US EPA ARCHIVE DOCUMENT

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM
Date: September 9, 2010

SUBJECT: Acephate and Methamidophos: Benchmark Dose Analysis of Acute Oral Studies and derivation of a Point of Departure and Relative Potency Factor.

PC Code: 103301
Decision No.: 440319
Petition No.: NA
Risk Assessment Type: NA
TXR No.: 0055521
MRID No.: NA

DP Barcode: D383706
Registration No.: NA
Regulatory Action: NA
Case No.: NA
CAS No.: NA
40 CFR: NA

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US EPA ARCHIVE DOCUMENT

I. CONCLUSIONS

RAB5 performed benchmark dose (BMD) analyses of several acute oral studies on acephate and methamidophos in order to establish a point of departure (POD) for acephate (single-chemical assessment) and an acephate-based relative potency factor (RPF) to convert methamidophos residues formed from the application of acephate to acephate-equivalent concentrations.

Based on the analyses, it is concluded that the use of acephate (POD of 0.304) as the index chemical will provide the most health-protective and most scientifically supportable approach for the acephate single-chemical assessment and that an RPF of 2.76 should be used to convert methamidophos residues to acephate-equivalent concentrations.

This memo summarizes the approach and presents the results of BMD analyses and POD and RPF derivation.

II. BACKGROUND

BMD analyses were performed with EPA's Benchmark Dose Software (Version 2.1.1) using an exponential model for continuous data. The data selected for evaluation consisted of decreased brain and red blood cell (RBC) cholinesterase (ChE) activities, the most relevant effects. The analyses focused on both pup and adult data from the comparative cholinesterase (CCA) studies that entailed single dose exposures. The CCA studies allow for the evaluation of pup vs. adult sensitivity and allow for removal of the FQPA factor since the most sensitive group (i.e., the pup) is considered. OPP has previously used the exponential model for modeling ChE activity. Model runs for ChE activity were conducted with an appropriate benchmark response level (10%), and statistical (e.g., goodness of fit values) and graphical results were used in model evaluation.

III. RESULTS

The results of the BMD analyses are summarized in Table 1 below. Details are included in the appendix.

TABLE 1: Results of BMD Exponential Modeling for Brain and RBC ChE Data on Acephate and Methamidophos

Chemical/Study	Sex/age	Endpoint	BMD Results	
			BMD10	BMDL10
Acephate MRID 44203302 Acute Study	Male	Hippocampus ChE	2.29167	1.30024
	Female	Hippocampus ChE	1.80914	1.17087
	Male	RBC ChE	(No adequate fit)	(No adequate fit)
	Female	RBC ChE	3.72746	2.52384
Acephate MRID 46151801 CCA Study	Adult Male	Brain ChE	1.65457	1.38198
	Adult Female	Brain ChE	(no adequate fit)	(no adequate fit)
	Adult Male	RBC ChE	(no adequate fit)	(no adequate fit)
	Adult Female	RBC ChE	(no adequate fit)	(no adequate fit)
Acephate MRID 46151801 CCA Study	Pup Male	Brain ChE	0.513127	0.303985
	Pup Female	Brain ChE	2.47396	1.01307
	Pup Male	RBC ChE	(no adequate fit)	(no adequate fit)
	Pup Female	RBC ChE	(no adequate fit)	(no adequate fit)
Methamidophos MRID 43025001 Acute Study	Male	Brain ChE	0.226159	0.208557
	Female	Brain ChE	(no adequate fit)	(no adequate fit)
Methamidophos MRID 43345801 ACN Study	Male	Brain ChE	(no adequate fit)	(no adequate fit)
	Female	Brain ChE	(no adequate fit)	(no adequate fit)
Methamidophos 46594003Ad	Adult Male	Brain ChE	0.293899	0.204274
	Adult Female	Brain ChE	(no adequate fit)	(no adequate fit)
Methamidophos 46594003Pup	Pup Male	Brain ChE	0.185773	0.136508
	Pup Female	Brain ChE	0.196438	0.144398
	Pup Male	RBC ChE	0.0629786	0.0345784
	Pup Female	RBC ChE	0.262528	0.125689

Table 2 below summarizes the oral RPFs for acephate and methamidophos based on the brain ChE data for pup. The RBC ChE data for pup was not amenable to BMD modeling and therefore oral RPFs are not presented for the RBC compartment.

Table 2. Acephate and Methamidophos ORAL RPFs for Pup Brain ChE Data

Pesticide	**Oral RPF** (acephate-based)	**Oral RPF** (methamidophos-based)	**BMD_{10}**	**$BMDL_{10}$**
Acephate	1.0	0.363	0.51	0.304
Methamidophos	2.76	1.0	0.186	0.137

Based on the results in Table 2, it is recommended that a BMDL10 of 0.304 mg/kg from the PND11 male brain ChE inhibition be used[1] as the POD for the combined acephate and methamidophos assesment. It is further recommended that a RPF of 2.76 be used to convert residues of methamidophos to acephate-equivalent concentrations.

[1] The methamidophos-based POD of 0.137 would be equivalent to 0.378 (2.76 x 0.137) POD for acephate.

APPENDIX

Acephate; MRID 44203302
Male RBC ChE

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Tue May 25 08:57:51 2010
 ================================================================

