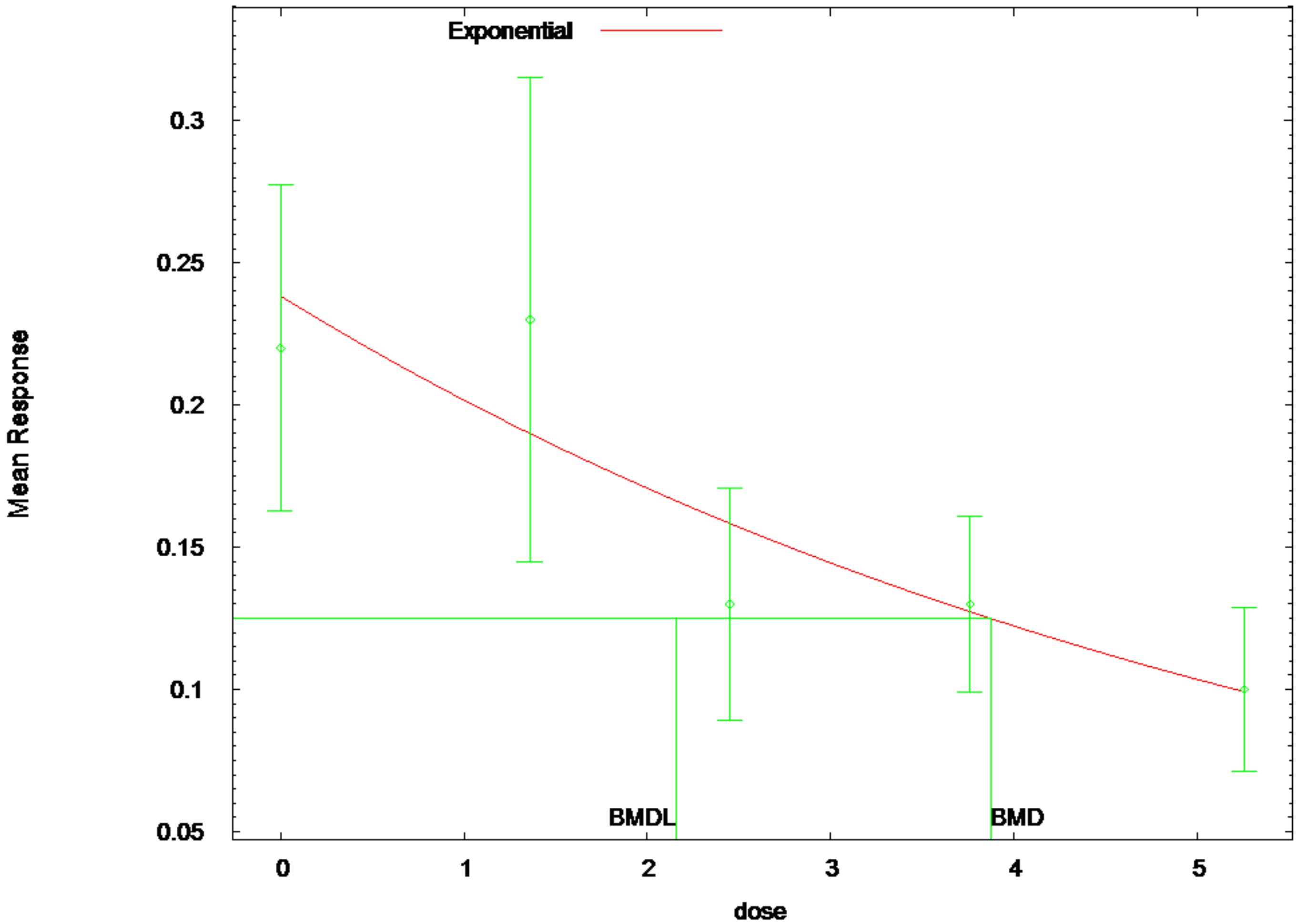
Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.35849

BMDL = 1.45524

Exponential Model 2, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:08 06/22 2014

```
====================================================================
===
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpNCV-1SD-5d.(d)
        Gnuplot Plotting File:
                                        Sun Jun 22 09:08:08 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 2
lnalpha	-1.08858
rho	2.4145
a	0.101819
b	0.164384
c	0
d	1

Parameter Estimates

Variable	Model 2
lnalpha	-0.590628
rho	2.62295
a	0.238331
b	0.166716
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2383	0.1135	-0.5108
1.361	0.19	0.08428	1.503
2.451	0.1584	0.0664	-1.282
3.761	0.1273	0.04987	0.1617
5.258	0.09919	0.03595	0.07097

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
               Var{e(ij)} = Sigma(i)^2

     Model A3:        Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:        Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
2	107.1483	4	-206.2965

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

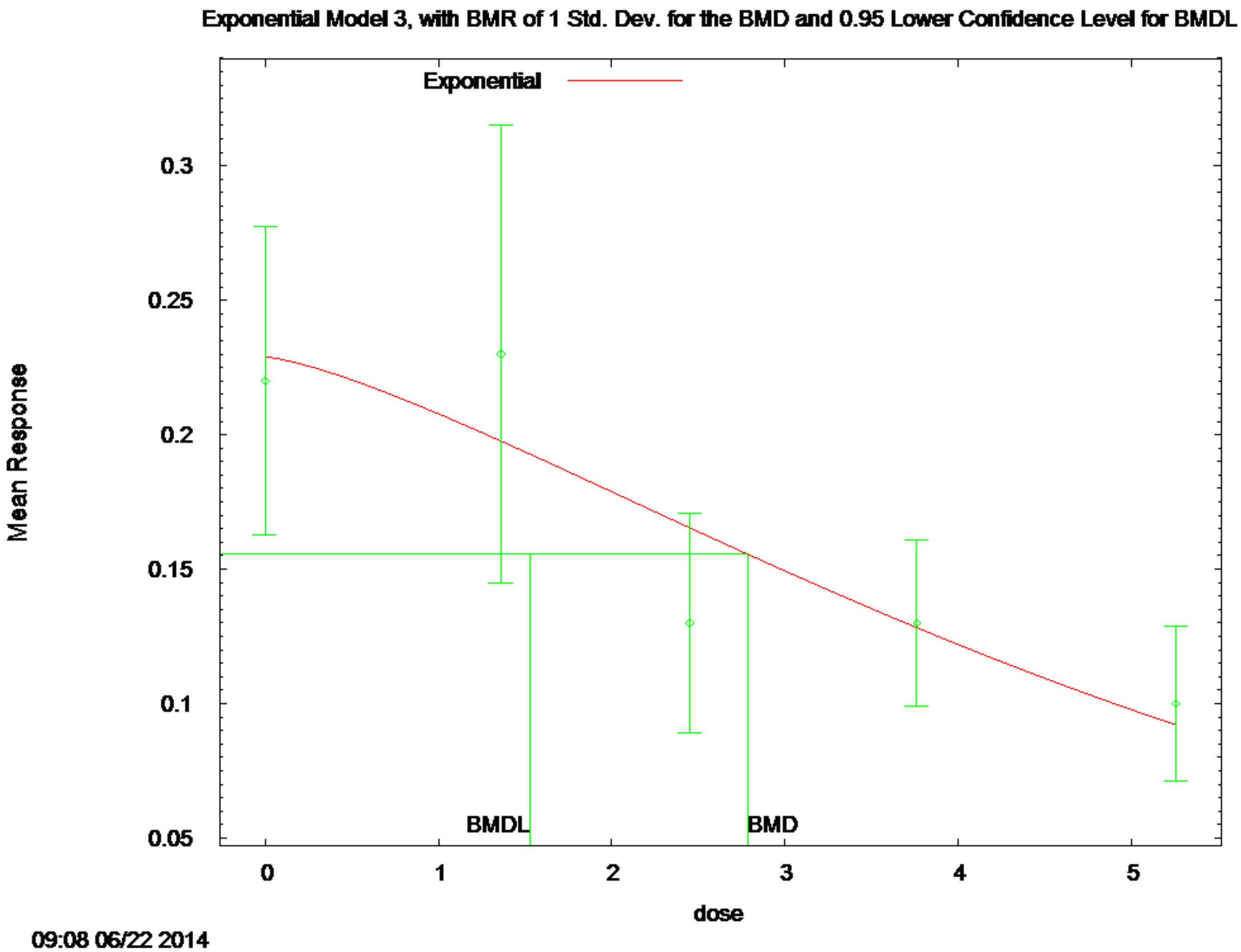
Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001
Test 2	18.17	4	

```
0.001142
     Test 3                              1.578           3
0.6643
     Test 4                              9.685           3
0.02145


     The p-value for Test 1 is less than .05.  There appears to
be a
     difference between response and/or variances among the dose
     levels, it seems appropriate to model the data.

     The p-value for Test 2 is less than .1.  A non-homogeneous
     variance model appears to be appropriate.

     The p-value for Test 3 is greater than .1.  The modeled
     variance appears to be appropriate here.

     The p-value for Test 4 is less than .1.  Model 2 may not
adequately
     describe the data; you may want to consider another model.