 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 = Mean
   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 = 250
   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          Model 3          Model 4          Model 5
     --------          -------          -------          -------          -------
      lnalpha           9.77394          9.77394          9.77394
9.77394
          rho(S)                0                0                0
0
            a           1451.32          1451.32           2725.8
2725.8
            b       0.00116256       0.00116256       0.00740575
0.00740575
```

c	--	--	0.412286	0.412286
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	11.7481	11.7481	10.6389	10.6389
rho	0	0	0	0
a	2056.26	2056.26	2424.92	2424.92
b	0.00147775	0.00147775	0.0426332	0.0426332
c	--	--	0.517415	0.517415
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	2596	193
5	2	1937	183.8
25	2	1778	207.2
125	2	1307	244.7
500	2	1180	43.1

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2056	355.7	2.146
	5	2041	355.7	-0.414
	25	1982	355.7	-0.8098
	125	1709	355.7	-1.6
	500	982.2	355.7	0.7865
3	0	2056	355.7	2.146
	5	2041	355.7	-0.414
	25	1982	355.7	-0.8098
	125	1709	355.7	-1.6
	500	982.2	355.7	0.7865
4	0	2425	204.3	1.184
	5	2200	204.3	-1.823
	25	1658	204.3	0.8324
	125	1260	204.3	0.3229
	500	1255	204.3	-0.5171
5	0	2425	204.3	1.184
	5	2200	204.3	-1.823
	25	1658	204.3	0.8324
	125	1260	204.3	0.3229
	500	1255	204.3	-0.5171

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	-53.86971	6	119.7394
A2	-51.68182	10	123.3636
A3	-53.86971	6	119.7394
R	-67.56781	2	139.1356
2	-63.74074	3	133.4815
3	-63.74074	3	133.4815
4	-58.1945	4	124.389
5	-58.1945	4	124.389

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.77	8	0.0001023
Test 2	4.376	4	0.3575
Test 3	4.376	4	0.3575
Test 4	19.74	3	0.000192
Test 5a	19.74	3	0.000192
Test 5b	-3.268e-013	0	N/A

Test 6a	8.65	2	0.01324
Test 6b	11.09	1	0.0008668
Test 7a	8.65	2	0.01324
Test 7b	11.09	1	0.0008668
Test 7c	-5.684e-014	0	N/A

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 greater than .1. A homogeneous variance model appears to be appropriate here.

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

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.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

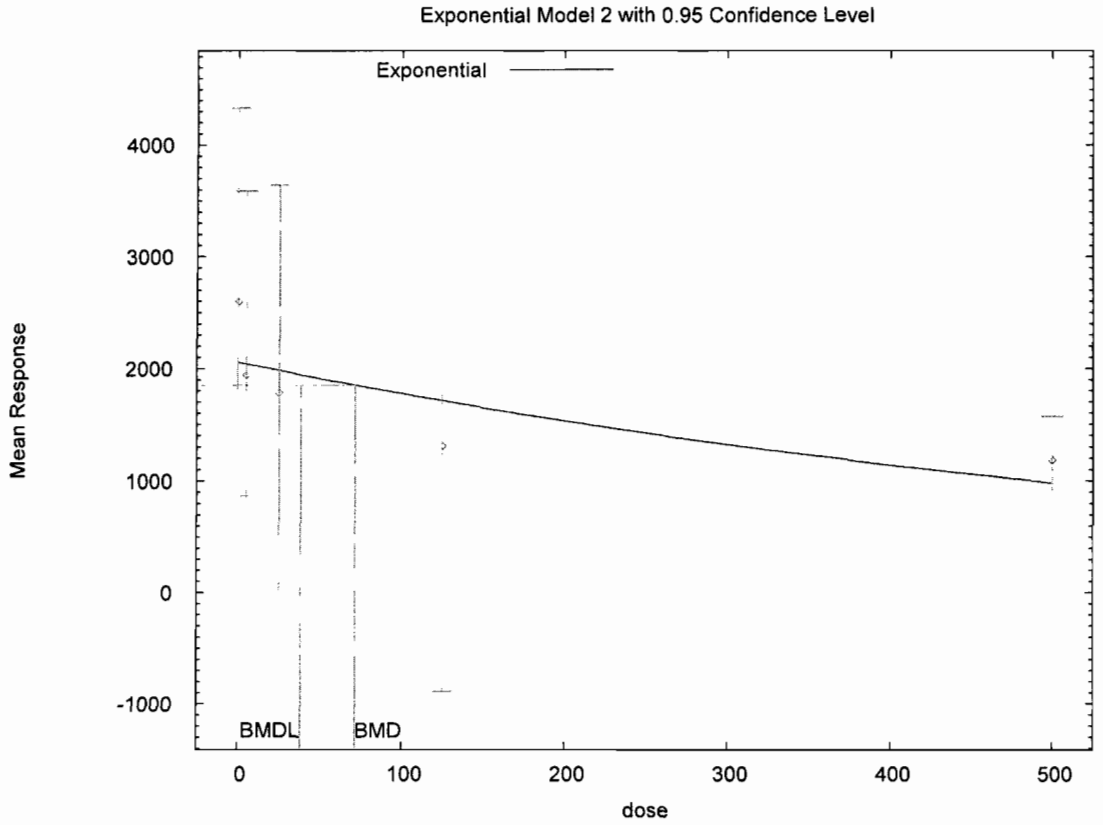
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	71.2978	38.0257
3	71.2978	38.0257
4	5.44661	1.47329
5	5.44661	1.47329


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
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3000
2000
1000
0
-1000
BMDL
BMD
0
100
200
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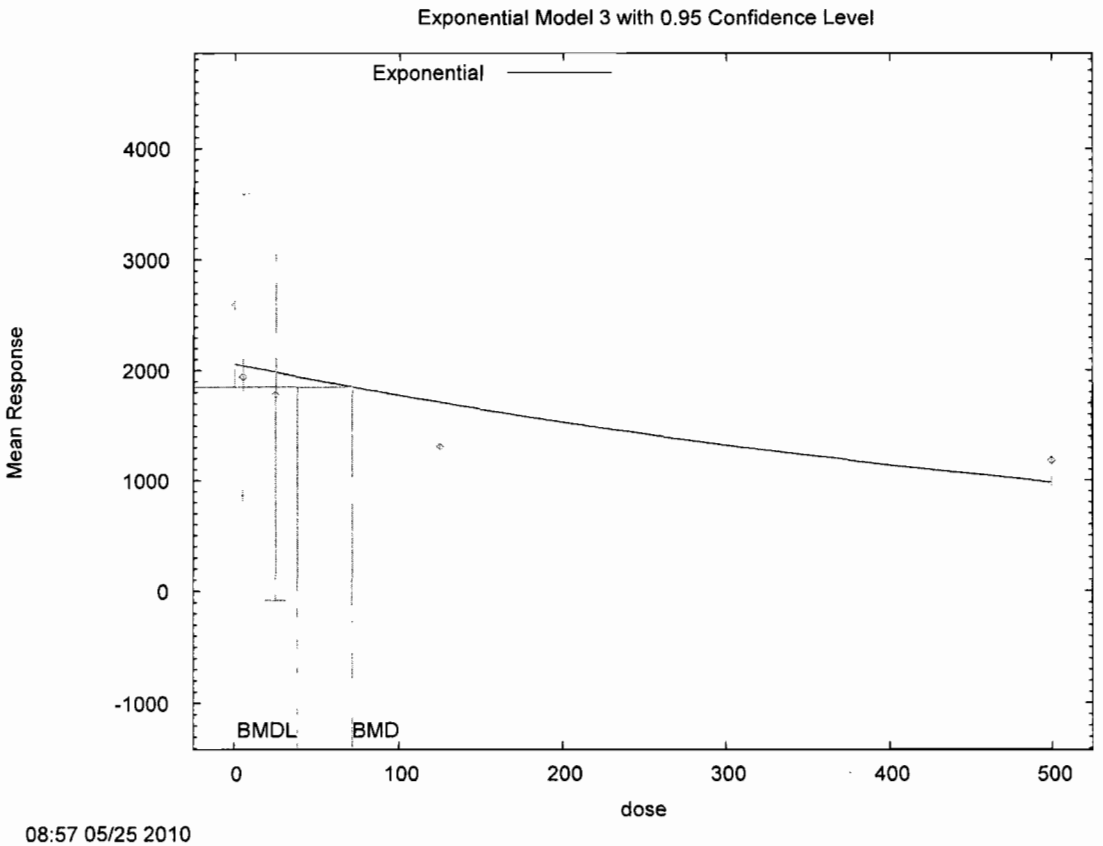
400
500
dose
08:57 05/25 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
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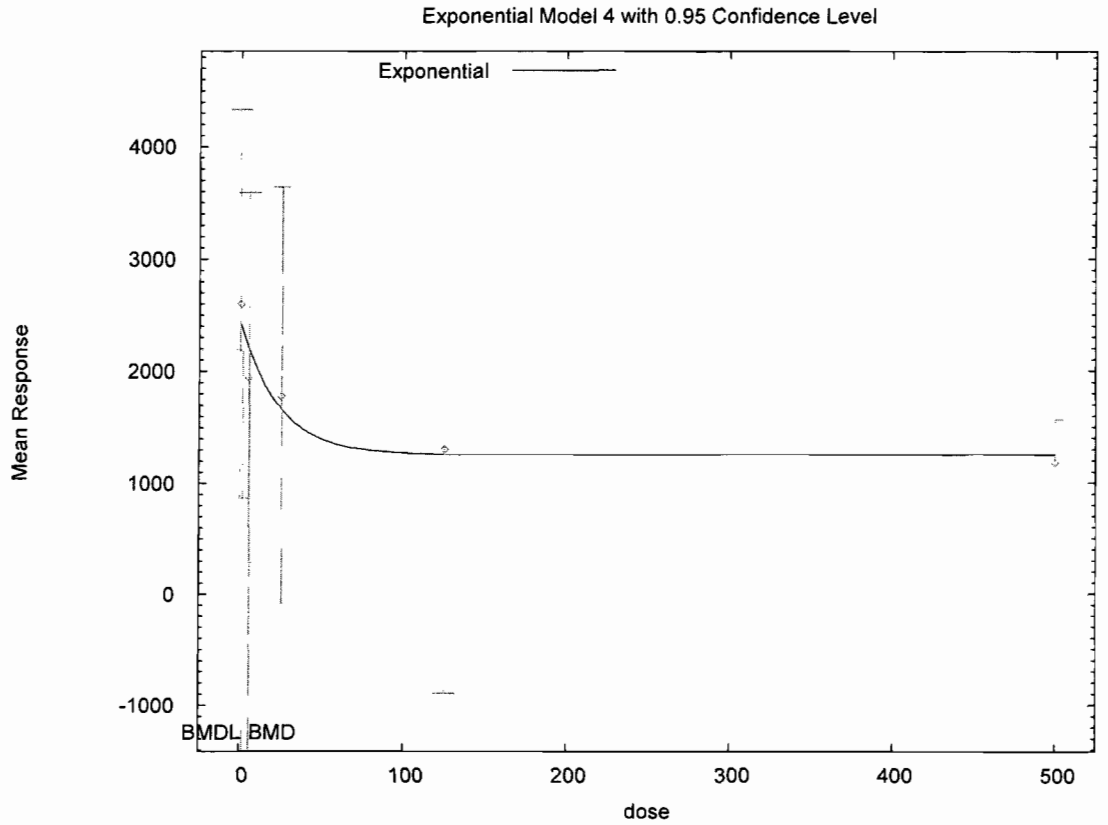
2000
1000
0
-1000
BMDL
BMD
0
100
200
300
400
500
dose
08:57 05/25 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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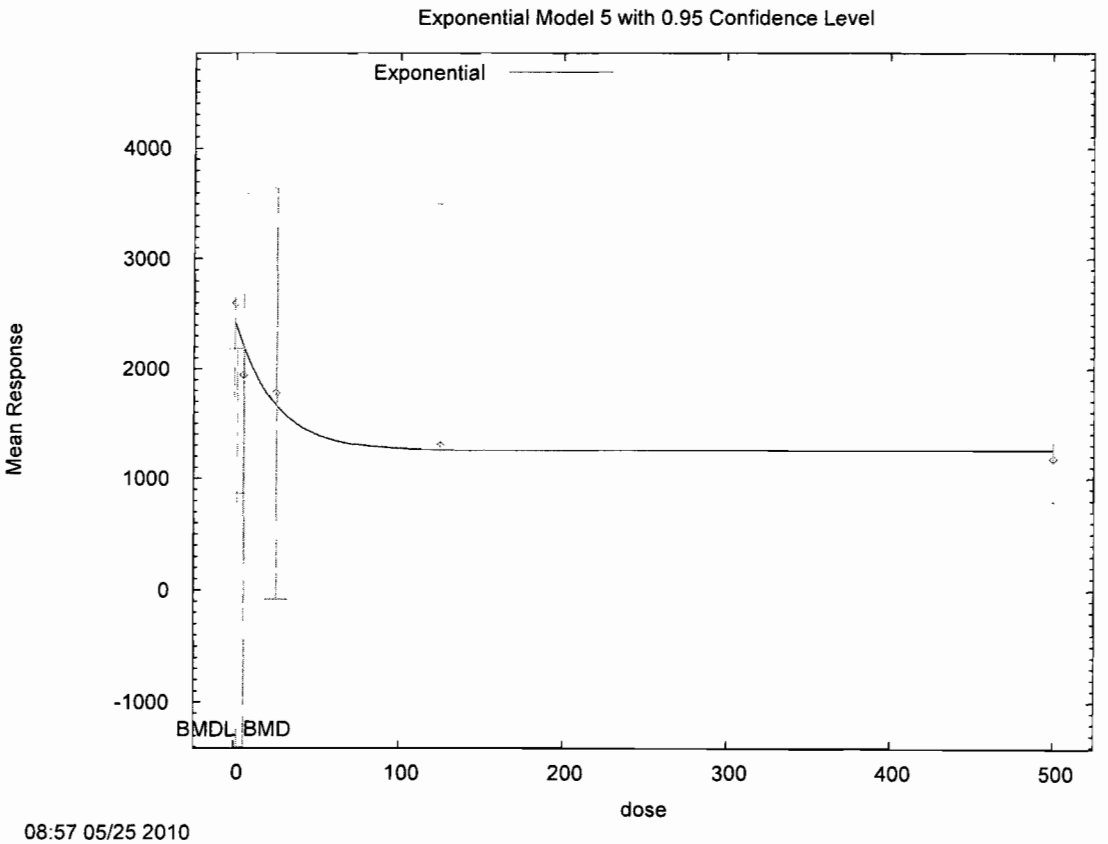
1000
0
-1000
BMDL BMD
0
100
200
300
400
500
dose
08:57 05/25 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
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1000
0
-1000
BMDL BMD
0
100
200
300
400
500
dose
08:57 05/25 2010

Acephate; MRID 44203302
Male RBC ChE

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Tue May 25 09:14:22 2010
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 BMDS Model Run
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   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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha          -7.58216          -7.58216            -7.58216          -
7.58216
          rho           2.36954           2.36954             2.36954
2.36954
            a           1451.32           1451.32              2725.8
2725.8
            b       0.00116256        0.00116256          0.00740575
0.00740575
            c                --                --              0.412286
0.412286
            d                --                 1                 --
1
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-83.282	-83.282	-7.72769	-7.7277
rho	12.769	12.769	2.44638	2.44638
a	1823.92	1823.92	2361.42	2361.42
b	0.000873882	0.000873882	0.0310877	0.0310877
c	--	--	0.52042	0.52042
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	2596	193
5	2	1937	183.8
25	2	1778	207.2
125	2	1307	244.7
500	2	1180	43.1

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1824	543.8	2.008
	5	1816	528.8	0.3237
	25	1785	473	-0.01945
	125	1635	270.7	-1.714
	500	1178	33.41	0.07319
3	0	1824	543.8	2.008
	5	1816	528.8	0.3237
	25	1785	473	-0.01945
	125	1635	270.7	-1.714
	500	1178	33.41	0.07319
4	0	2361	280.5	1.183
	5	2198	257	-1.438
	25	1750	194.4	0.2071
	125	1252	129.1	0.6004
	500	1229	126.2	-0.5484
5	0	2361	280.5	1.183
	5	2198	257	-1.438
	25	1750	194.4	0.2071
	125	1252	129.1	0.6004
	500	1229	126.2	-0.5484

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	-53.86971	6	119.7394
A2	-51.68182	10	123.3636
A3	-53.8118	7	121.6236
R	-67.56781	2	139.1356
2	-60.677	4	129.354
3	-60.677	4	129.354
4	-57.30858	5	124.6172
5	-57.30858	5	124.6172

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	31.77	8	0.0001023
Test 2	4.376	4	0.3575
Test 3	4.26	3	0.2347
Test 4	13.73	3	0.003296
Test 5a	13.73	3	0.003296
Test 5b	0	0	N/A
Test 6a	6.994	2	0.03029
Test 6b	6.737	1	0.009444
Test 7a	6.994	2	0.03029
Test 7b	6.737	1	0.009444
Test 7c	-8.811e-013	0	N/A

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 greater than .1. Consider
running a homogeneous model.

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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.

The p-value for Test 6b is less than .05. Model 4 appears
to fit the data better than Model 2.

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.

The p-value for Test 7b is less than .05. Model 5 appears
to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

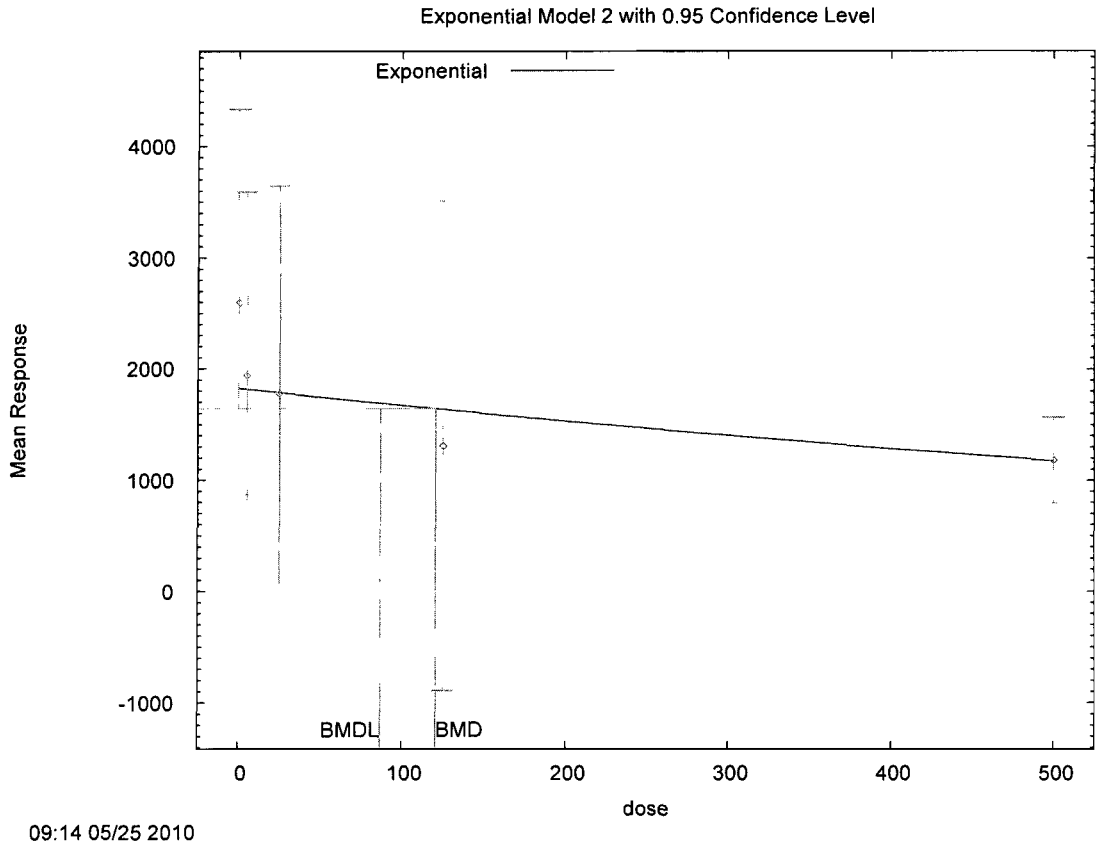
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	120.566	86.8319
3	120.566	86.8319
4	7.52211	3.25401
5	7.52211	3.25401


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
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BMDL
BMD
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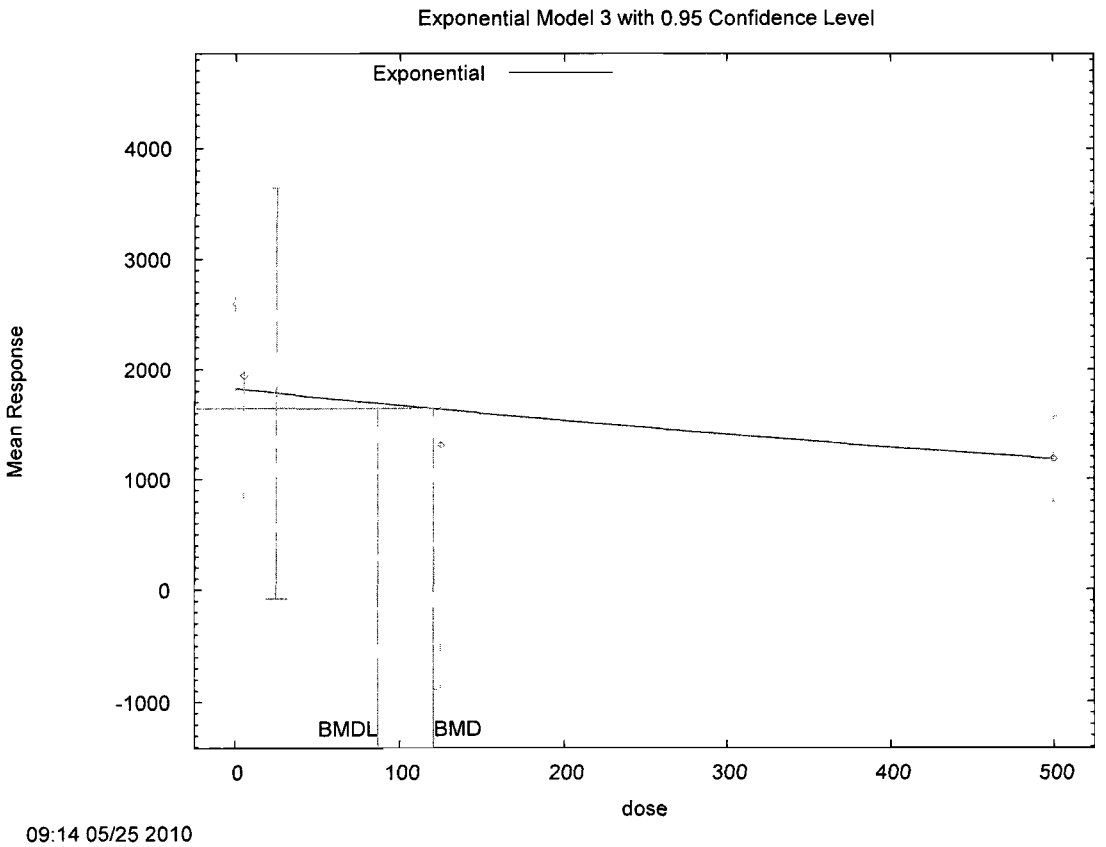
09:14 05/25 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
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3000
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1000
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-1000
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BMD
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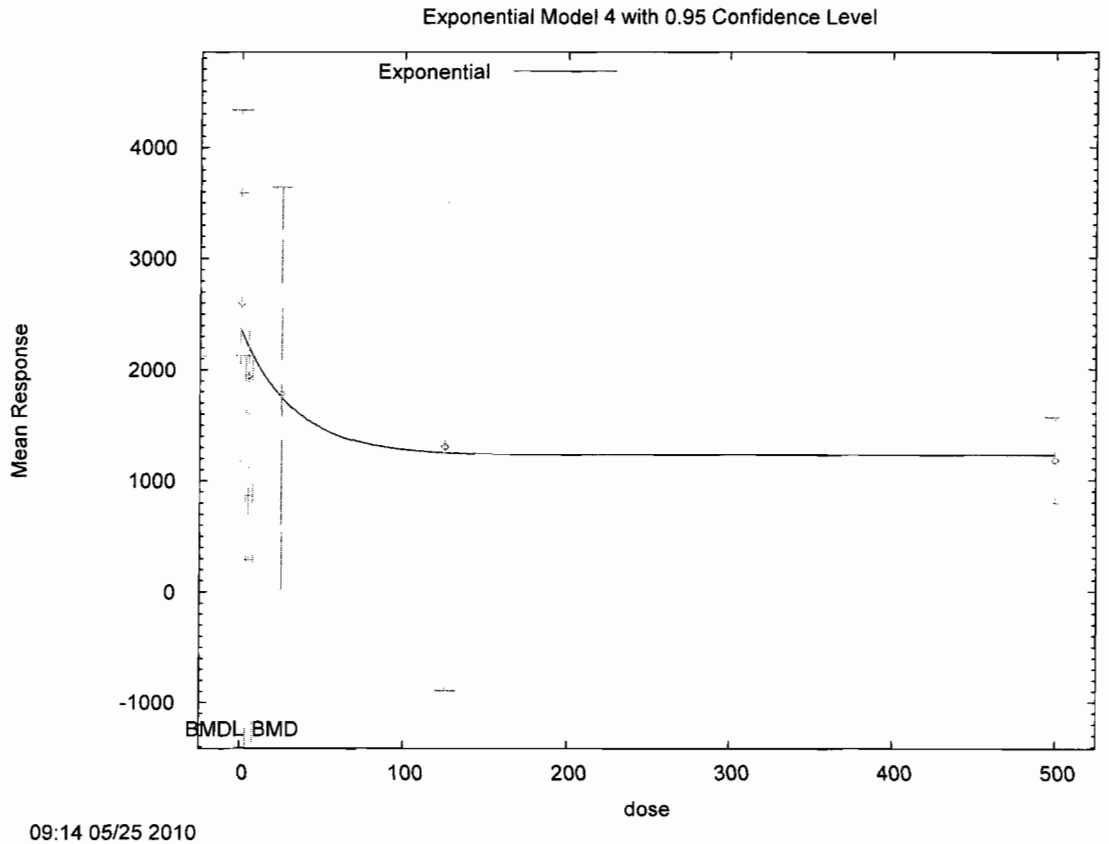
dose
09:14 05/25 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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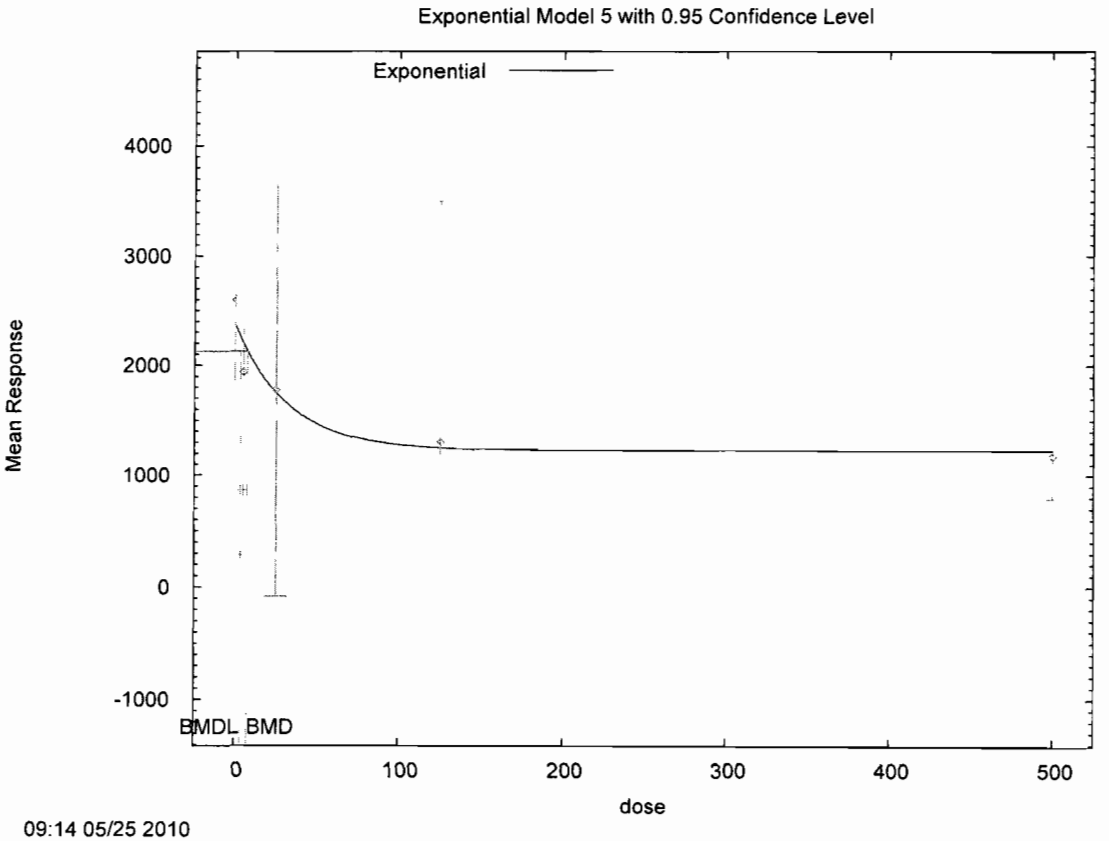
3000
2000
1000
0
-1000
BMDL BMD
0
100
200
300
400
500
dose
09:14 05/25 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
4000
3000
2000
1000
0
-1000
BMDL BMD
0
100
200
300
400
500
dose
09:14 05/25 2010

Acephate; MRID 44203302
Male Hippocampus ChE

```
Warning:  optimum may not have been found form model 1 (BMDL).  Bad process completion
in Optimization routine.


 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Mon May 24 09:40:23 2010
 ================================================================

 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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha          -2.58609          -2.58609            -2.58609          -
2.58609
          rho          0.977311          0.977311            0.977311
0.977311
            a           1.98017           1.98017              6.6675
6.6675
            b         0.0024492         0.0024492          0.00993515
0.00993515
            c                --                --               0.185691
0.185691
```

d	--	1	--
1			

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.301276	-0.301276	-2.62861	-2.62861
rho	-0.0942359	-0.094236	1.08434	1.08434
a	5.79844	5.79843	5.93956	5.93956
b	0.0287506	0.0287506	0.0521014	0.0521014
c	--	--	0.237421	0.237421
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	6.35	0.792
5	2	4.37	0.382
25	2	2.78	0.714
125	2	1.51	0.148
500	2	1.3	0.566

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	5.798	0.7918	0.9851
	5	5.022	0.7972	-1.157
	25	2.826	0.8191	-0.07923
	125	0.1594	0.9379	2.036
	500	3.313e-006	1.559	1.179
3	0	5.798	0.7918	0.9851
	5	5.022	0.7972	-1.157
	25	2.826	0.8191	-0.07923
	125	0.1594	0.9379	2.036
	500	3.313e-006	1.559	1.179
4	0	5.94	0.7058	0.8224
	5	4.901	0.636	-1.18
	25	2.641	0.4549	0.4307
	125	1.417	0.3245	0.4057
	500	1.41	0.3237	-0.4814
5	0	5.94	0.7058	0.8224
	5	4.901	0.636	-1.18
	25	2.641	0.4549	0.4307
	125	1.417	0.3245	0.4057
	500	1.41	0.3237	-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	4.084636	6	3.830729
A2	6.489946	10	7.020108
A3	4.415234	7	5.169531
R	-11.60272	2	27.20545
2	-4.440097	4	16.88019
3	-4.440097	4	16.88019
4	2.683894	5	4.632213
5	2.683894	5	4.632213

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	36.19	8	< 0.0001
Test 2	4.811	4	0.3073
Test 3	4.149	3	0.2458
Test 4	17.71	3	0.0005046
Test 5a	17.71	3	0.0005046
Test 5b	-7.319e-013	0	N/A
Test 6a	3.463	2	0.177
Test 6b	14.25	1	0.0001602
Test 7a	3.463	2	0.177
Test 7b	14.25	1	0.0001602

Test 7c	-2.629e-013	0	N/A

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 greater than .1. Consider running a homogeneous model.

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

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

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

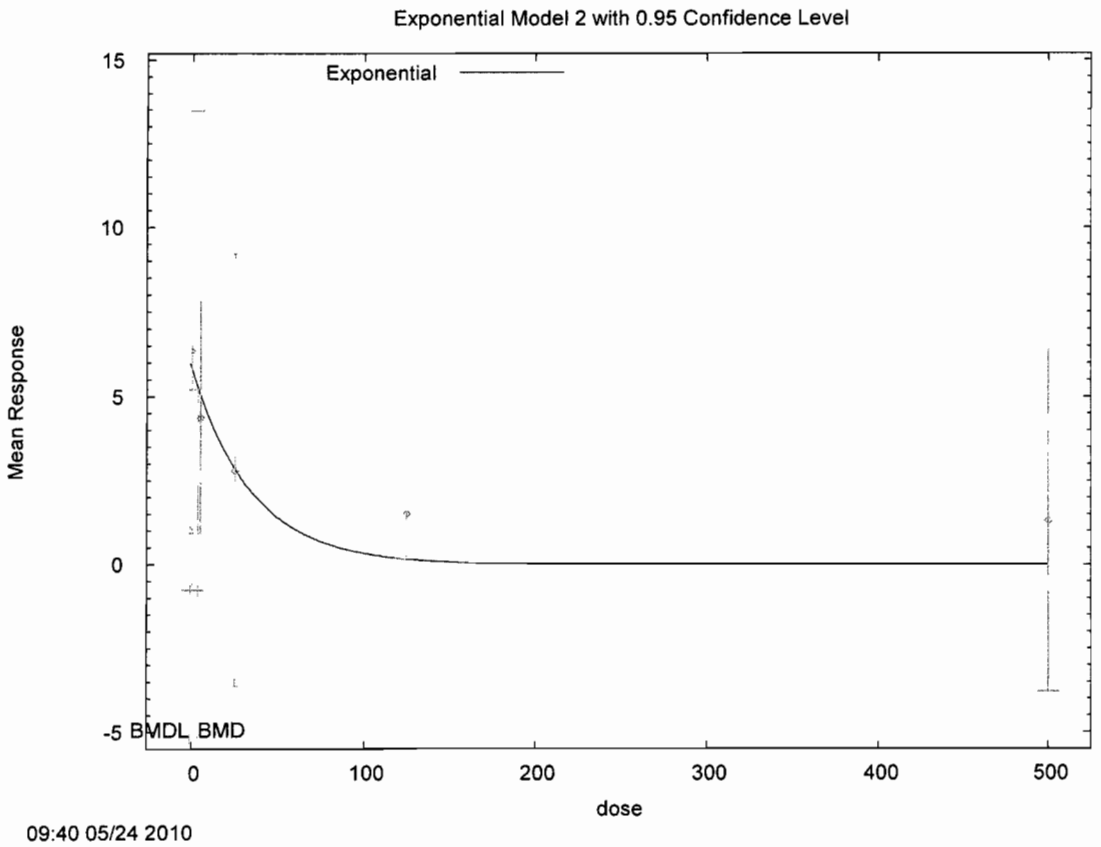
Specified Effect = 0.100000

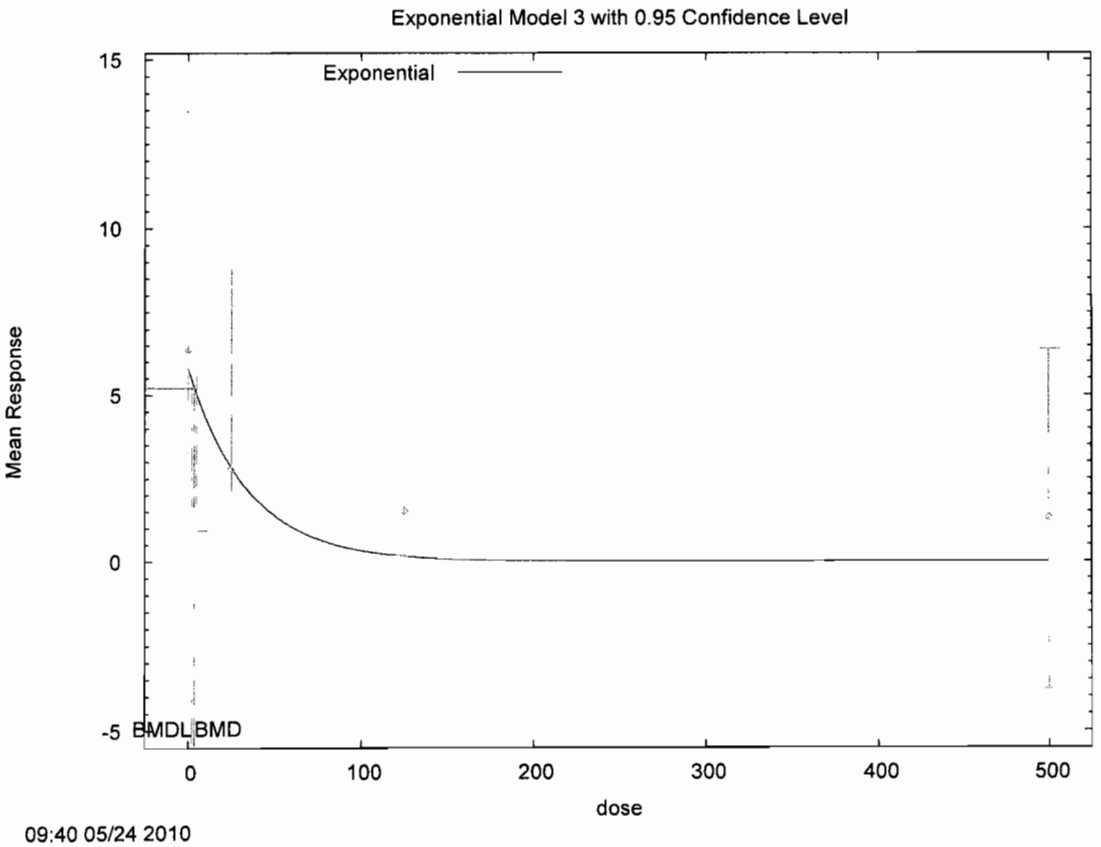
Risk Type = Relative deviation

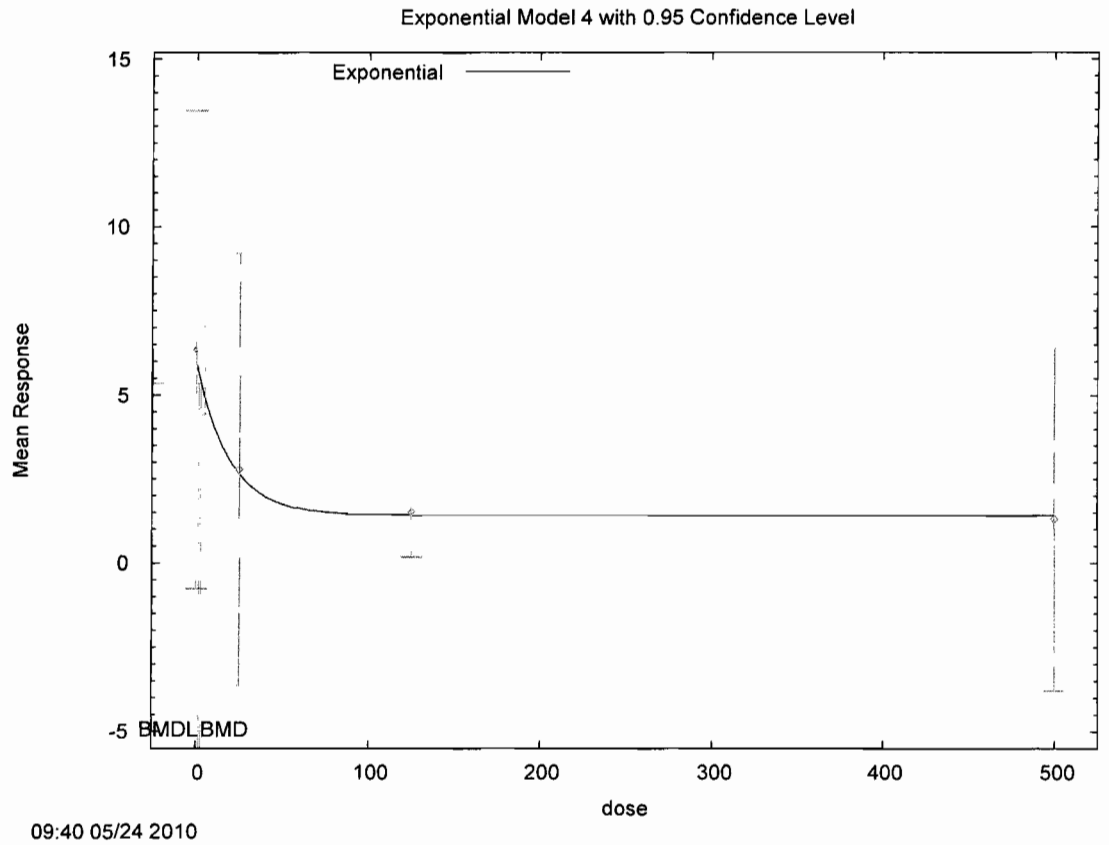
Confidence Level = 0.950000

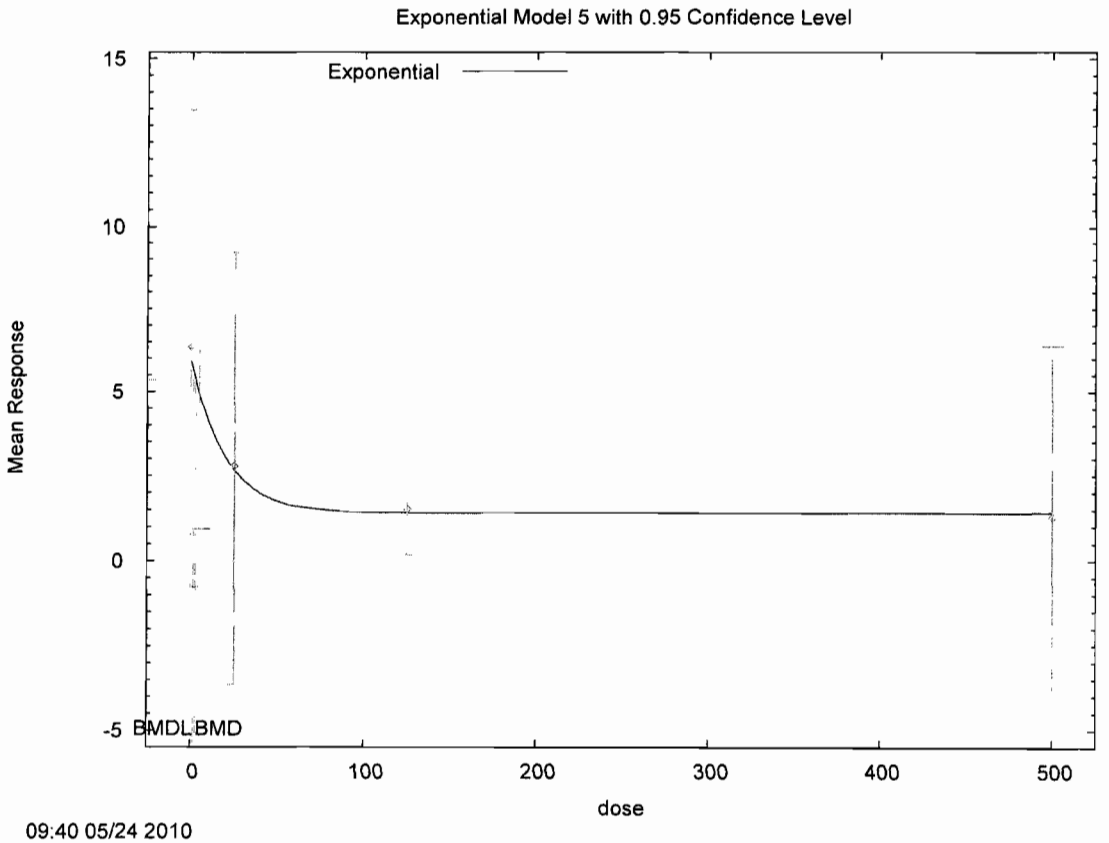
BMD and BMDL by Model

Model	BMD	BMDL
2	3.66464	Bad completion
3	3.66464	2.16271
4	2.69794	1.64328
5	2.69794	1.64328


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL BMD
0
100
200
300
400
500
dose
09:40 05/24 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL BMD
0
100
200
300
400
500
dose
09:40 05/24 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL BMD
0
100
200
300
400
500
dose
09:40 05/24 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL BMD
0
100
200
300
400
500
dose
09:40 05/24 2010

Acephate; MRID 44203302
Male Hippocampus ChE

```
Warning:  optimum may not have been found form model 1 (BMDL).  Bad process completion
in Optimization routine.
Warning:  optimum may not have been found form model 2 (BMDL).  Bad process completion
in Optimization routine.