   Benchmark Dose Computations:

     Specified Effect = 1.000000

            Risk Type = Estimated standard deviations from
control

     Confidence Level = 0.950000

                  BMD =       3.8783

                 BMDL =      2.16072
```


Exponential Model 3, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:08:07 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-5.32056
rho(S)	0
a	0.23917
b	0.0958051
c	0
d	2

(S) = Specified

Parameter Estimates

Variable	Model 3
lnalpha	-5.22632
rho	0
a	0.228926
b	0.177375
c	0
d	1.34953

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2289	0.0733	-0.385
1.361	0.1977	0.0733	1.396
2.451	0.1654	0.0733	-1.449
3.761	0.1283	0.0733	0.06992
5.258	0.09213	0.0733	0.3394

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
3	101.4317	4	-194.8633

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 5a	4.523	2	0.1042

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Benchmark Dose Computations:

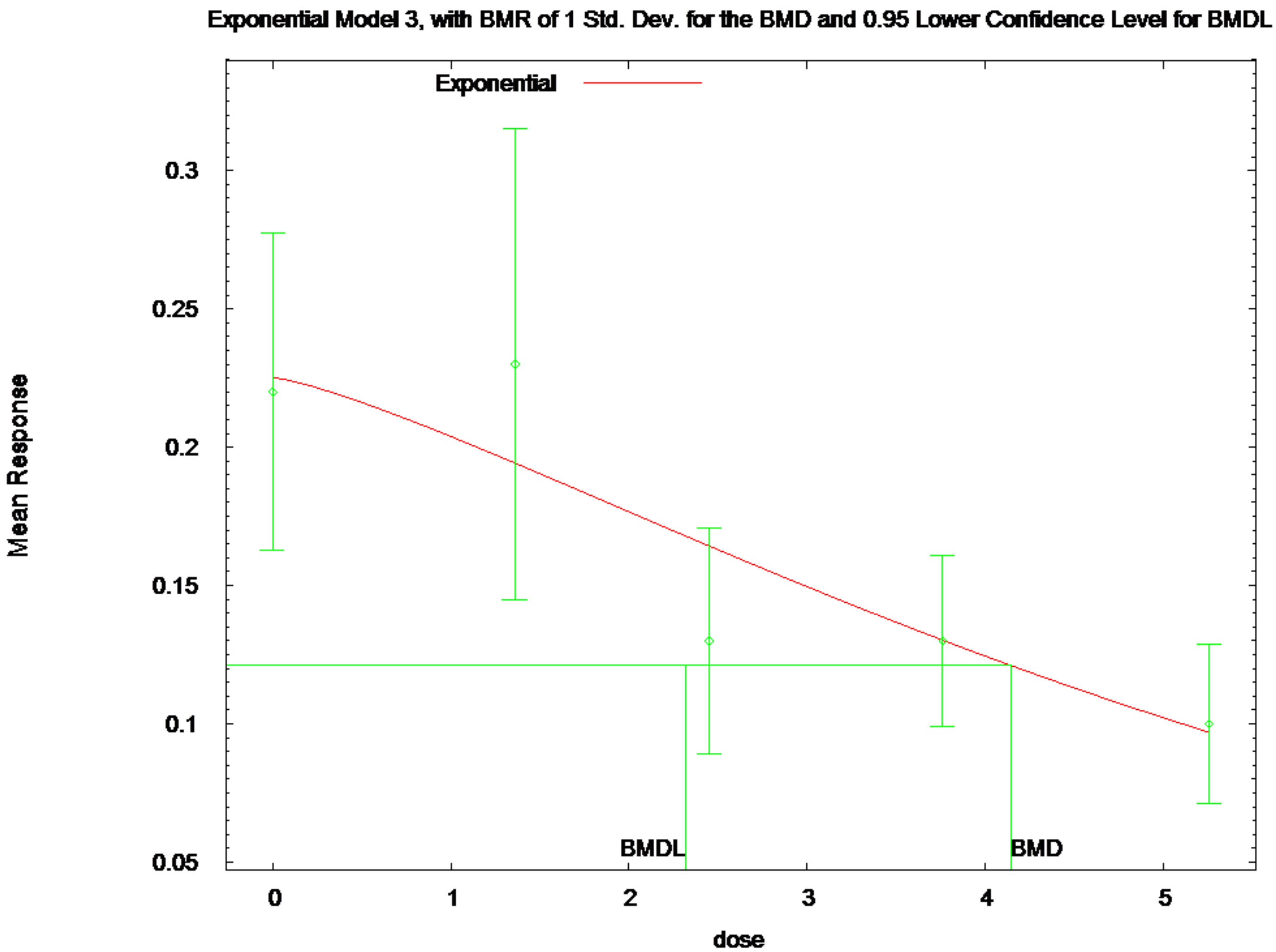
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.78443

BMDL = 1.53251



09:08 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:08:08 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 3
lnalpha	-1.08858
rho	2.4145
a	0.23917
b	0.0958051
c	0
d	2

Parameter Estimates

Variable	Model 3
lnalpha	-0.659547
rho	2.5928
a	0.225175
b	0.166469
c	0
d	1.28789

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2252	0.1041	-0.1572
1.361	0.1942	0.08594	1.316
2.451	0.1643	0.06917	-1.487
3.761	0.1303	0.05121	-0.0169
5.258	0.09698	0.03492	0.2734

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
3	107.4993	5	-204.9986

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 5a: Does Model 3 fit the data? (A3 vs 3)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 5a	8.983	2	0.01121

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

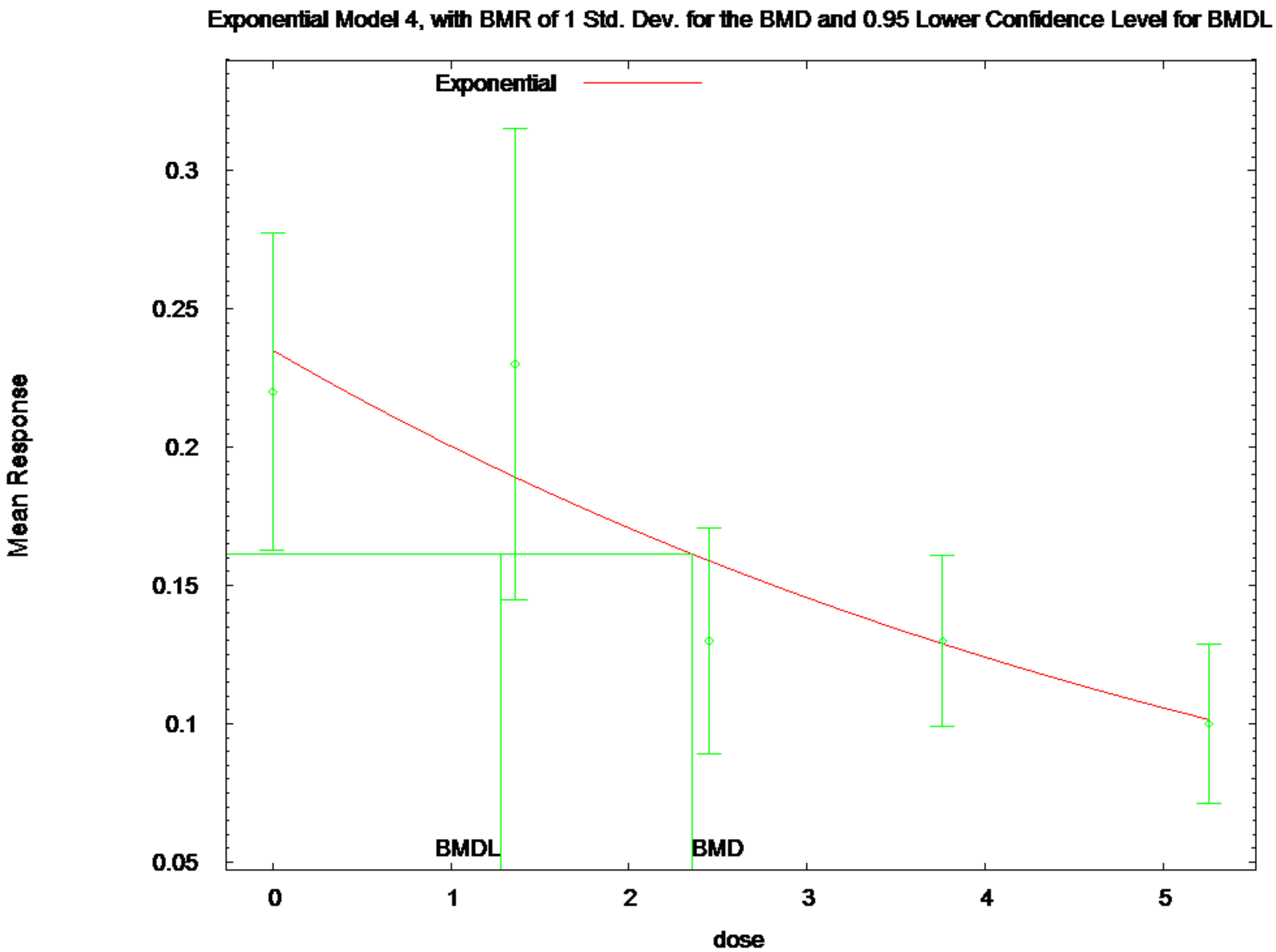
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 4.14625

BMDL = 2.32125



09:08 06/22 2014

```
=================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                      Sun Jun 22 09:08:07 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-5.32056
rho(S)	0
a	0.2415
b	0.172301
c	0.000414079
d	1

(S) = Specified

Parameter Estimates

Variable	Model 4
lnalpha	-5.21349
rho	0
a	0.235092
b	0.159679
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2351	0.07377	-0.6469
1.361	0.1892	0.07377	1.75
2.451	0.159	0.07377	-1.177
3.761	0.129	0.07377	0.0427
5.258	0.1015	0.07377	-0.06572

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
```

```
Model A2:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:         Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model  R:         Yij = Mu + e(i)
           Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
4	101.1239	3	-196.2477

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 6a	5.139	3	0.1619

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Benchmark Dose Computations:

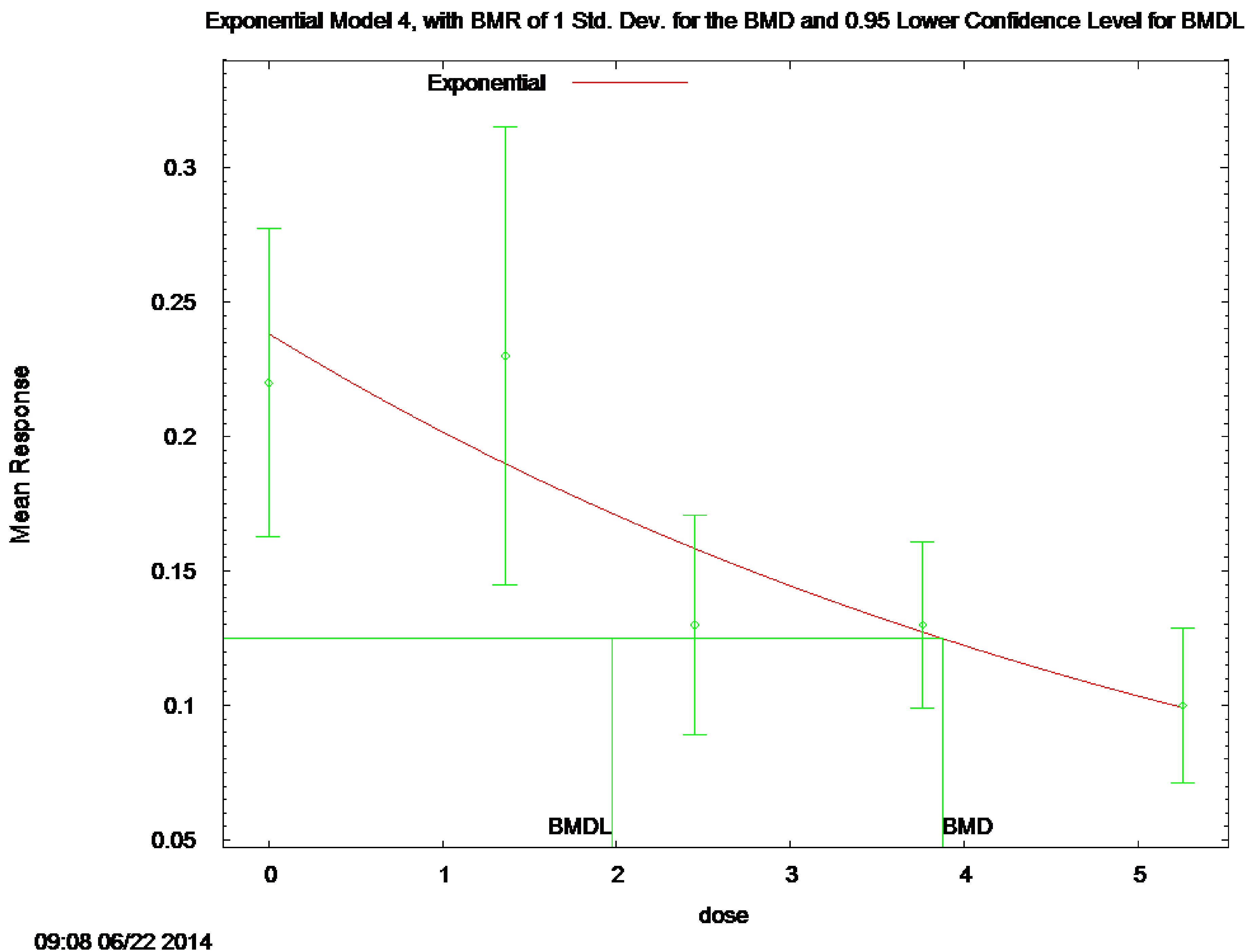
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.35849

BMDL = 1.28226



Exponential Model 4, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
0
1
2
3
4
5
dose
BMDL
BMD
09:08 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:08:08 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 4
lnalpha	-1.08858
rho	2.4145
a	0.2415
b	0.172301
c	0.000414079
d	1

Parameter Estimates

Variable	Model 4
lnalpha	-0.59063
rho	2.62295
a	0.238331
b	0.166716
c	0
d	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2383	0.1135	-0.5108
1.361	0.19	0.08428	1.503
2.451	0.1584	0.0664	-1.282
3.761	0.1273	0.04987	0.1617
5.258	0.09919	0.03595	0.07097

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
             Var{e(ij)} = Sigma(i)^2

     Model A3:          Yij = Mu(i) + e(ij)
             Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:          Yij = Mu + e(i)
             Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
4	107.1483	4	-206.2965

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 6a: Does Model 4 fit the data? (A3 vs 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 6a	9.685	3	0.02145

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

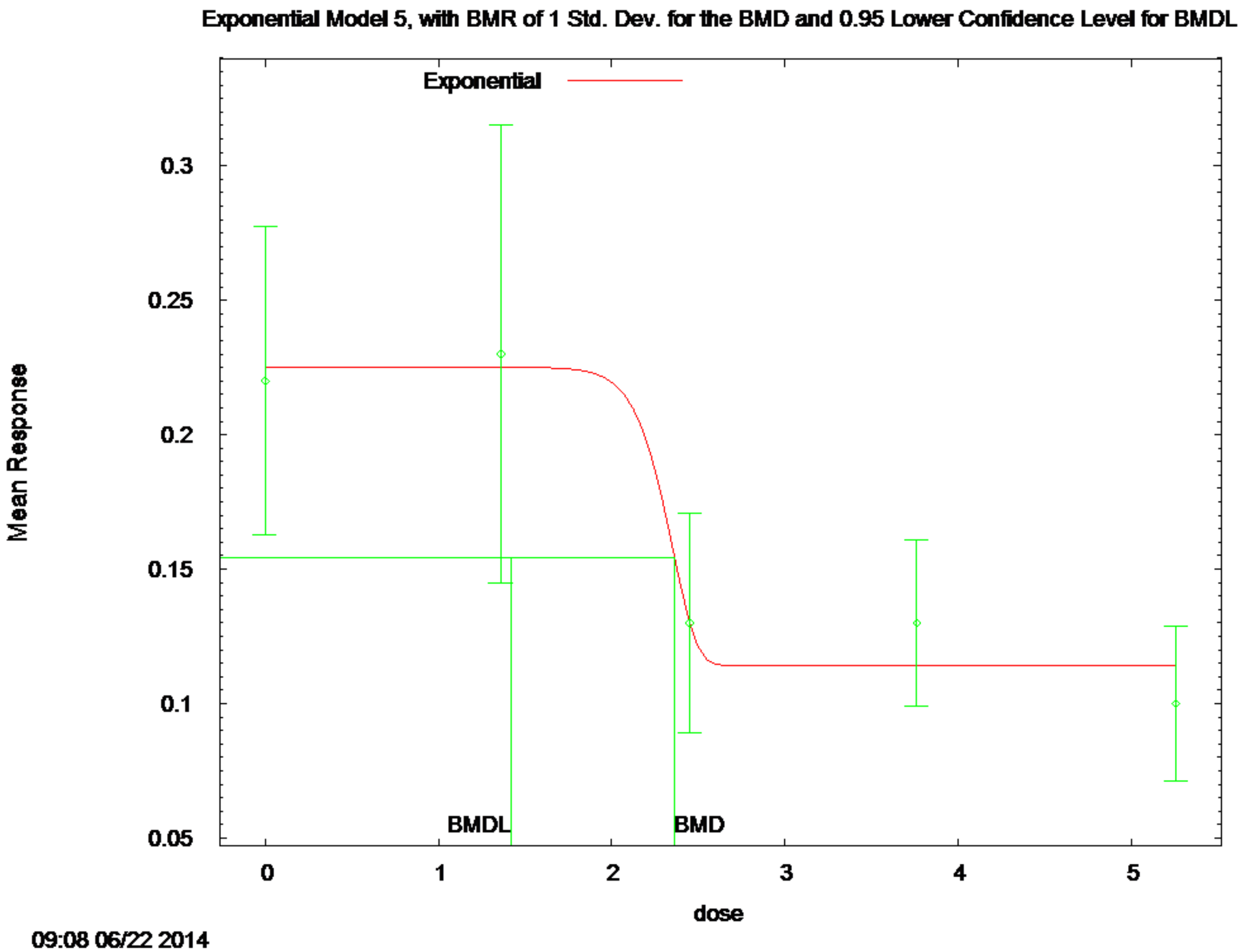
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 3.8783

BMDL = 1.97412



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
====================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:08:07 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-5.32056
rho(S)	0
a	0.2415
b	0.172301
c	0.000414079
d	1

(S) = Specified

Parameter Estimates

Variable	Model 5
lnalpha	-5.30047
rho	0
a	0.225003
b	0.423397
c	0.507595
d	18

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.225	0.07063	-0.224
1.361	0.225	0.07063	0.224
2.451	0.13	0.07063	-4.191e-005
3.761	0.1142	0.07063	0.6706
5.258	0.1142	0.07063	-0.6362

Other models for which likelihoods are calculated:

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
```

```
     Model A2:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = Sigma(i)^2

     Model A3:         Yij = Mu(i) + e(ij)
               Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

     Model  R:         Yij = Mu + e(i)
               Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	103.6934	6	-195.3868
R	92.68104	2	-181.3621
5	103.2112	5	-196.4224

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value

Test 1	40.2	8	< 0.0001
Test 2	18.17	4	0.001142
Test 3	18.17	4	0.001142
Test 7a	0.9644	1	0.3261

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

Benchmark Dose Computations:

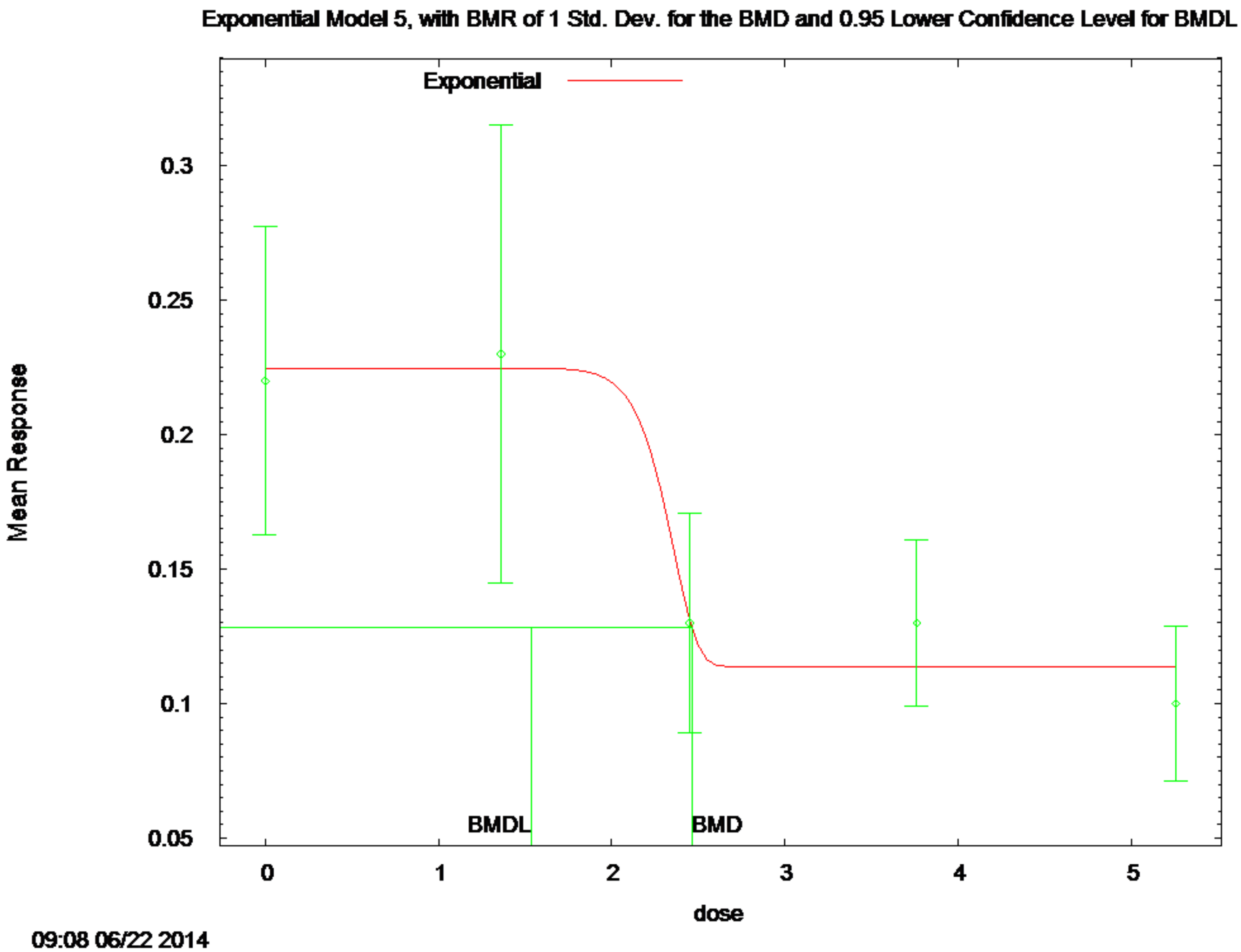
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.36378

BMDL = 1.42021



Exponential Model 5, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL
Exponential
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
==================================================================
===
       Exponential Model. (Version: 1.9;  Date: 01/29/2013)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-ExpNCV-1SD-5d.(d)
       Gnuplot Plotting File:
                                       Sun Jun 22 09:08:08 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = MeanResponse
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                  Initial Parameter Values
```

Variable	Model 5
lnalpha	-1.08858
rho	2.4145
a	0.2415
b	0.172301
c	0.000414079
d	1

Parameter Estimates

Variable	Model 5
lnalpha	-0.920058
rho	2.51647
a	0.224792
b	0.42243
c	0.506715
d	18

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	0.22	0.08
1.361	10	0.23	0.119
2.451	9	0.13	0.053
3.761	9	0.13	0.04
5.258	10	0.1	0.04

Estimated Values of Interest

Dose	Est Mean	Est Std	Scaled Residual
0	0.2248	0.09652	-0.157
1.361	0.2248	0.09651	0.1708
2.451	0.131	0.04893	-0.06142
3.761	0.1139	0.04103	1.177
5.258	0.1139	0.04103	-1.072

Other models for which likelihoods are calculated:

```
  Model A1:        Yij = Mu(i) + e(ij)
             Var{e(ij)} = Sigma^2

  Model A2:        Yij = Mu(i) + e(ij)
```

```
              Var{e(ij)} = Sigma(i)^2

    Model A3:         Yij = Mu(i) + e(ij)
              Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

    Model  R:         Yij = Mu + e(i)
              Var{e(ij)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	103.6934	6	-195.3868
A2	112.7799	10	-205.5597
A3	111.9906	7	-209.9812
R	92.68104	2	-181.3621
5	110.5929	6	-209.1858

Additive constant for all log-likelihoods = -44.11. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)

Test 7a: Does Model 5 fit the data? (A3 vs 5)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	40.2	8	< 0.0001

Test 2	18.17	4	0.001142
Test 3	1.578	3	0.6643
Test 7a	2.795	1	0.09454

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

Benchmark Dose Computations:

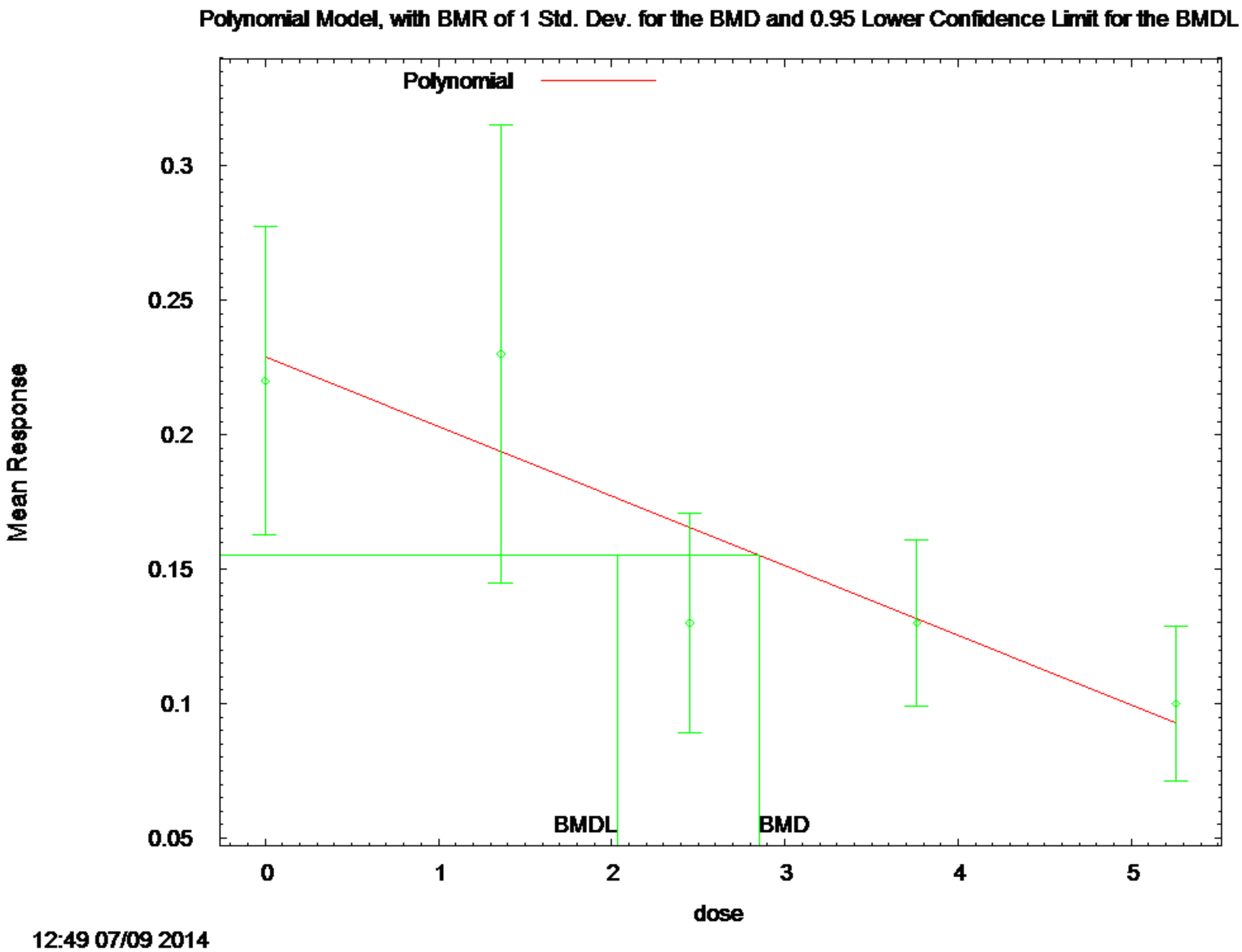
Specified Effect = 1.000000

Risk Type = Estimated standard deviations from control

Confidence Level = 0.950000

BMD = 2.46312

BMDL = 1.53813


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly2CV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly2CV-1SD-
5d.plt
                                        Wed Jul 09 12:49:38 2014
====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =     0.232604
                         beta_1 =   -0.0320749
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-1.7e-007	2.7e-007
beta_0	-1.7e-007	1	-0.81
beta_1	2.7e-007	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00542838	0.00110806	0.00325661	0.00760014
beta_0	0.229102	0.0180267	0.193771	0.264434
beta_1	-0.0258556	0.00572228	-0.037071	-0.0146401
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.229	0.08	0.0737	-0.391
1.361	10	0.23	0.194	0.119	0.0737	1.55
2.451	9	0.13	0.166	0.053	0.0737	-1.45
3.761	9	0.13	0.132	0.04	0.0737	-0.0757
5.258	10	0.1	0.0932	0.04	0.0737	0.294

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	101.186766	3	-196.373532
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	5.01329	3	0.1708

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose

levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is greater than .1. The model chosen
seems
to adequately describe the data