 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Mon May 24 09:33:31 2010
 ================================================================

 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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha          -1.81693          -1.81693            -1.81693          -
1.81693
         rho(S)                0                 0                   0
0
```

a	1.98017	1.98017	6.6675	6.6675
b	0.0024492	0.0024492	0.00993515	0.00993515
c	--	--	0.185691	0.185691
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	0.00263274	0.0026326	-1.38055	-1.38055
rho	0	0	0	0
a	5.6065	5.6065	6.06937	6.06937
b	0.0224156	0.0224156	0.0617464	0.0617463
c	--	--	0.242118	0.242118
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	6.35	0.792
5	2	4.37	0.382
25	2	2.78	0.714
125	2	1.51	0.148
500	2	1.3	0.566

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	5.606	1.001	1.05
	5	5.012	1.001	-0.9068
	25	3.201	1.001	-0.5949
	125	0.3403	1.001	1.652
	500	7.607e-005	1.001	1.836
3	0	5.607	1.001	1.05
	5	5.012	1.001	-0.9068
	25	3.201	1.001	-0.5949
	125	0.3403	1.001	1.652
	500	7.607e-005	1.001	1.836
4	0	6.069	0.5014	0.7915
	5	4.848	0.5014	-1.347
	25	2.452	0.5014	0.925
	125	1.472	0.5014	0.1084
	500	1.47	0.5014	-0.4781
5	0	6.069	0.5014	0.7915
	5	4.848	0.5014	-1.347
	25	2.452	0.5014	0.925

125	1.472	0.5014	0.1084
500	1.47	0.5014	-0.4781

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	4.084636	6	3.830729
A2	6.489946	10	7.020108
A3	4.084636	6	3.830729
R	-11.60272	2	27.20545
2	-5.013164	3	16.02633
3	-5.013164	3	16.02633
4	1.902758	4	4.194484
5	1.902758	4	4.194484

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	36.19	8	< 0.0001
Test 2	4.811	4	0.3073

Test 3	4.811	4	0.3073
Test 4	18.2	3	0.0004008
Test 5a	18.2	3	0.0004008
Test 5b	-3.57e-013	0	N/A
Test 6a	4.364	2	0.1128
Test 6b	13.83	1	0.0001999
Test 7a	4.364	2	0.1128
Test 7b	13.83	1	0.0001999
Test 7c	-6.759e-013	0	N/A

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 greater than .1. A homogeneous variance model appears to be appropriate here.

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

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

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

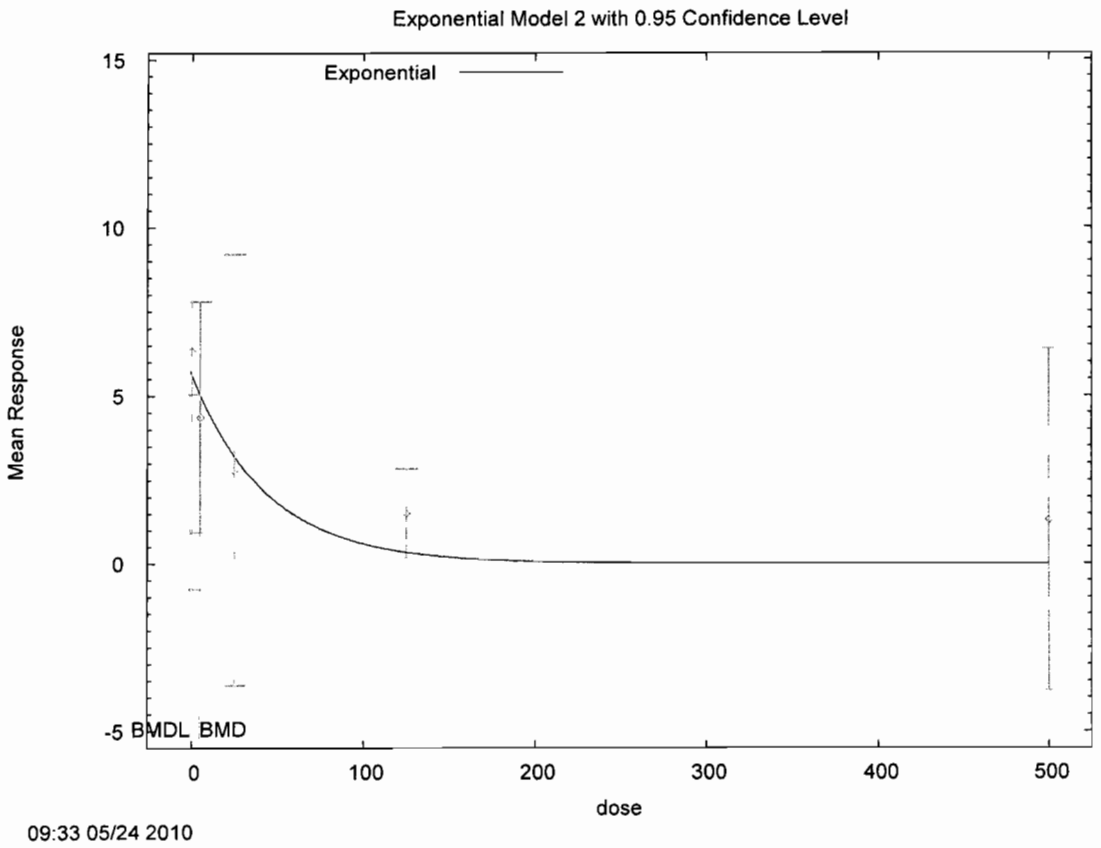
Specified Effect = 0.100000

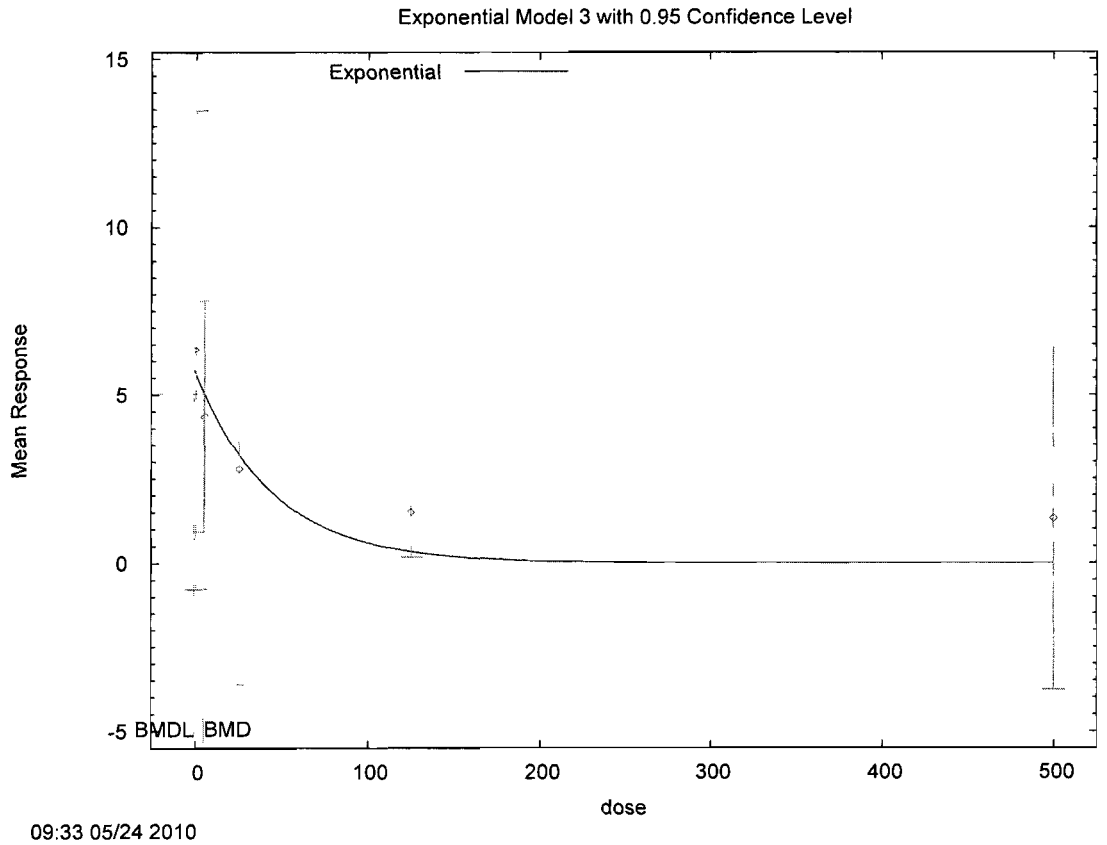
Risk Type = Relative deviation

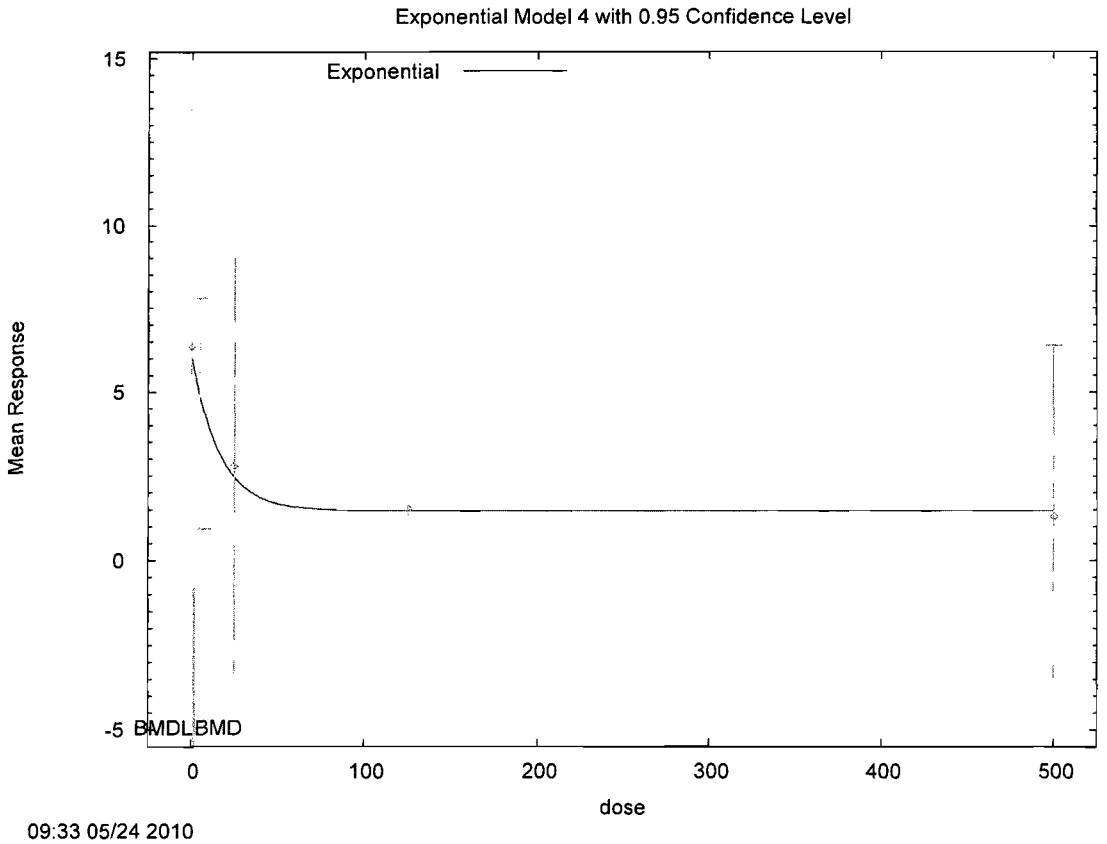
Confidence Level = 0.950000

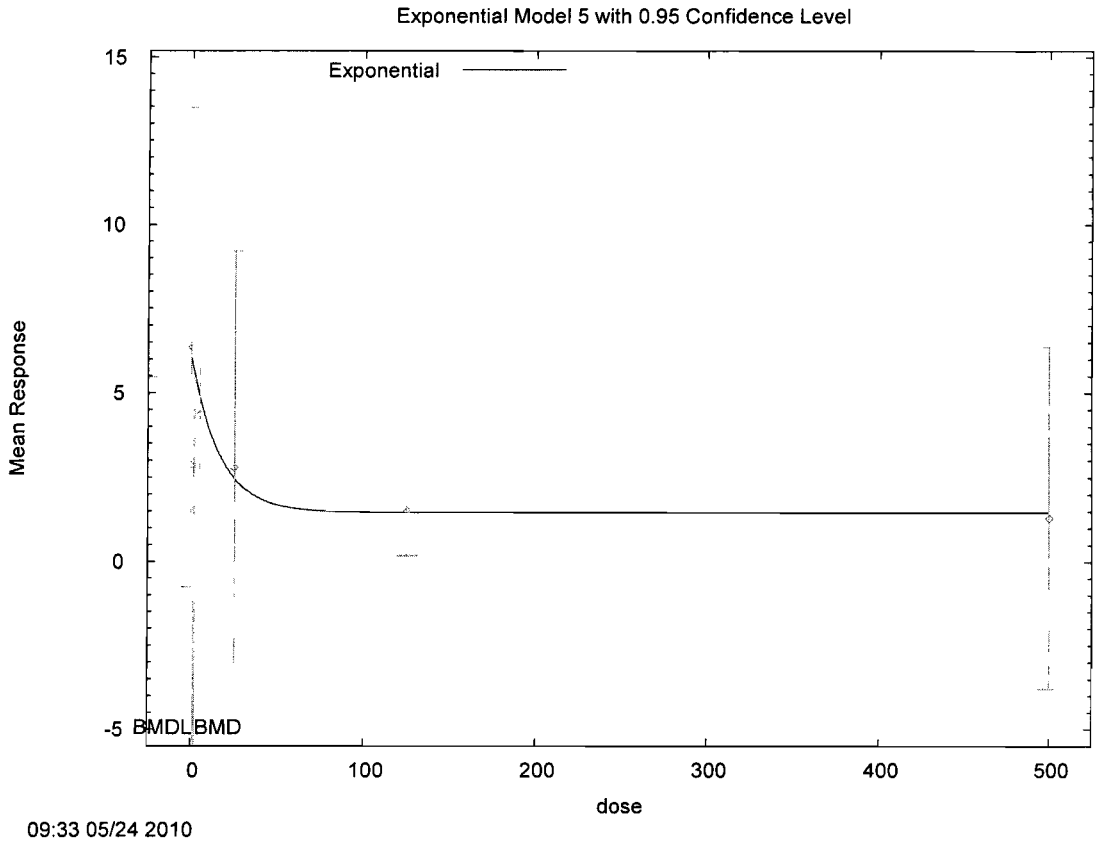
BMD and BMDL by Model

Model	BMD	BMDL
2	4.70032	Bad completion
3	4.70032	Bad completion
4	2.29167	1.30024
5	2.29167	1.30024


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL
BMD
0
100
200
300
400
500
dose
09:33 05/24 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
09:33 05/24 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
09:33 05/24 2010



Acephate; MRID 44203302
Female RBC ChE

```
!!! Warning:  optimum may not have been found for Model 3          !!!
!!! Bad completion code in maximum likelihood optimization routine  !!!
!!! Try choosing different initial values                          !!!

Warning:  optimum may not have been found form model 2 (BMDL).  Bad process completion
in Optimization routine.


 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Tue May 25 09:42:00 2010
 ================================================================

 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-15.1994	-15.1994	-15.1994	-15.1994
rho	3.35564	3.35564	3.35564	3.35564
a	1407.04	1407.04	2797.2	2797.2
b	0.0013541	0.0013541	0.00767472	0.00767472
c	--	--	0.376567	0.376567
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-46.3595	-15.1994	-0.517925	-0.517925
rho	7.81719	3.35564	1.40019	1.40019
a	1921.62	1407.04	2648.03	2648.03
b	0.00111594	0.0013541	0.0535526	0.0535526
c	--	--	0.447374	0.447374
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	2664	281.4
5	2	2288	173.2
25	2	1565	263.8
125	2	1269	31.1
500	2	1106	89.8

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1922	585.7	1.792
	5	1911	573.1	0.9305
	25	1869	525.2	-0.8179
	125	1671	339.5	-1.676
	500	1100	66.15	0.1309
3	0	0	0	1.#IO
	5	0	0	1.#IO
	25	0	0	1.#IO
	125	0	0	1.#IO
	500	0	0	1.#IO
4	0	2648	192.3	0.1175
	5	2304	174.4	-0.1319
	25	1568	133.2	-0.0349
	125	1186	109.6	1.065
	500	1185	109.5	-1.016
5	0	2648	192.3	0.1175
	5	2304	174.4	-0.1319
	25	1568	133.2	-0.0349
	125	1186	109.6	1.065
	500	1185	109.5	-1.016

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	-54.2029	6	120.4058
A2	-50.14268	10	120.2854
A3	-52.93776	7	119.8755
R	-69.22654	2	142.4531
2	-63.01435	4	134.0287
3	-484.9148	4	977.8296
4	-54.41036	5	118.8207
5	-54.41036	5	118.8207

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	38.17	8	< 0.0001
Test 2	8.12	4	0.08726
Test 3	5.59	3	0.1333
Test 4	20.15	3	0.0001578
Test 5a	864	3	< 0.0001
Test 5b	-843.8	0	N/A
Test 6a	2.945	2	0.2293
Test 6b	17.21	1	< 0.0001
Test 7a	2.945	2	0.2293
Test 7b	861	1	< 0.0001
Test 7c	-2.842e-014	0	N/A

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.

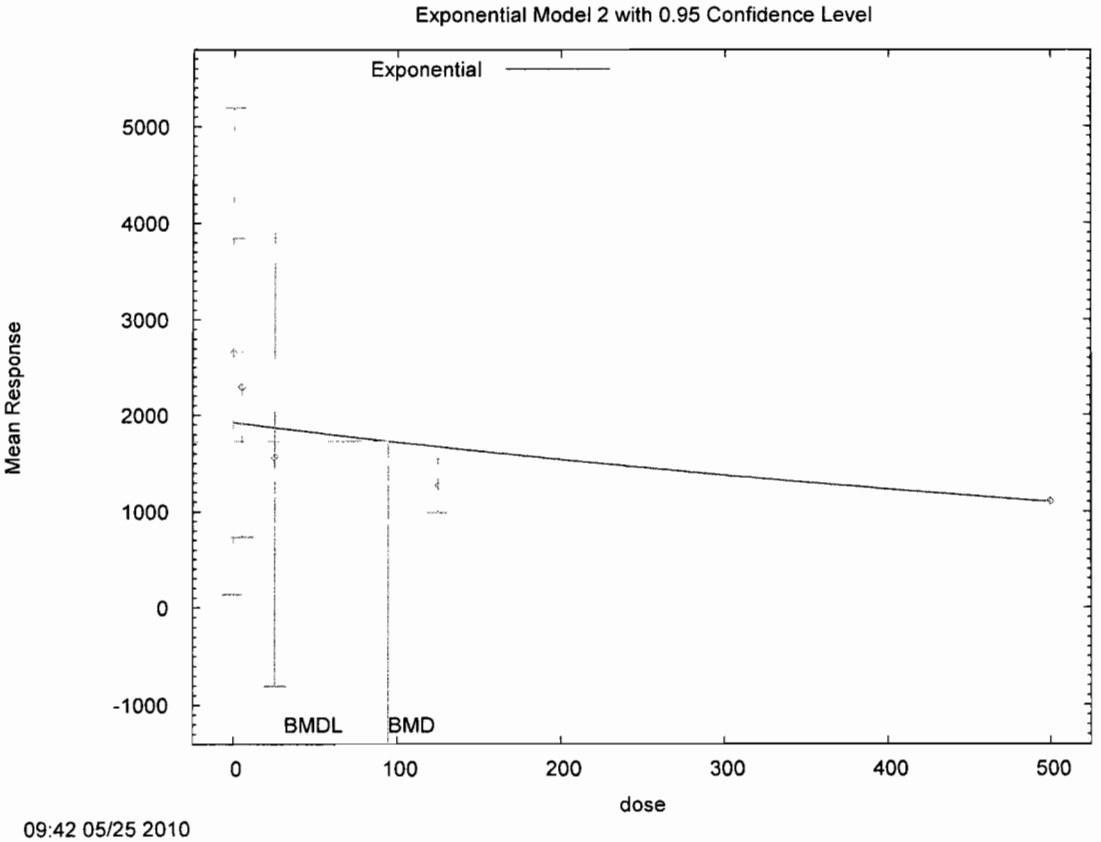
The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

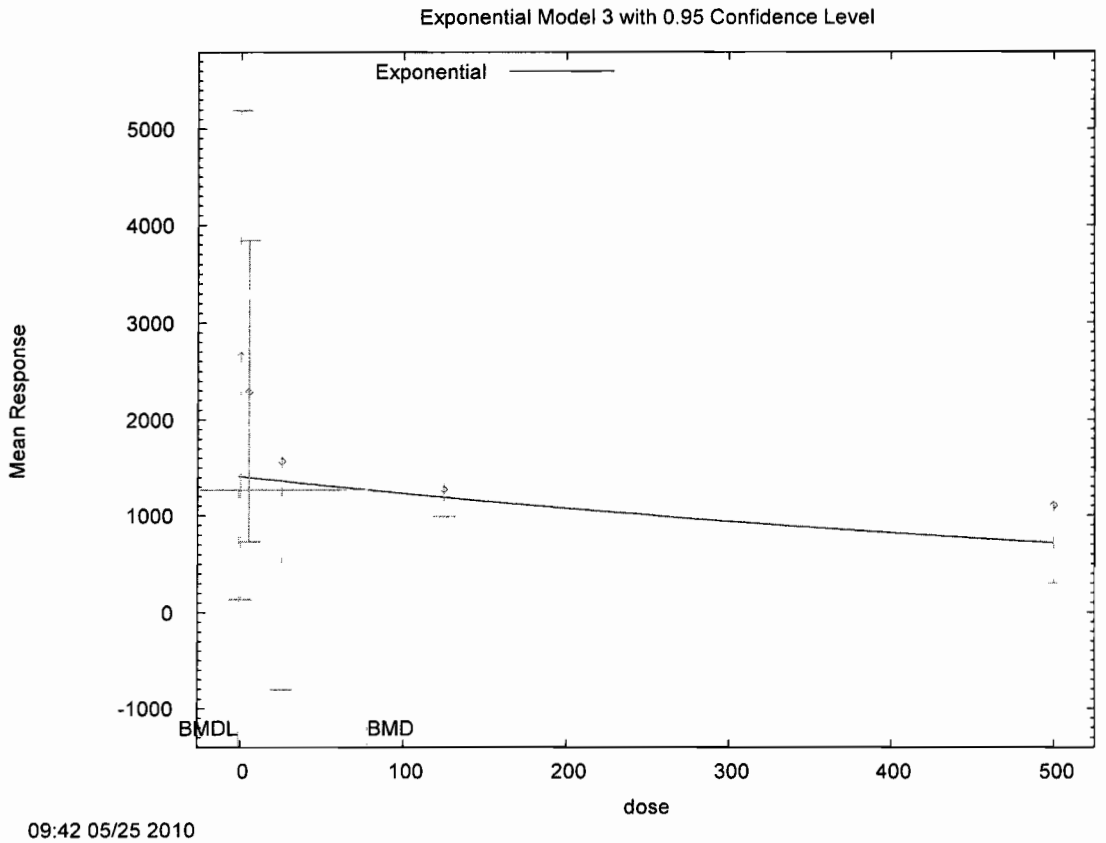
The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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

```
The p-value for Test 6b is less than .05.  Model 4 appears
to fit the data better than Model 2.

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

The p-value for Test 7b is less than .05.  Model 5 appears
to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.


Benchmark Dose Computations:

  Specified Effect = 0.100000

         Risk Type = Relative deviation

  Confidence Level = 0.950000


             BMD and BMDL by Model

 Model              BMD                 BMDL
-------          -----------          ----------
   2               94.414              66.7705
   3              77.8088         Bad completion
   4              3.72746              2.52378
   5              3.72746              2.52384
```




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
5000
4000
3000
2000
1000
0
-1000
BMDL
BMD
0
100
200
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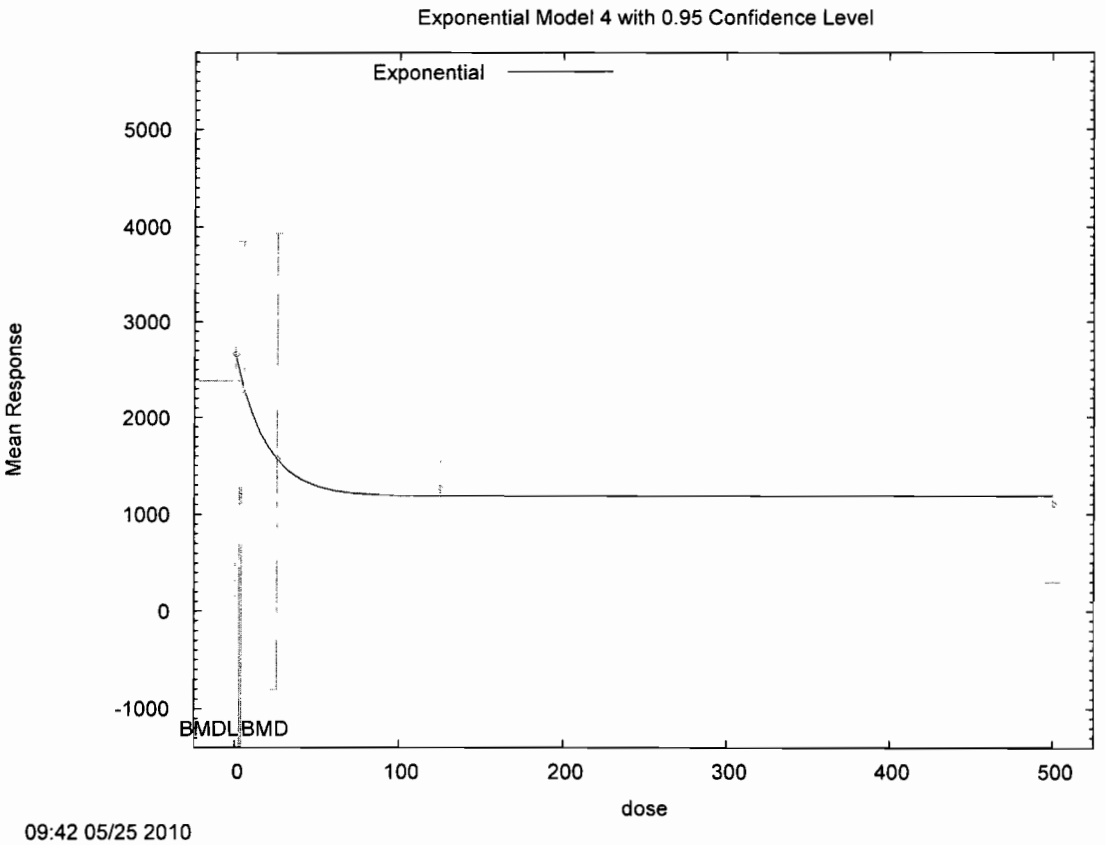
dose
09:42 05/25 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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0
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BMDL
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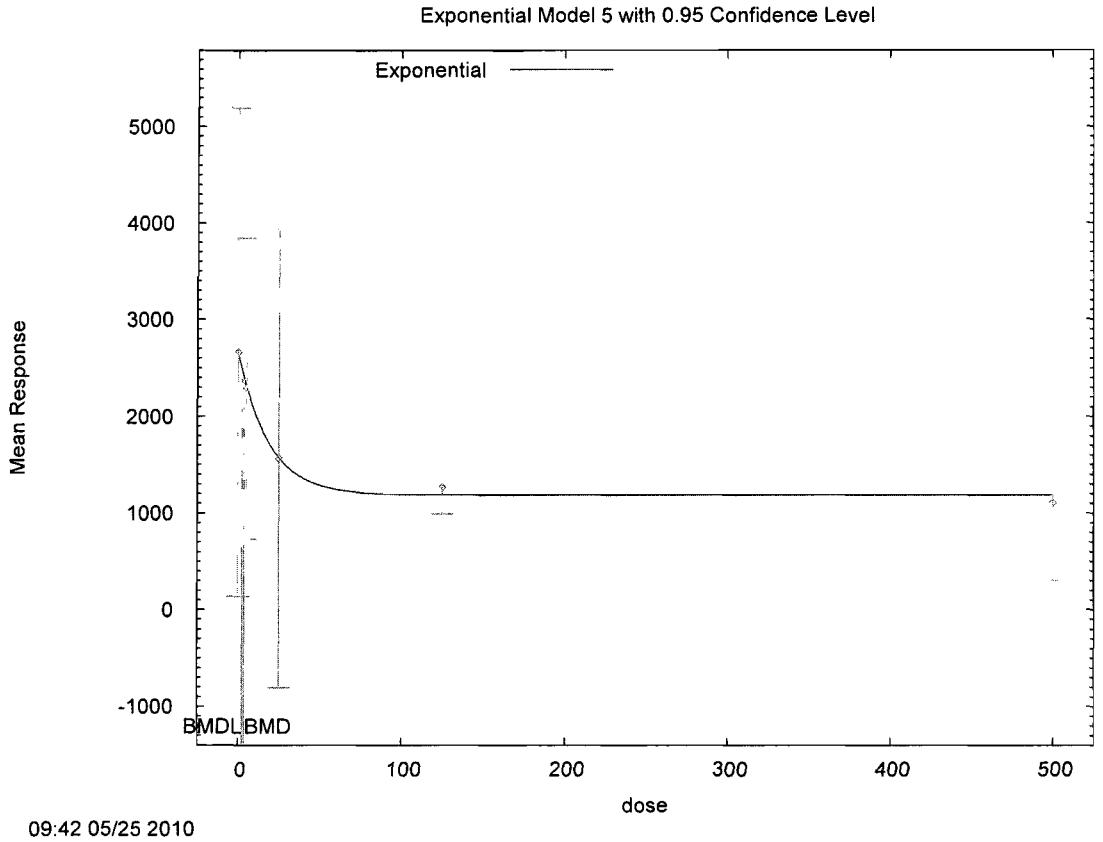
dose
09:42 05/25 2010



Acephate; MRID 44203302
Female RBC ChE

```
==============================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Tue May 25 09:35:54 2010
==============================================================================

 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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	9.84058	9.84058	9.84058	9.84058
rho(S)	0	0	0	0
a	1407.04	1407.04	2797.2	2797.2
b	0.0013541	0.0013541	0.00767472	0.00767472
c	--	--	0.376567	0.376567
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	12.0733	12.0733	9.97363	9.97363
rho	0	0	0	0
a	2141.72	2141.72	2655.15	2655.15
b	0.00187867	0.00187867	0.0550475	0.0550475
c	--	--	0.447269	0.447269
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev

0	2	2664	281.4
5	2	2288	173.2
25	2	1565	263.8
125	2	1269	31.1
500	2	1106	89.8

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2142	418.5	1.765
	5	2122	418.5	0.562
	25	2043	418.5	-1.617
	125	1693	418.5	-1.434
	500	837.2	418.5	0.9085
3	0	2142	418.5	1.765
	5	2122	418.5	0.562
	25	2043	418.5	-1.617
	125	1693	418.5	-1.434
	500	837.2	418.5	0.9085
4	0	2655	146.5	0.08549
	5	2302	146.5	-0.1355
	25	1558	146.5	0.06579
	125	1189	146.5	0.7717
	500	1188	146.5	-0.7875
5	0	2655	146.5	0.08549
	5	2302	146.5	-0.1355
	25	1558	146.5	0.06579
	125	1189	146.5	0.7717
	500	1188	146.5	-0.7875

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	-54.2029	6	120.4058
A2	-50.14268	10	120.2854
A3	-54.2029	6	120.4058
R	-69.22654	2	142.4531
2	-65.36667	3	136.7333
3	-65.36667	3	136.7333
4	-54.86814	4	117.7363
5	-54.86814	4	117.7363

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	38.17	8	< 0.0001
Test 2	8.12	4	0.08726
Test 3	8.12	4	0.08726
Test 4	22.33	3	< 0.0001
Test 5a	22.33	3	< 0.0001
Test 5b	-2.302e-012	0	N/A
Test 6a	1.33	2	0.5141
Test 6b	21	1	< 0.0001
Test 7a	1.33	2	0.5141
Test 7b	21	1	< 0.0001
Test 7c	0	0	N/A

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears

to fit the data better than Model 2.

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

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

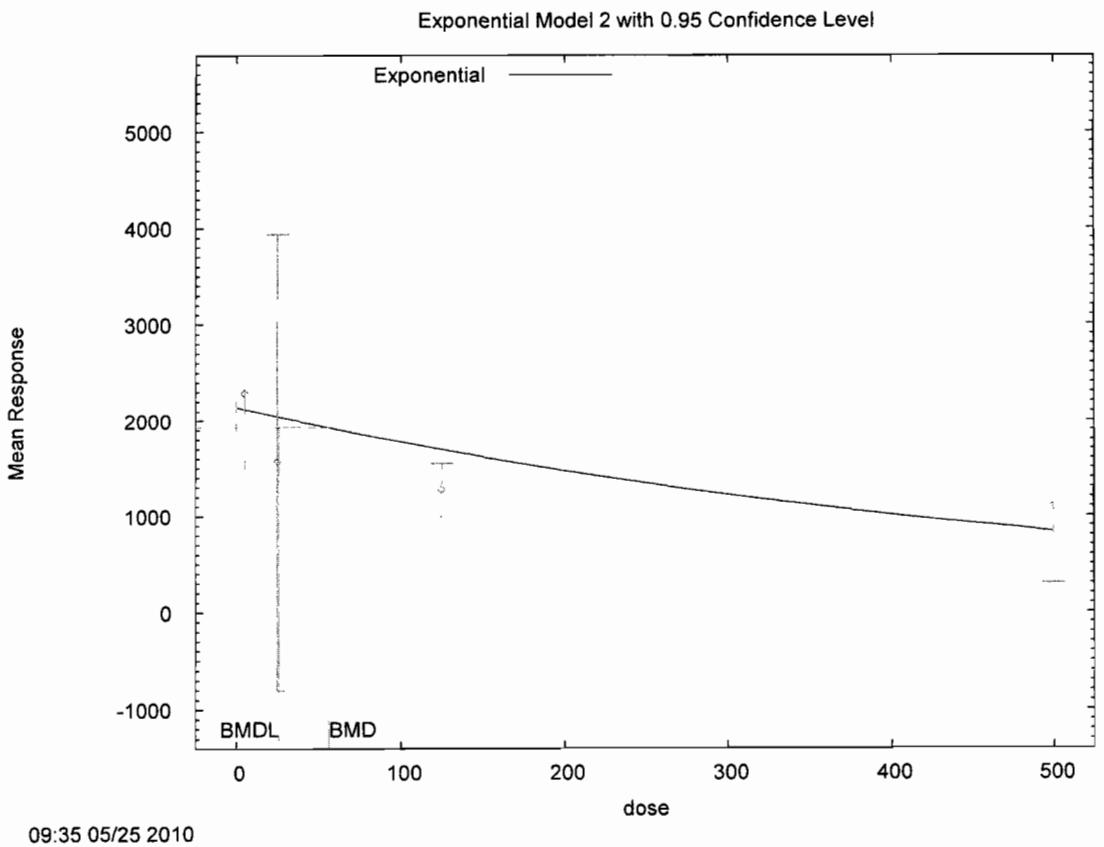
Specified Effect = 0.100000

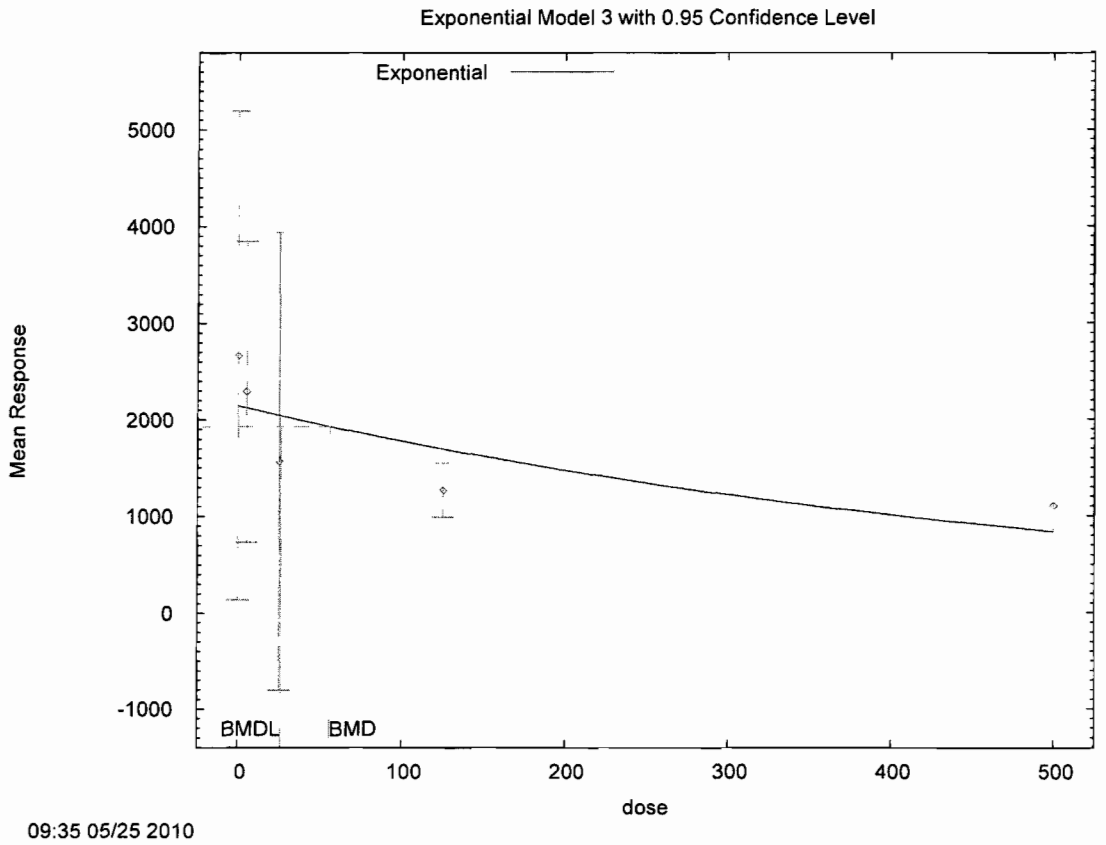
Risk Type = Relative deviation

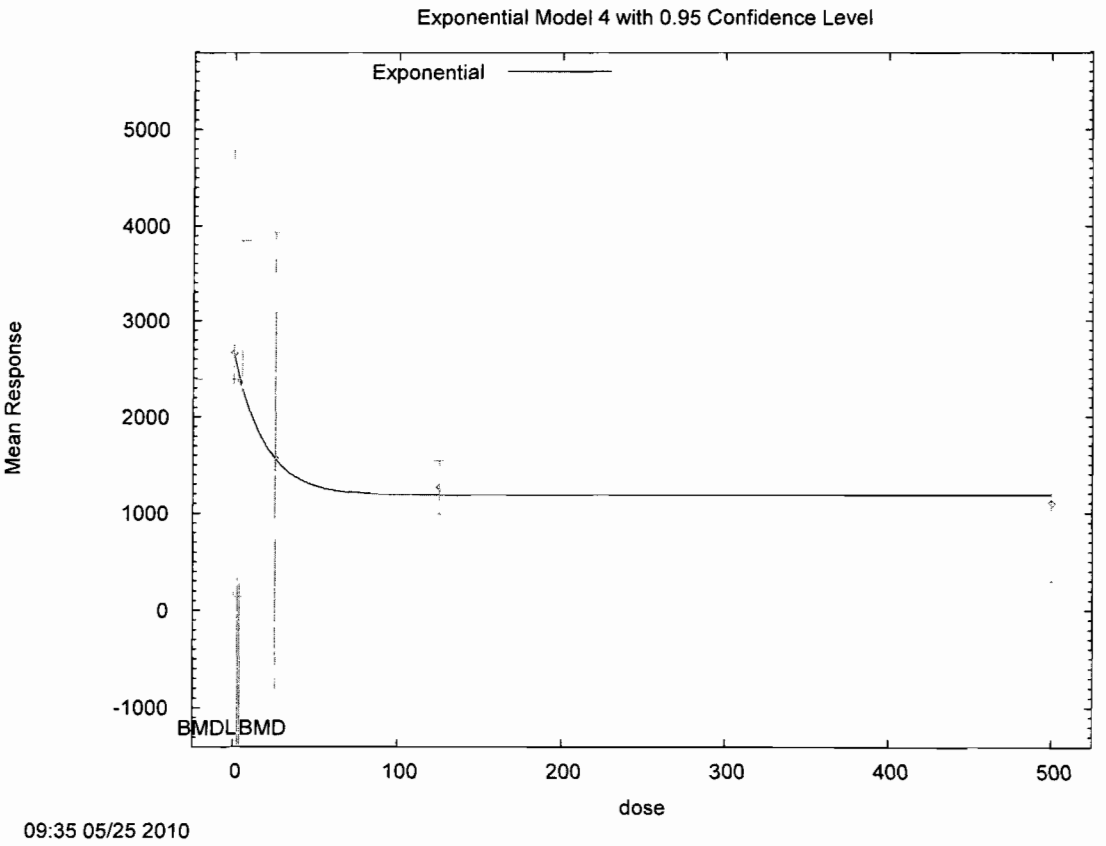
Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	56.0824	26.0497
3	56.0825	26.0497
4	3.62547	2.42415
5	3.62547	2.42415




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
5000
4000
3000
2000
1000
0
-1000
BMDL
BMD
0
100
200
300
400
500
dose
09:35 05/25 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
5000
4000
3000
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1000
0
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BMD
0
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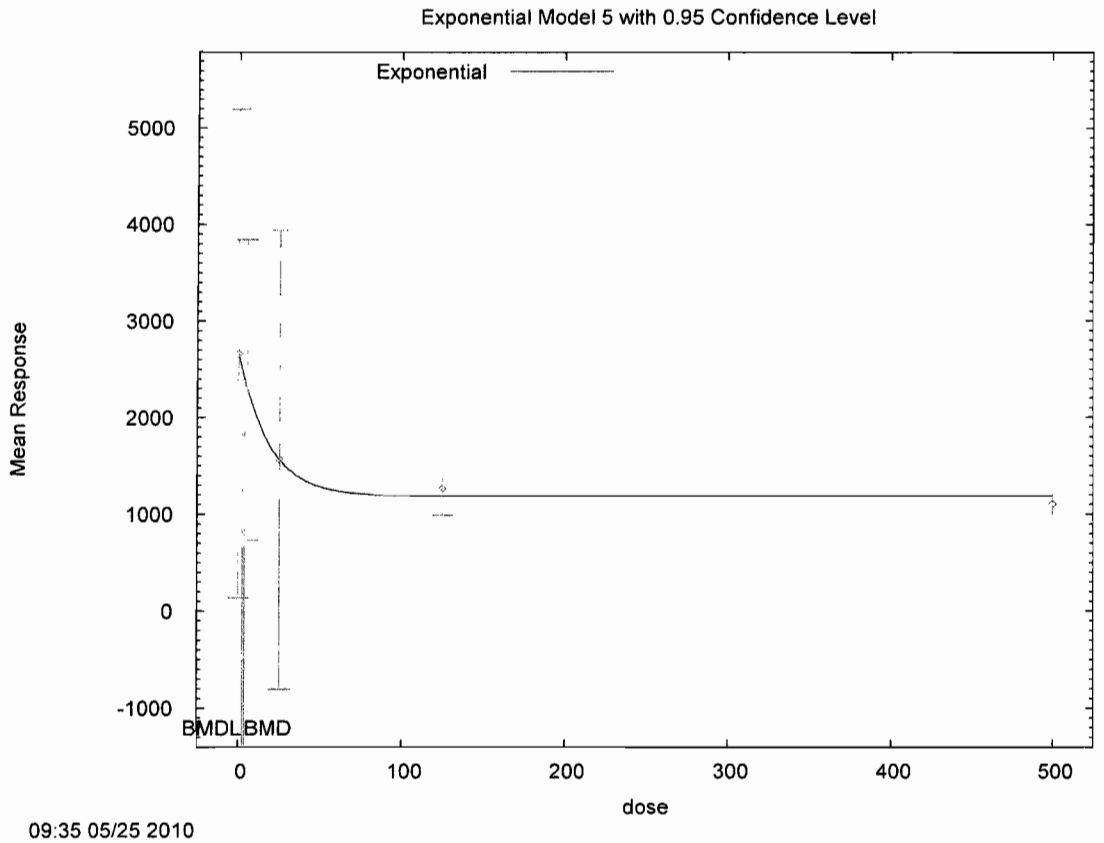
09:35 05/25 2010



Acephate; MRID 44203302
Female Hippocampus ChE