Benchmark Dose Computation

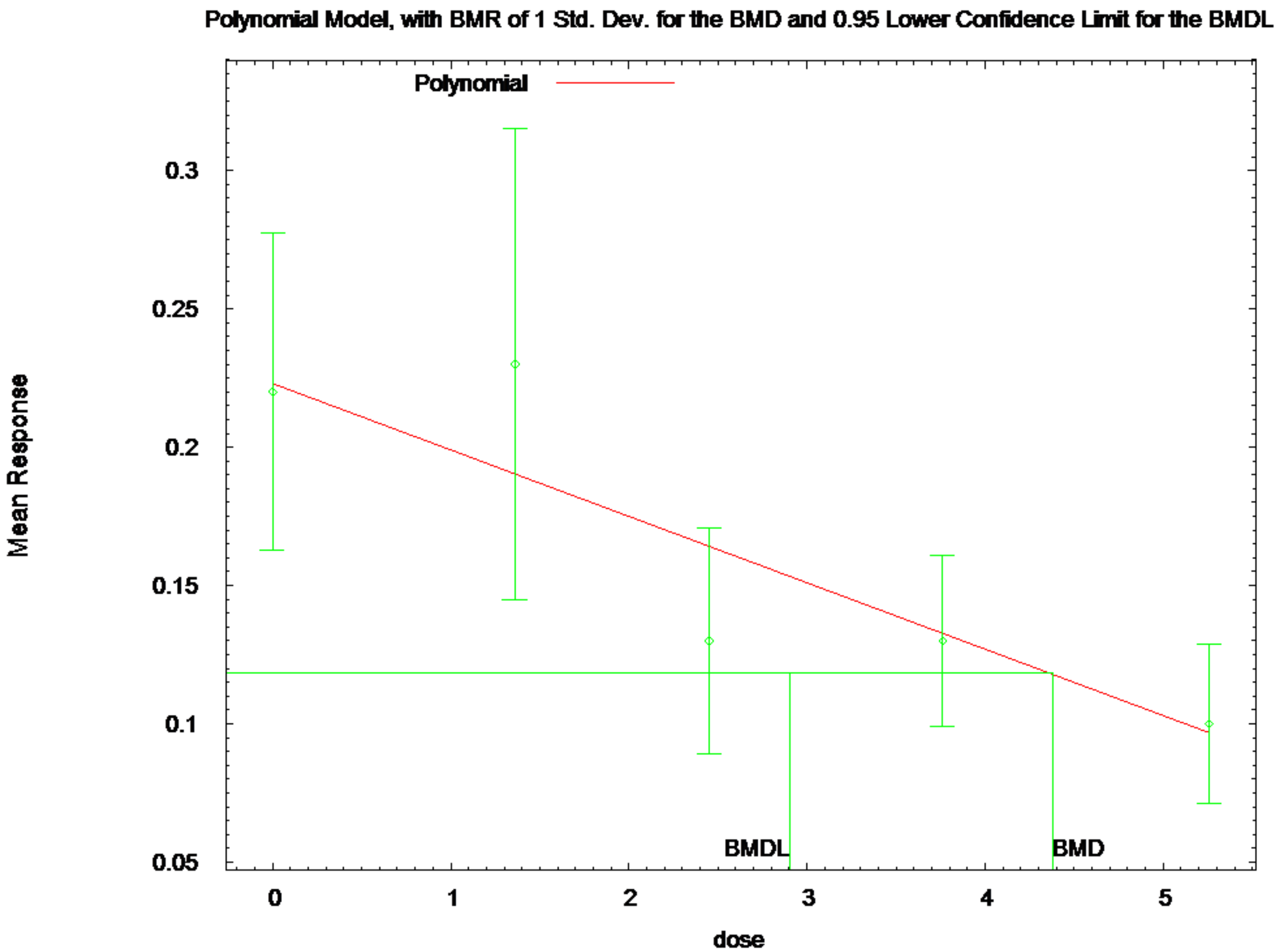
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.84958

BMDL = 2.03295



12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly2NCV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly2NCV-1SD-
5d.plt
                                       Wed Jul 09 12:49:39 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =     0.232604
                         beta_1 =   -0.0320749
                         beta_2 =            0


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.076	0.083
rho	0.99	1	-0.076	0.083
beta_0	-0.076	-0.076	1	-0.92
beta_1	0.083	0.083	-0.92	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.557387	1.30166	-3.1086	1.99383
rho	2.63613	0.691385	1.28104	3.99122
beta_0	0.22329	0.0212241	0.181691	0.264888
beta_1	-0.0239544	0.00497926	-0.0337136	-0.0141953
beta_2	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.223	0.08	0.105	-0.0992
1.361	10	0.23	0.191	0.119	0.0852	1.46
2.451	9	0.13	0.165	0.053	0.0702	-1.48

3.761	9	0.13	0.133	0.04	0.0531	-0.181
5.258	10	0.1	0.0973	0.04	0.0351	0.24

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	107.004496	4	-206.008991
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643

Test 4	9.97226	3	0.0188

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

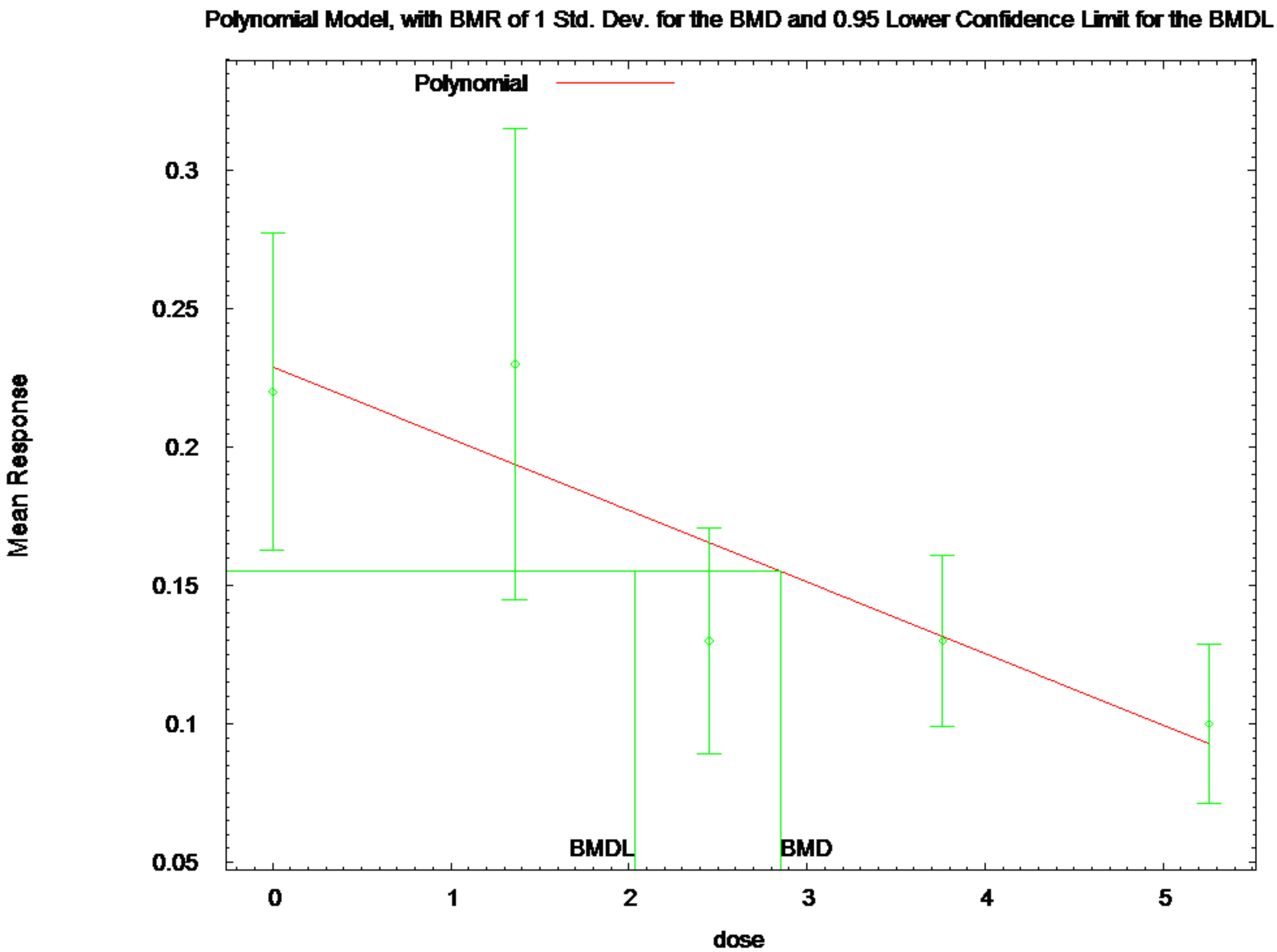
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.37872

BMDL = 2.90647



12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly3CV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly3CV-1SD-
5d.plt
                                       Wed Jul 09 12:49:38 2014
====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =     0.224911
                         beta_1 =            0
                         beta_2 =   -0.0222894
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -rho -beta_2 -beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	1.1e-010	1.8e-010
beta_0	1.1e-010	1	-0.81
beta_1	1.8e-010	-0.81	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00542838	0.00110806	0.00325661	0.00760014
beta_0	0.229102	0.0180267	0.193771	0.264434
beta_1	-0.0258556	0.00572228	-0.037071	-0.0146401
beta_2	-0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.229	0.08	0.0737	-0.391
1.361	10	0.23	0.194	0.119	0.0737	1.55
2.451	9	0.13	0.166	0.053	0.0737	-1.45
3.761	9	0.13	0.132	0.04	0.0737	

-0.0757
5.258   10   0.1   0.0932   0.04   0.0737
0.294

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	101.186766	3	-196.373532
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels?
(A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	5.01329	3	0.1708