```
Warning:  optimum may not have been found form model 1 (BMDL).  Bad process completion
in Optimization routine.


 ======================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                 Mon May 24 14:46:48 2010
 ======================================================================

 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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-6.71031	-6.71031	-6.71031	-6.71031
rho	3.62984	3.62984	3.62984	3.62984
a	1.61695	1.51496	6.72	6.72
b	0.00302024	2.49752e-006	0.0104996	0.0104996
c	--	--	0.131803	0.131803
d	--	2	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.41653	-6.19457	-6.80547	-6.80547
rho	-0.031723	7.14528	5.37127	5.37127
a	6.07609	3.0169	4.38937	4.38937
b	0.0425953	0.00235576	0.0172136	0.0172136
c	--	--	0.212161	0.212161
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	6.4	1.216
5	2	4.44	0.332
25	2	2.24	0.354
125	2	1.35	0.021
500	2	0.93	0.049

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.076	0.7891	0.5805
	5	4.911	0.7918	-0.8405
	25	2.095	0.8025	0.2558
	125	0.0296	0.8586	2.175
	500	3.421e-009	1.106	1.189
3	0	3.017	2.334	2.05
	5	2.982	2.238	0.9215
	25	2.844	1.891	-0.4519
	125	2.247	0.8152	-1.557
	500	0.929	0.03472	0.04091
4	0	4.389	1.768	1.608
	5	4.104	1.476	0.3217
	25	3.18	0.744	-1.787
	125	1.333	0.07208	0.326
	500	0.9319	0.02754	-0.09692
5	0	4.389	1.768	1.608
	5	4.104	1.476	0.3217
	25	3.18	0.744	-1.787
	125	1.333	0.07208	0.326
	500	0.9319	0.02754	-0.09692

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	3.809922	6	4.380156
A2	16.1151	10	-12.23019
A3	12.78946	7	-11.57893
R	-12.41965	2	28.83929
2	-3.516221	4	15.03244
3	-2.451957	4	12.90391
4	6.117484	5	-2.234969
5	6.117484	5	-2.234969

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	57.07	8	< 0.0001
Test 2	24.61	4	< 0.0001
Test 3	6.651	3	0.08388
Test 4	32.61	3	< 0.0001
Test 5a	30.48	3	< 0.0001
Test 5b	2.129	0	N/A
Test 6a	13.34	2	0.001266
Test 6b	19.27	1	< 0.0001
Test 7a	13.34	2	0.001266
Test 7b	17.14	1	< 0.0001
Test 7c	-1.599e-014	0	N/A

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 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.

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.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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.

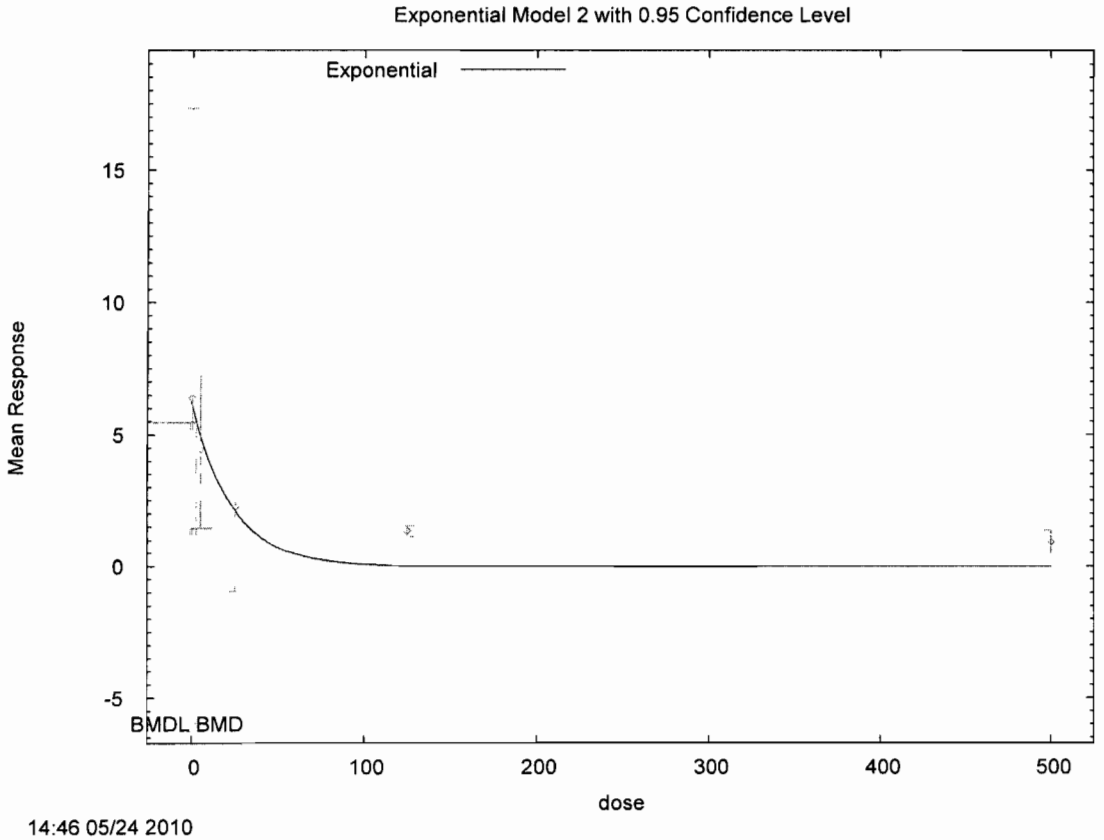
The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

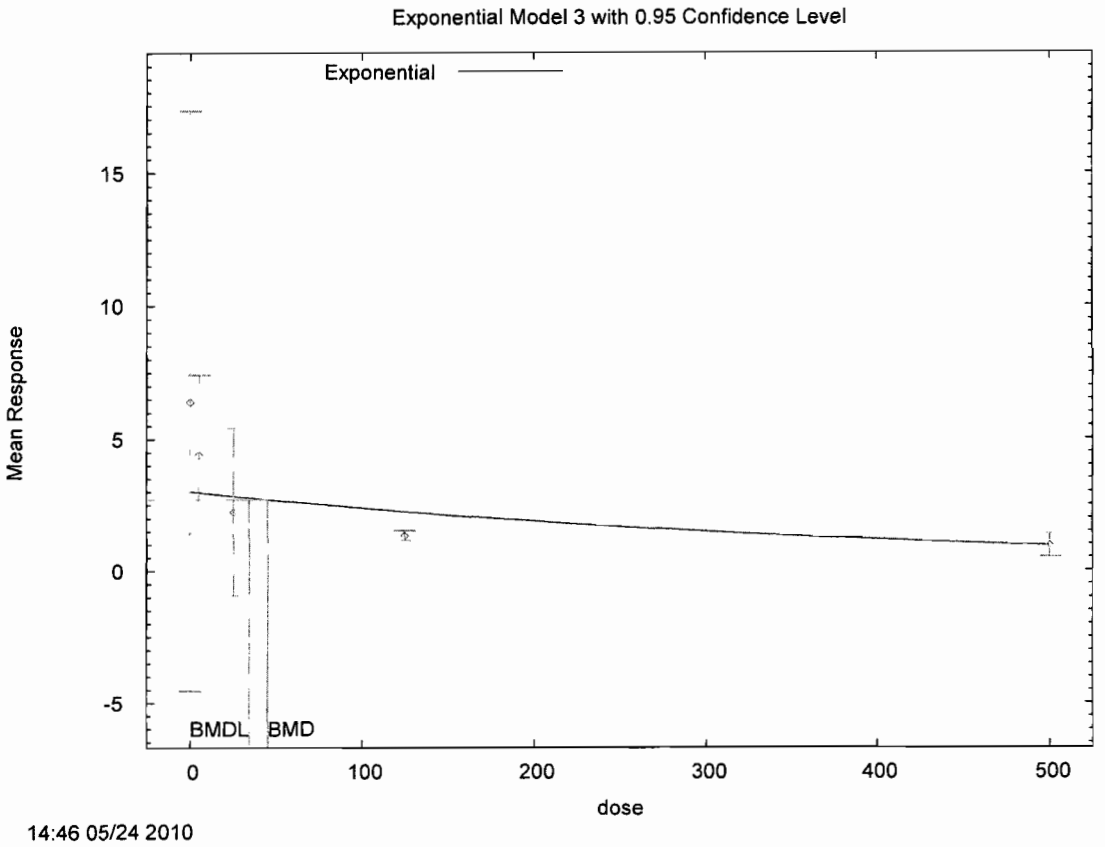
The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

```
The p-value for Test 7b is less than .05.  Model 5 appears
to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.


Benchmark Dose Computations:

  Specified Effect = 0.100000

         Risk Type = Relative deviation

  Confidence Level = 0.950000
```

BMD and BMDL by Model

Model	BMD	BMDL
2	2.47352	Bad completion
3	44.7247	34.1588
4	7.88558	6.42746
5	7.88558	6.42746




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
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5
0
-5
BMDL
BMD
0
100
200
300
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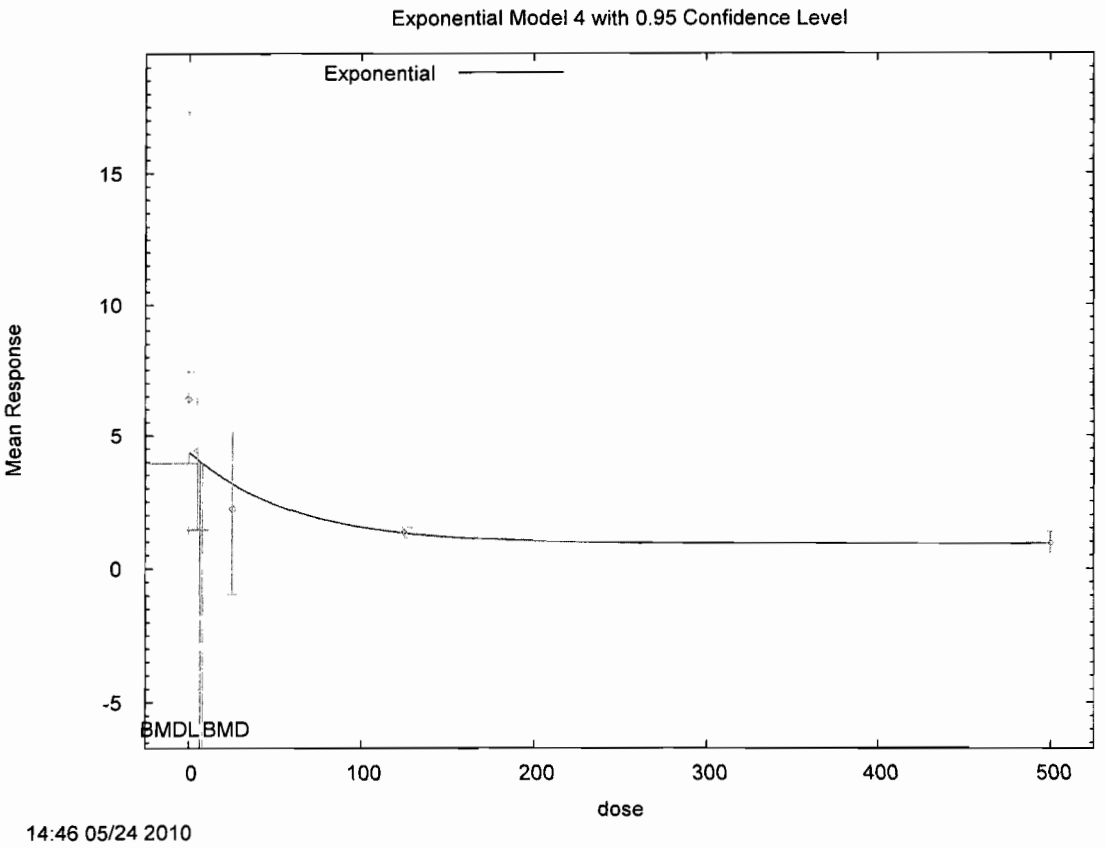
500
dose
14:46 05/24 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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0
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BMDL
BMD
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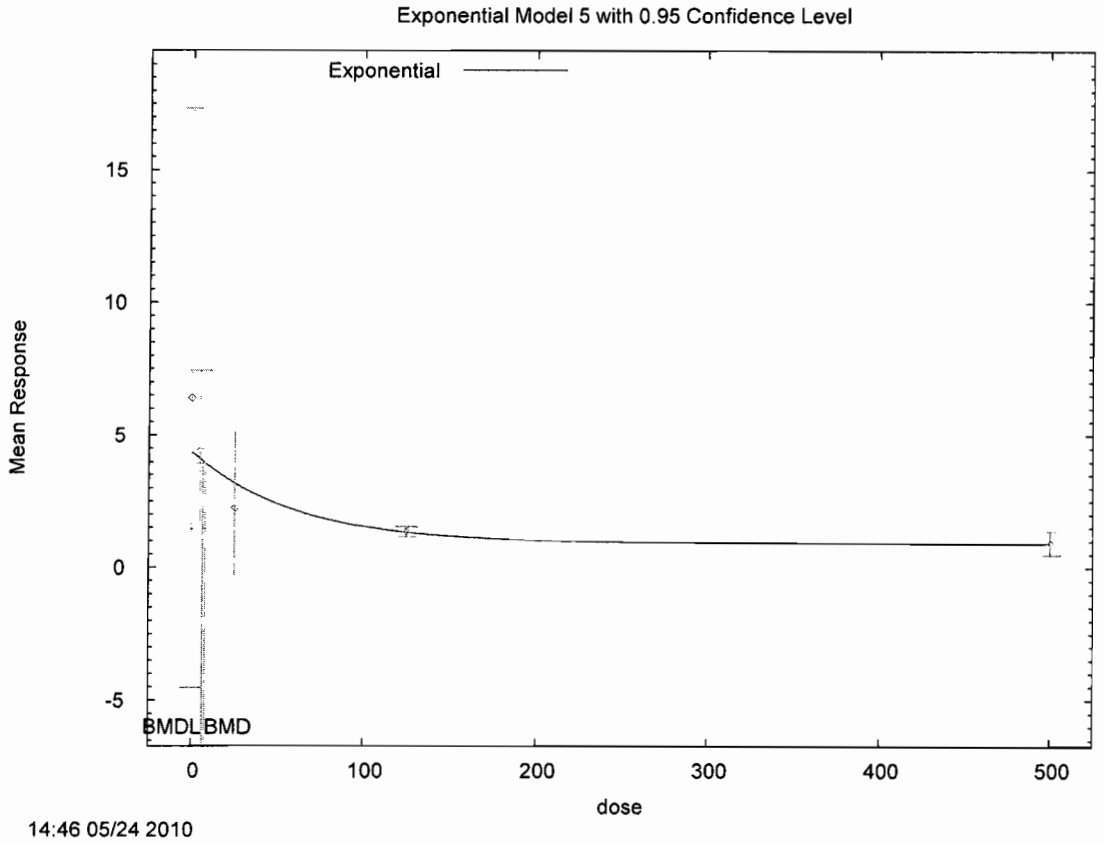
dose
14:46 05/24 2010



Acephate; MRID 44203302
Female Hippocampus ChE

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Warning:  optimum may not have been found form model 1 (BMDL).  Bad process completion
in Optimization routine.


 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Mon May 24 09:49:43 2010
 ================================================================

 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-1.76198	-1.76198	-1.76198	-1.76198
rho(S)	0	0	0	0
a	1.61695	1.61695	6.72	6.72
b	0.00302024	0.00302024	0.0104996	0.0104996
c	--	--	0.131803	0.131803
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.270811	-0.270811	-1.51614	-1.51614
rho	0	0	0	0
a	6.0652	6.0652	6.25191	6.25191
b	0.0420851	0.0420851	0.0729433	0.0729433
c	--	--	0.191122	0.191122
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	2	6.4	1.216
5	2	4.44	0.332
25	2	2.24	0.354
125	2	1.35	0.021
500	2	0.93	0.049

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.065	0.8734	0.5421
	5	4.914	0.8734	-0.768
	25	2.118	0.8734	0.1977
	125	0.03149	0.8734	2.135
	500	4.407e-009	0.8734	1.506
3	0	6.065	0.8734	0.5421
	5	4.914	0.8734	-0.768
	25	2.118	0.8734	0.1977
	125	0.03149	0.8734	2.135
	500	4.407e-009	0.8734	1.506
4	0	6.252	0.4686	0.4469
	5	4.706	0.4686	-0.8042
	25	2.011	0.4686	0.6902
	125	1.195	0.4686	0.4665
	500	1.195	0.4686	-0.7994
5	0	6.252	0.4686	0.4469
	5	4.706	0.4686	-0.8042
	25	2.011	0.4686	0.6902
	125	1.195	0.4686	0.4665
	500	1.195	0.4686	-0.7994

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	3.809922	6	4.380156
A2	16.1151	10	-12.23019
A3	3.809922	6	4.380156
R	-12.41965	2	28.83929
2	-3.645947	3	13.29189
3	-3.645947	3	13.29189
4	2.580688	4	2.838625
5	2.580688	4	2.838625

Additive constant for all log-likelihoods = -9.189. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	57.07	8	< 0.0001
Test 2	24.61	4	< 0.0001
Test 3	24.61	4	< 0.0001
Test 4	14.91	3	0.001894
Test 5a	14.91	3	0.001894
Test 5b	3.109e-014	0	N/A
Test 6a	2.458	2	0.2925
Test 6b	12.45	1	0.0004173
Test 7a	2.458	2	0.2925
Test 7b	12.45	1	0.0004173
Test 7c	-1.457e-012	0	N/A

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

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

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

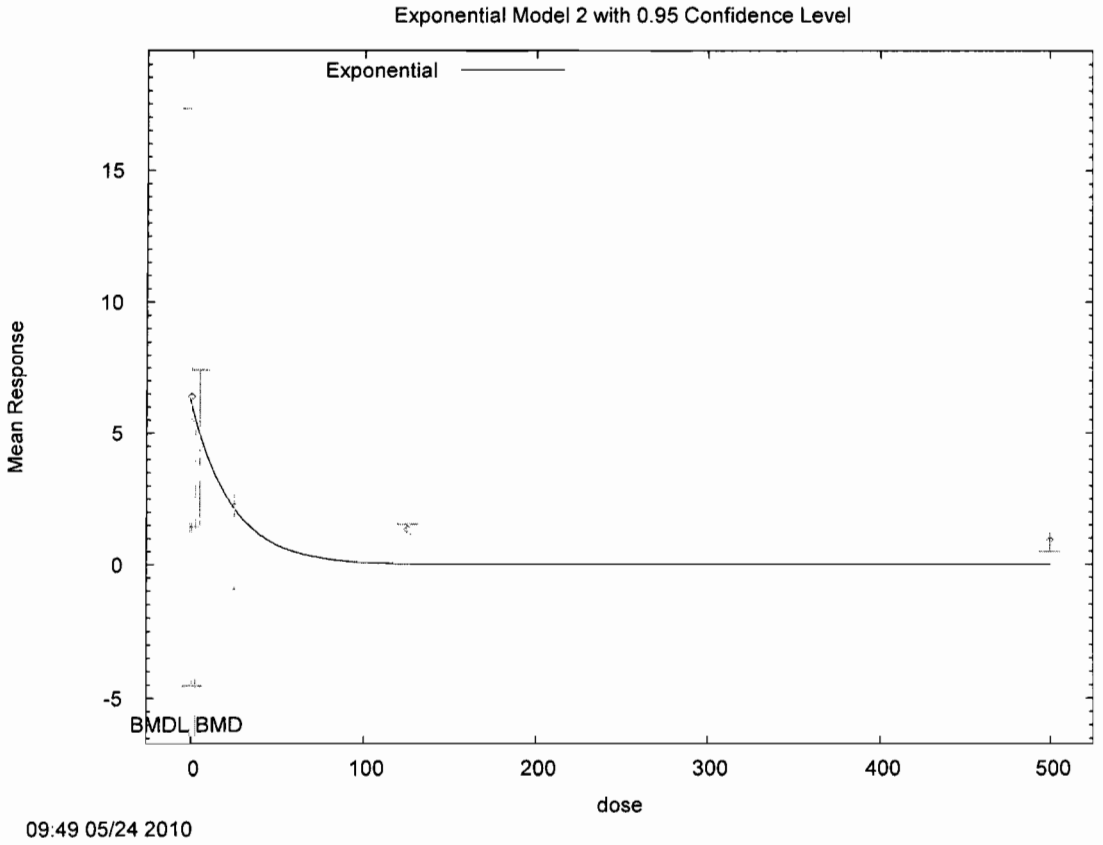
Specified Effect = 0.100000

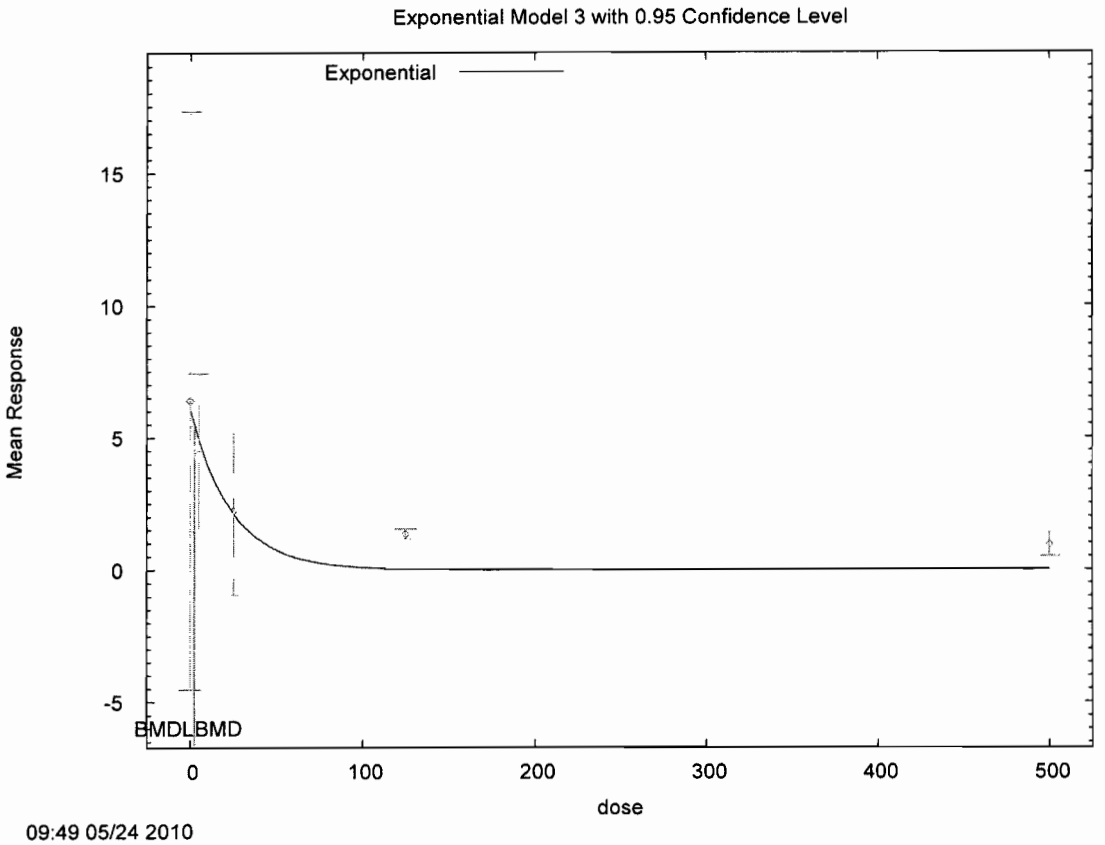
Risk Type = Relative deviation

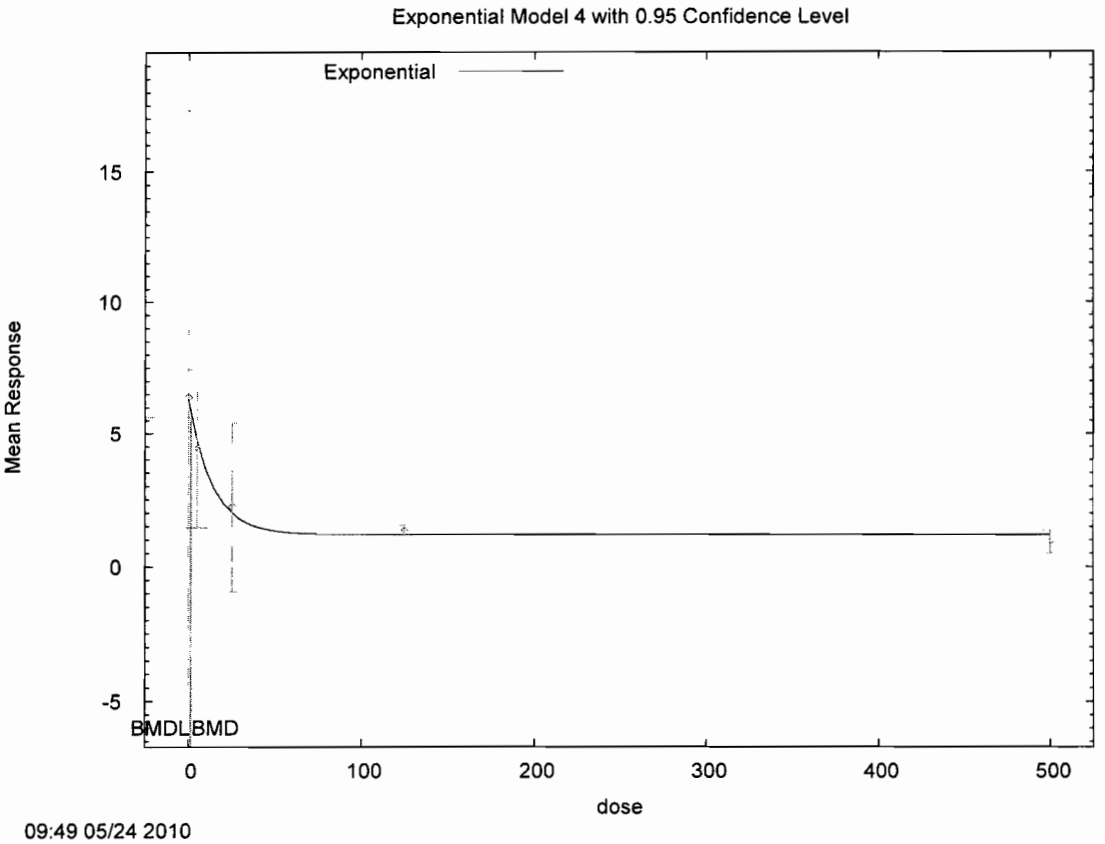
Confidence Level = 0.950000

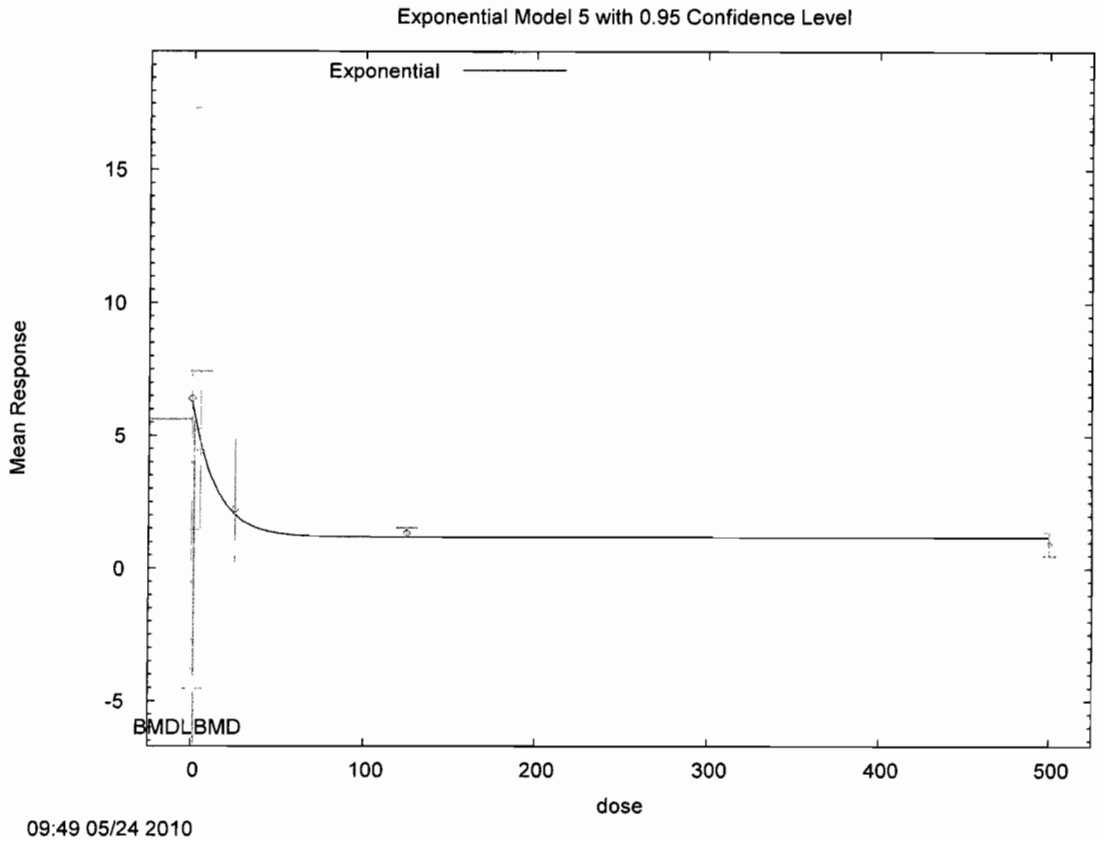
BMD and BMDL by Model

Model	BMD	BMDL
2	2.50351	Bad completion
3	2.50351	2.14639
4	1.80914	1.17087
5	1.80914	1.17087