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

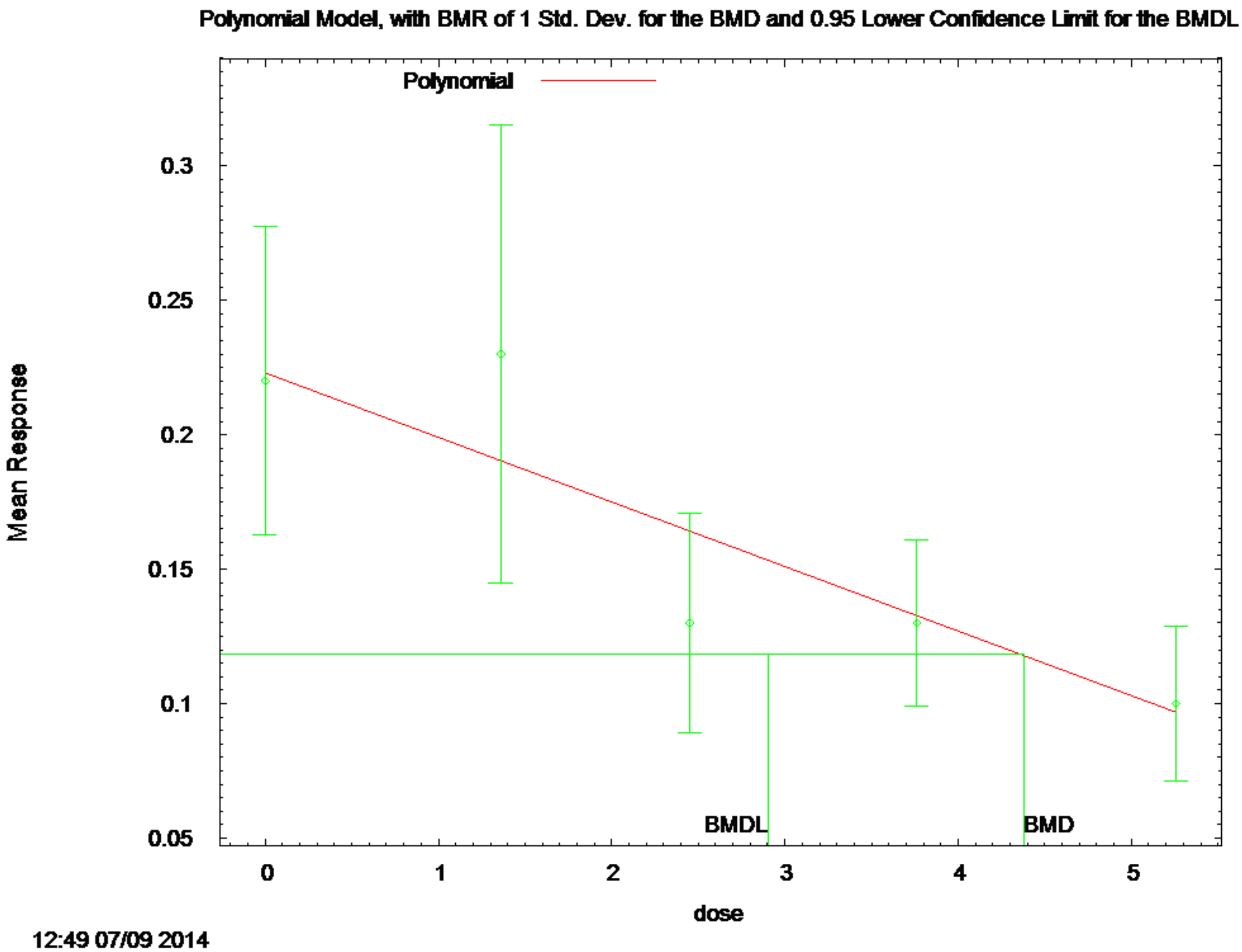
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.84958

BMDL = 2.03295


Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly3NCV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly3NCV-1SD-
5d.plt
                                        Wed Jul 09 12:49:39 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =     0.224911
                         beta_1 =            0
                         beta_2 =   -0.0222894
                         beta_3 =            0


           Asymptotic Correlation Matrix of Parameter Estimates
```

(*** The model parameter(s) -beta_2 -beta_3
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.076	0.083
rho	0.99	1	-0.076	0.083
beta_0	-0.076	-0.076	1	-0.92
beta_1	0.083	0.083	-0.92	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.557383	1.30166	-3.1086	1.99383
rho	2.63613	0.691385	1.28104	3.99122
beta_0	0.22329	0.0212241	0.181691	0.264888
beta_1	-0.0239544	0.00497926	-0.0337136	-0.0141953
beta_2	0	NA		
beta_3	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.223	0.08	0.105	-0.0992
1.361	10	0.23	0.191	0.119	0.0852	1.46

```
2.451      9       0.13        0.165        0.053       0.0702
-1.48
3.761      9       0.13        0.133         0.04       0.0531
-0.181
5.258     10        0.1       0.0973         0.04       0.0351
0.24
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	107.004496	4	-206.008991
R	92.681036	2	-181.362073

Explanation of Tests

```
 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001

Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	9.97226	3	0.0188

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

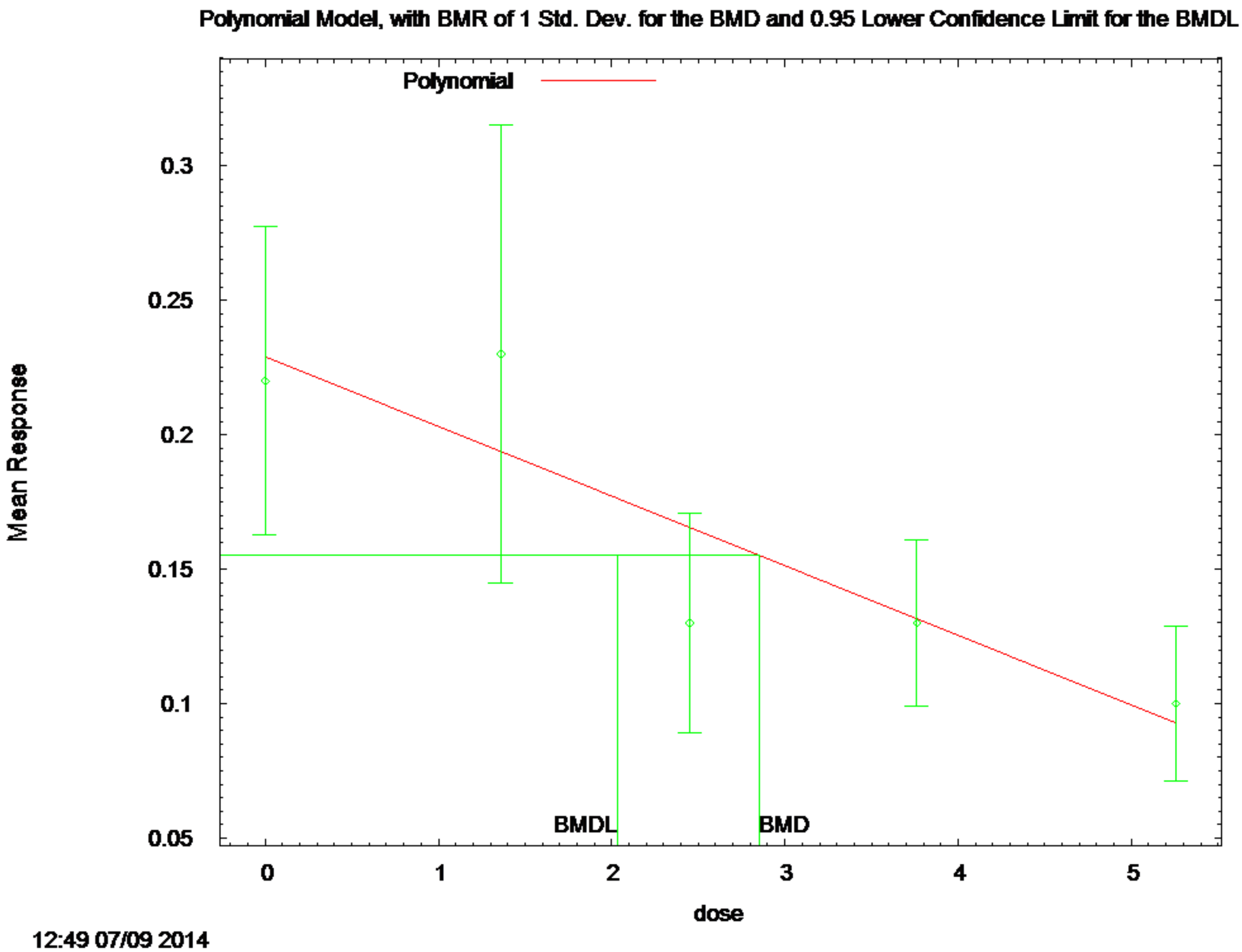
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.37872

BMDL = 2.90647



Polynomial Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Polynomial
0.3
0.25
0.2
0.15
0.1
0.05
Mean Response
BMDL
BMD
0
1
2
3
4
5
dose
12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly4CV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly4CV-1SD-
5d.plt
                                      Wed Jul 09 12:49:38 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The polynomial coefficients are restricted to be negative
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                         beta_0 =         0.22
                         beta_1 =            0
                         beta_2 =     -0.22957
                         beta_3 =            0
                         beta_4 =  -0.00619142
```

Asymptotic Correlation Matrix of Parameter Estimates

(*** The model parameter(s) -rho -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	alpha	beta_0	beta_1
alpha	1	-6.5e-012	-1e-012
beta_0	-6.5e-012	1	-0.81
beta_1	-1e-012	-0.81	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
alpha	0.00542838	0.00110806	0.00325661	0.00760014
beta_0	0.229102	0.0180267	0.193771	0.264434
beta_1	-0.0258556	0.00572228	-0.037071	-0.0146401
beta_2	-2.80498e-027	NA		
beta_3	-1.77823e-028	NA		
beta_4	-0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.229	0.08	0.0737	-0.391
1.361	10	0.23	0.194	0.119	0.0737	1.55
2.451	9	0.13	0.166	0.053	0.0737	

```
-1.45
3.761     9       0.13        0.132         0.04       0.0737
-0.0757
5.258    10        0.1       0.0932         0.04       0.0737
0.294
```

Model Descriptions for likelihoods calculated

```
 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	101.186766	3	-196.373532
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142

Test 3	18.1729	4	0.001142
Test 4	5.01329	3	0.1708

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider a
different variance model

The p-value for Test 4 is greater than .1. The model chosen seems
to adequately describe the data

Benchmark Dose Computation

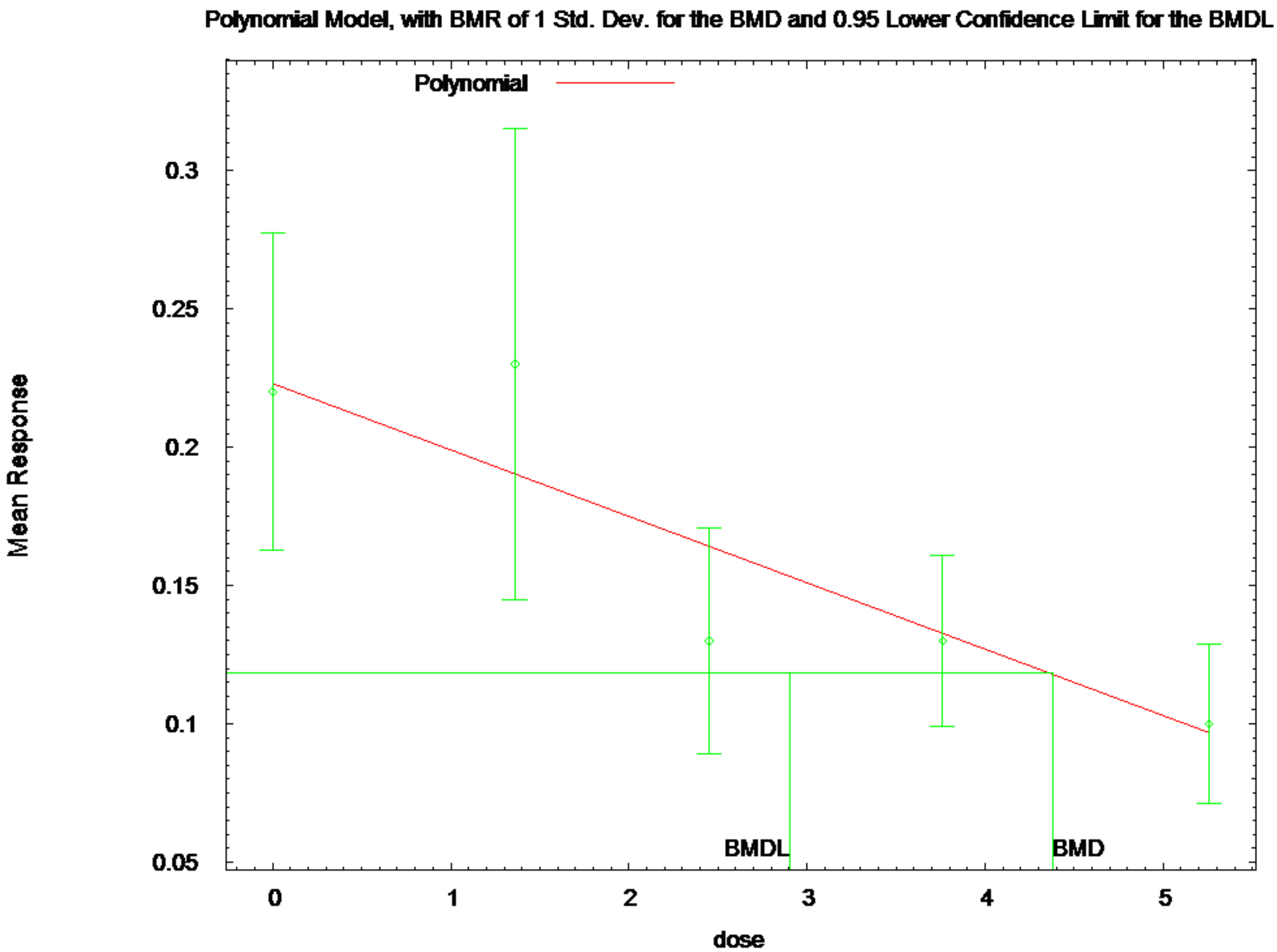
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 2.84958

BMDL = 2.03295



12:49 07/09 2014

```
====================================================================
===
       Polynomial Model. (Version: 2.19;  Date: 06/25/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly4NCV-1SD-
5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Rat_Monocyte_Concurrent
_Ln/Monocyte_Concurrent_Ln-HLS 2001-Monocyte Count-Poly4NCV-1SD-
5d.plt
                                        Wed Jul 09 12:49:39 2014

====================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = beta_0 + beta_1*dose + beta_2*dose^2 + ...


   Dependent variable = MeanResponse
   Independent variable = Dose
   The polynomial coefficients are restricted to be negative
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                         beta_0 =         0.22
                         beta_1 =            0
                         beta_2 =     -0.22957
                         beta_3 =            0
                         beta_4 =  -0.00619142
```

Asymptotic Correlation Matrix of Parameter Estimates

(*** The model parameter(s) -beta_2 -beta_3 -beta_4
have been estimated at a boundary point, or have been specified by the user,
and do not appear in the correlation matrix)

	lalpha	rho	beta_0	beta_1
lalpha	1	0.99	-0.076	0.083
rho	0.99	1	-0.076	0.083
beta_0	-0.076	-0.076	1	-0.92
beta_1	0.083	0.083	-0.92	1

Parameter Estimates

Variable	Estimate	Std. Err.	95.0% Wald Confidence Interval Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.557384	1.30166	-3.1086	1.99383
rho	2.63613	0.691385	1.28104	3.99122
beta_0	0.22329	0.0212241	0.181691	0.264888
beta_1	-0.0239544	0.00497926	-0.0337136	-0.0141953
beta_2	0	NA		
beta_3	0	NA		
beta_4	0	NA		

NA - Indicates that this parameter has hit a bound
implied by some inequality constraint and thus
has no standard error.

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.223	0.08	0.105	

```
-0.0992
1.361    10       0.23        0.191        0.119       0.0852
1.46
2.451     9       0.13        0.165        0.053       0.0702
-1.48
3.761     9       0.13        0.133         0.04       0.0531
-0.181
5.258    10        0.1       0.0973         0.04       0.0351
0.24
```

```
 Model Descriptions for likelihoods calculated


 Model A1:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma^2

 Model A2:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = Sigma(i)^2

 Model A3:        Yij = Mu(i) + e(ij)
           Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
     Model A3 uses any fixed variance parameters that
     were specified by the user

 Model  R:         Yi = Mu + e(i)
            Var{e(i)} = Sigma^2


                       Likelihoods of Interest

            Model      Log(likelihood)   # Param's      AIC
             A1          103.693409           6    -195.386818
             A2          112.779870          10    -205.559741
             A3          111.990624           7    -209.981248
         fitted          107.004496           4    -206.008991
              R           92.681036           2    -181.362073


                   Explanation of Tests

 Test 1:  Do responses and/or variances differ among Dose levels?
          (A2 vs. R)
 Test 2:  Are Variances Homogeneous? (A1 vs A2)
 Test 3:  Are variances adequately modeled? (A2 vs. A3)
 Test 4:  Does the Model for the Mean Fit? (A3 vs. fitted)
 (Note:  When rho=0 the results of Test 3 and Test 2 will be the
same.)

                     Tests of Interest
```

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	9.97226	3	0.0188

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

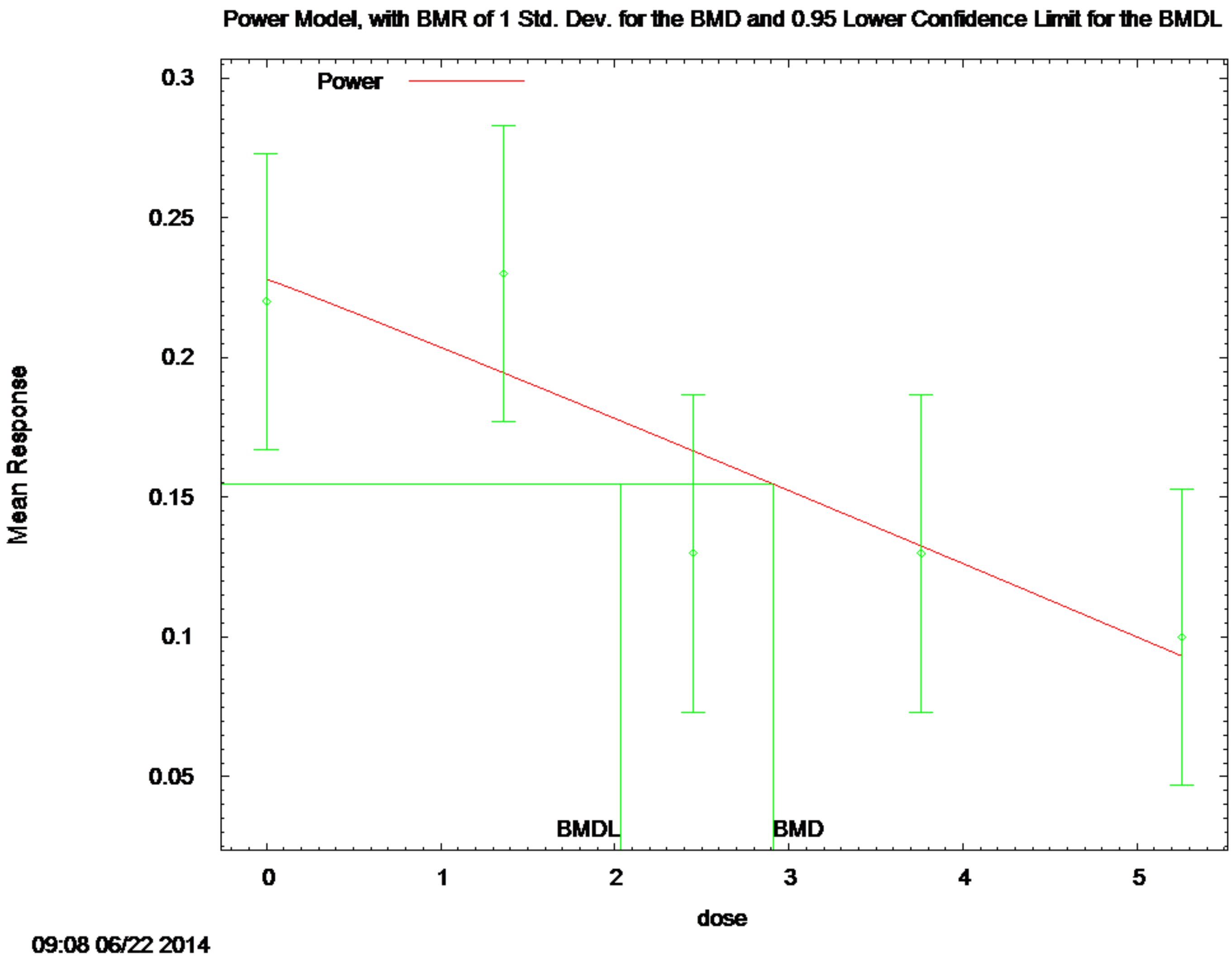
Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.37872

BMDL = 2.90647


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
=================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-PowerCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-PowerCV-1SD-5d.plt
                                      Sun Jun 22 09:08:08 2014

=================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   rho is set to 0
   The power is restricted to be greater than or equal to 1
   A constant variance model is fit

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                          alpha =   0.00545863
                            rho =            0   Specified
                        control =          0.1
                          slope =     0.174099
                          power =     -1.50587


           Asymptotic Correlation Matrix of Parameter Estimates

           ( *** The model parameter(s)  -rho
                 have been estimated at a boundary point, or have
```

been specified by the user,
and do not appear in the correlation matrix)

	alpha	control	slope	power
alpha	1	4e-008	-1.2e-007	-1.5e-007
control	4e-008	1	-0.72	-0.55
slope	-1.2e-007	-0.72	1	0.96
power	-1.5e-007	-0.55	0.96	1

Parameter Estimates

95.0% Wald Confidence Interval

Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
alpha	0.00542766	0.00110792	0.00325618	0.00759914
control	0.228176	0.0214028	0.186228	0.270125
slope	-0.0244404	0.018427	-0.0605565	0.0116758
power	1.03286	0.419442	0.210769	1.85495

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.228	0.08	0.0737	-0.351
1.361	10	0.23	0.195	0.119	0.0737	1.52
2.451	9	0.13	0.166	0.053	0.0737	-1.49
3.761	9	0.13	0.132	0.04	0.0737	-0.0882
5.258	10	0.1	0.0925	0.04	0.0737	0.323

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	103.693409	6	-195.386818
fitted	101.189934	4	-194.379868
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	18.1729	4	0.001142
Test 4	5.00695	2	0.0818

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. Consider running a
non-homogeneous variance model

The p-value for Test 3 is less than .1. You may want to consider
a
different variance model

The p-value for Test 4 is less than .1. You may want to try a
different
model

Benchmark Dose Computation

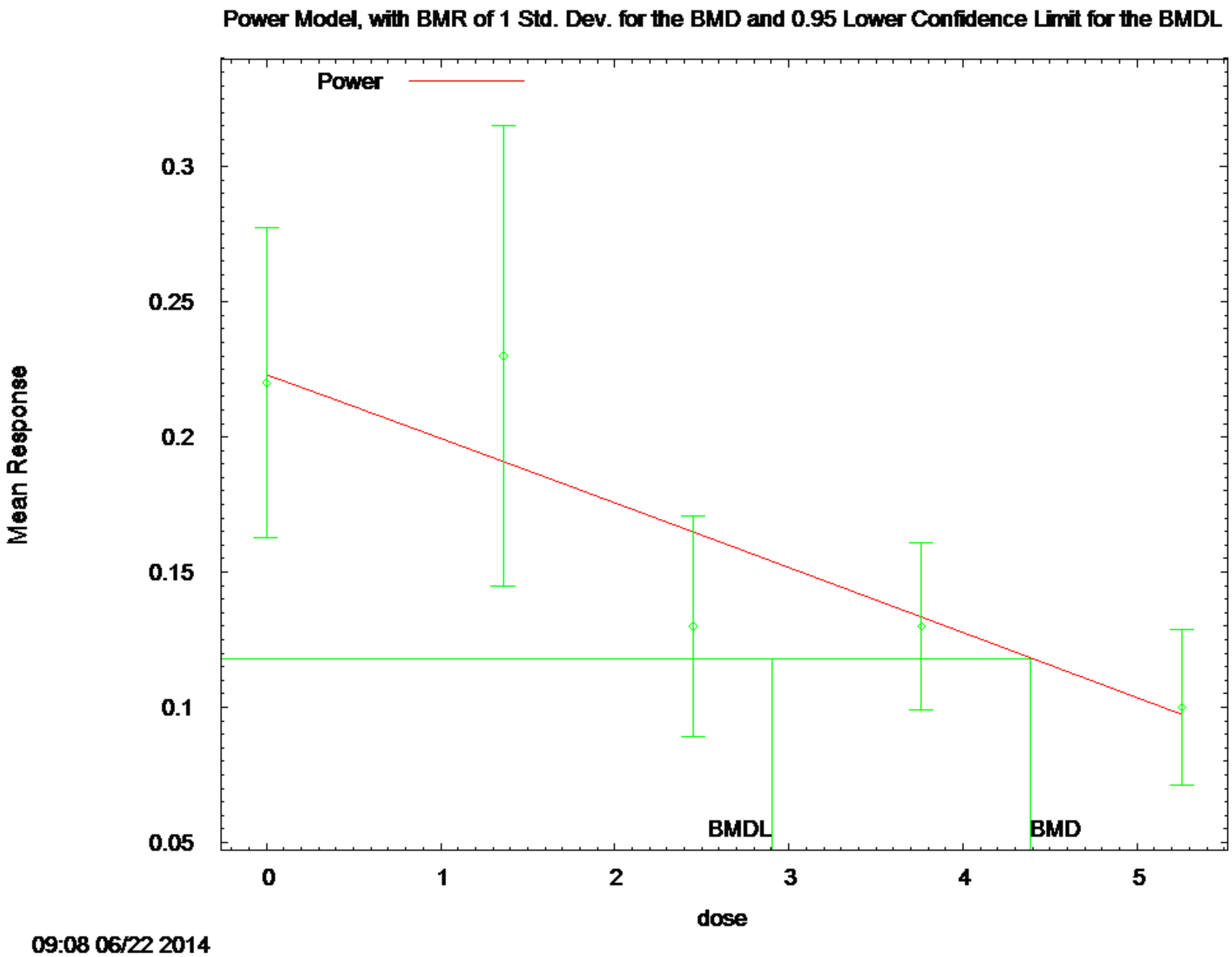
Specified effect = 1

Risk Type = Estimated standard deviations from the
control mean

Confidence level = 0.95

BMD = 2.9104

BMDL = 2.03363


Power Model, with BMR of 1 Std. Dev. for the BMD and 0.95 Lower Confidence Limit for the BMDL
Power
Mean Response
0.3
0.25
0.2
0.15
0.1
0.05
BMDL
BMD
0
1
2
3
4
5
dose
09:08 06/22 2014

```
==================================================================
===
       Power Model. (Version: 2.18;  Date: 05/19/2014)
       Input Data File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-PowerNCV-1SD-5d.(d)
       Gnuplot Plotting File:
C:/Users/dmayfield/Desktop/Norm/Monocyte_Concurrent_Ln-HLS 2001-
Monocyte Count-PowerNCV-1SD-5d.plt
                                       Sun Jun 22 09:08:09 2014

==================================================================
===

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
~~~~

   The form of the response function is:

   Y[dose] = control + slope * dose^power


   Dependent variable = MeanResponse
   Independent variable = Dose
   The power is restricted to be greater than or equal to 1
   The variance is to be modeled as Var(i) = exp(lalpha + log
(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008



                  Default Initial Parameter Values
                         lalpha =     -5.21056
                            rho =            0
                        control =          0.1
                          slope =     0.174099
                          power =     -1.50587


           Asymptotic Correlation Matrix of Parameter Estimates

                 lalpha          rho      control        slope
power
```

lalpha	1	0.99	-0.5	0.26	0.081
rho	0.99	1	-0.45	0.25	0.081
control	-0.5	-0.45	1	-0.81	-0.64
slope	0.26	0.25	-0.81	1	0.96
power	0.081	0.081	-0.64	0.96	1

Parameter Estimates

			95.0% Wald Confidence Interval	
Variable	Estimate	Std. Err.	Lower Conf. Limit	Upper Conf. Limit
lalpha	-0.553873	1.75668	-3.9969	2.88915
rho	2.63797	0.921616	0.831639	4.44431
control	0.222847	0.0276528	0.168649	0.277045
slope	-0.0235189	0.0181588	-0.0591095	0.0120718
power	1.00904	0.366939	0.289854	1.72823

Table of Data and Estimated Values of Interest

Dose	N	Obs Mean	Est Mean	Obs Std Dev	Est Std Dev	Scaled Res.
0	10	0.22	0.223	0.08	0.105	-0.086
1.361	10	0.23	0.191	0.119	0.0852	1.46
2.451	9	0.13	0.165	0.053	0.0703	-1.48
3.761	9	0.13	0.133	0.04	0.0532	-0.188

5.258 10 0.1 0.0973 0.04 0.0351
0.242

Model Descriptions for likelihoods calculated

```
Model A1:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma^2

Model A2:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = Sigma(i)^2

Model A3:        Yij = Mu(i) + e(ij)
          Var{e(ij)} = exp(lalpha + rho*ln(Mu(i)))
    Model A3 uses any fixed variance parameters that
    were specified by the user

Model  R:         Yi = Mu + e(i)
           Var{e(i)} = Sigma^2
```

Likelihoods of Interest

Model	Log(likelihood)	# Param's	AIC
A1	103.693409	6	-195.386818
A2	112.779870	10	-205.559741
A3	111.990624	7	-209.981248
fitted	107.004802	5	-204.009605
R	92.681036	2	-181.362073

Explanation of Tests

Test 1: Do responses and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A1 vs A2)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does the Model for the Mean Fit? (A3 vs. fitted)
(Note: When rho=0 the results of Test 3 and Test 2 will be the same.)

Tests of Interest

Test	-2*log(Likelihood Ratio)	Test df	p-value
Test 1	40.1977	8	<.0001
Test 2	18.1729	4	0.001142
Test 3	1.57849	3	0.6643
Test 4	9.97164	2	0.006834

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels
It seems appropriate to model the data

The p-value for Test 2 is less than .1. A non-homogeneous variance
model appears to be appropriate

The p-value for Test 3 is greater than .1. The modeled variance appears
to be appropriate here

The p-value for Test 4 is less than .1. You may want to try a different
model

Benchmark Dose Computation

Specified effect = 1

Risk Type = Estimated standard deviations from the control mean

Confidence level = 0.95

BMD = 4.39068

BMDL = 2.90659