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL
BMD
0
100
200
300
400
500
dose
09:49 05/24 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
15
10
5
0
-5
BMDL
BMD
0
100
200
300
400
500
dose
09:49 05/24 2010



Acephate
MRID 46151801
Male RBC ChE

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 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                          Mon May 17 10:42:49 2010
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 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-3.96558	-3.96558	-3.96558	-3.96558
rho	2.24783	2.24783	2.24783	2.24783
a	2.22082	2.22082	2.688	2.688
b	0.00804937	0.00804937	0.136697	0.136697
c	--	--	0.690901	0.690901
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-1.71988	-2.73738	-1.71988	-2.73738
rho	0.0466741	1.23293	0.0466745	1.23293
a	2.33515	2.3375	2.33515	2.3375
b	0.00805998	0.0858792	0.00805998	0.0869045
c	--	--	0	0.231851
d	--	13.8448	--	12.9977

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.95	0.28
0.5	10	2.49	0.42
1	10	2.35	0.19

2.5	10	2.56	0.53
10	10	2.07	0.42

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2.335	0.4316	-2.822
	0.5	2.326	0.4316	1.203
	1	2.316	0.4316	0.2462
	2.5	2.289	0.4314	1.99
	10	2.154	0.4308	-0.6189
3	0	2.337	0.4294	-2.853
	0.5	2.337	0.4294	1.123
	1	2.337	0.4294	0.09205
	2.5	2.337	0.4294	1.638
	10	2.07	0.3984	-1.109e-007
4	0	2.335	0.4316	-2.822
	0.5	2.326	0.4316	1.203
	1	2.316	0.4316	0.2462
	2.5	2.289	0.4314	1.99
	10	2.154	0.4308	-0.6189
5	0	2.338	0.4294	-2.853
	0.5	2.338	0.4294	1.123
	1	2.338	0.4294	0.09205
	2.5	2.337	0.4294	1.638
	10	2.07	0.3984	-3.331e-008

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	25.12208	6	-38.24417
A2	30.66978	10	-41.33955
A3	26.3927	7	-38.7854
R	16.4211	2	-28.8422
2	17.03384	4	-26.06767
3	18.01219	5	-26.02438
4	17.03384	4	-26.06767
5	18.01219	6	-24.02438

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	28.5	8	0.0003884
Test 2	11.1	4	0.02551
Test 3	8.554	3	0.03585
Test 4	18.72	3	0.0003127
Test 5a	16.76	2	0.0002293
Test 5b	1.957	1	0.1619
Test 6a	18.72	3	0.0003127
Test 6b	-2.132e-014	0	N/A
Test 7a	16.76	1	< 0.0001
Test 7b	-8.299e-008	1	N/A
Test 7c	1.957	2	0.3759

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 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.

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.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

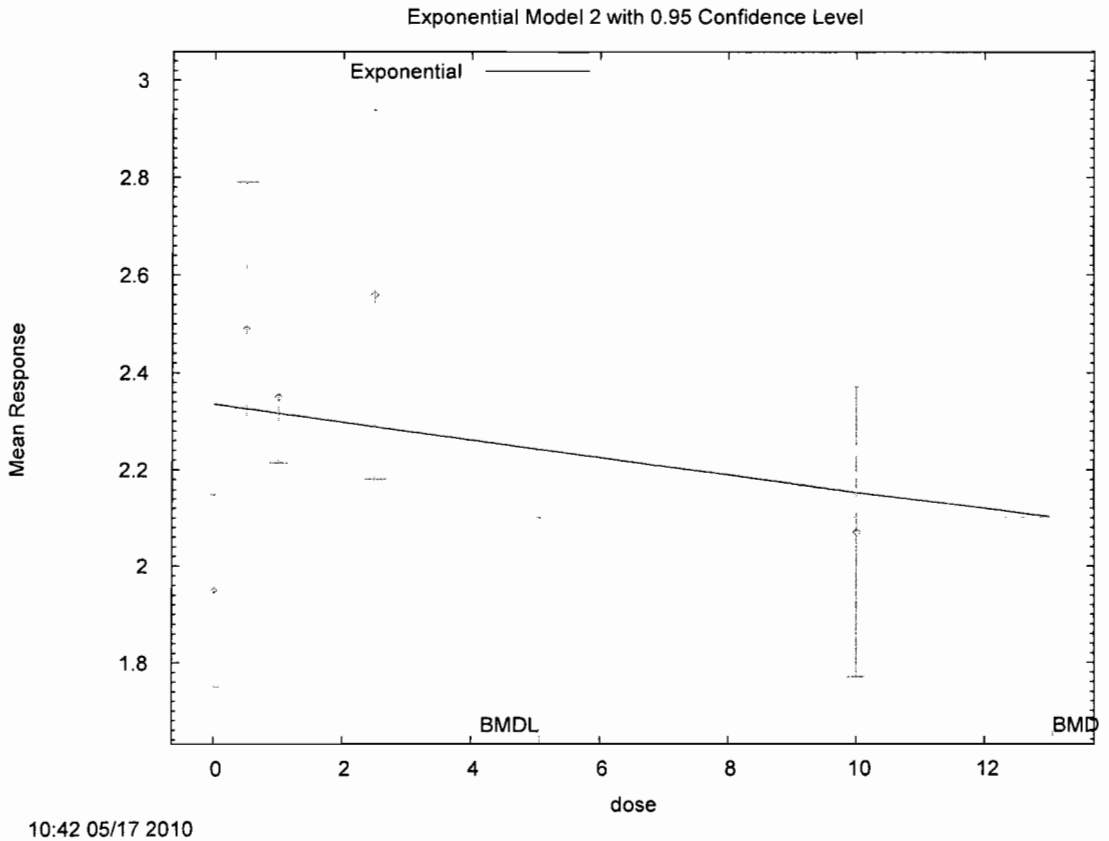
Specified Effect = 0.100000

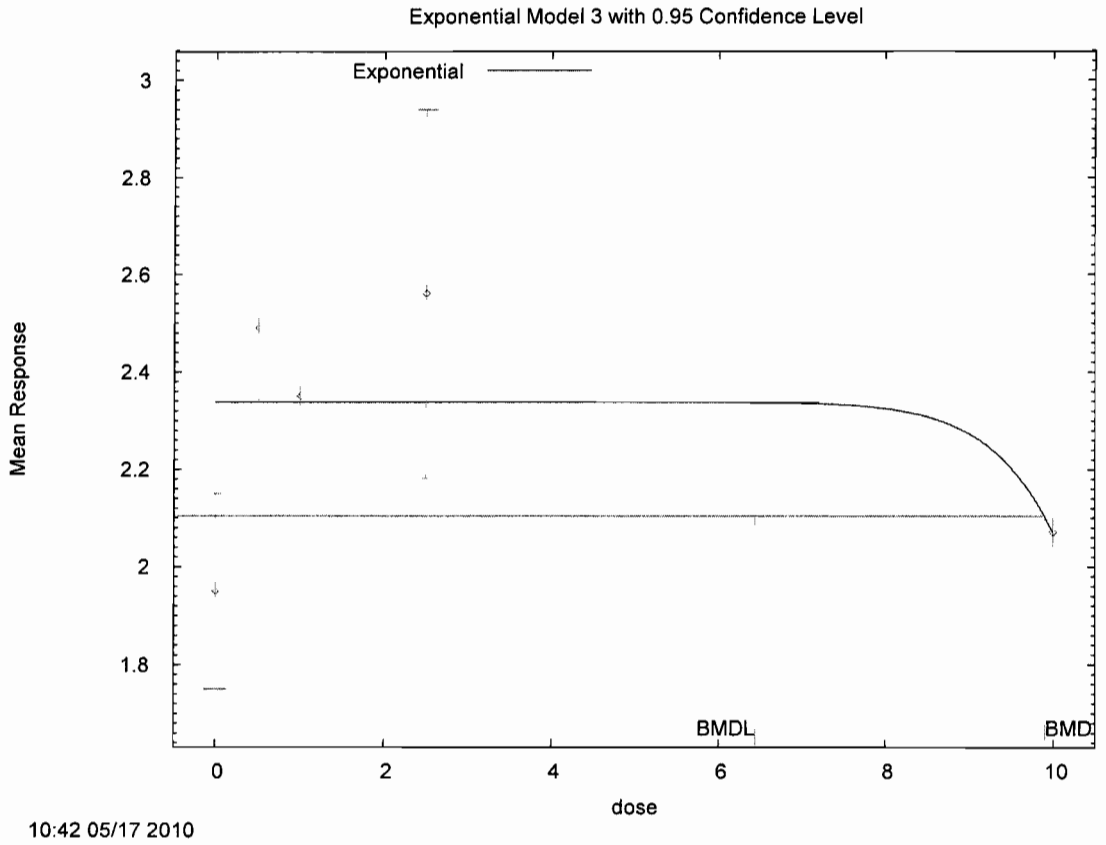
Risk Type = Relative deviation

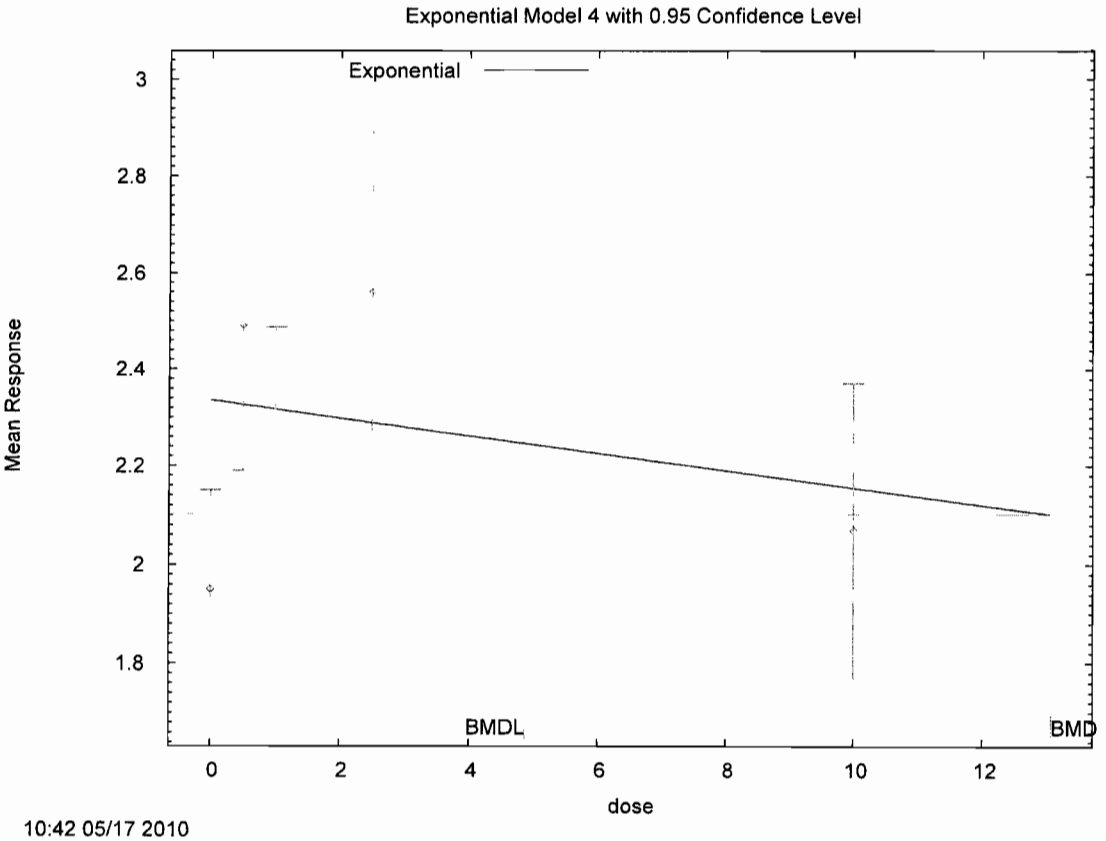
Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	13.0721	5.0665
3	9.89739	6.44146
4	13.0721	4.87449
5	9.88867	2.6943




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
10
dose
10:42 05/17 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
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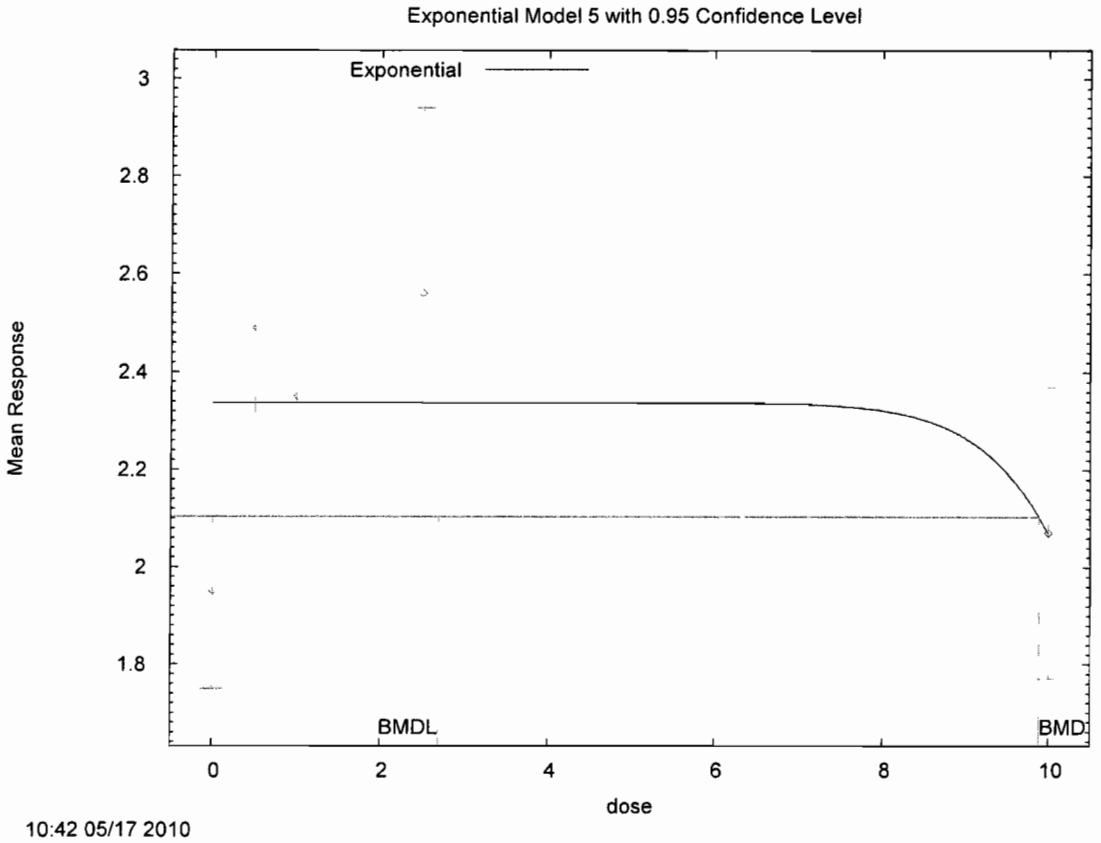
12
dose
10:42 05/17 2010



Acephate 4615180
pup female brain che

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 ***********************************************************************
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Fri May 28 13:04:09 2010
 ***********************************************************************

 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	0.344074	0.344074	0.344074	0.344074
rho(S)	0	0	0	0
a	3.89058	3.89058	5.65562	5.65562
b	0.0438513	0.0438513	0.282882	0.282882
c	--	--	0.533747	0.533747
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	0.432266	0.419565	0.432266	0.413324
rho	0	0	0	0
a	4.97422	4.84179	4.97422	4.8707
b	0.0425878	0.0623952	0.0425878	0.367017
c	--	--	0	0.650748
d	--	1.81214	--	18

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	4.844	0.8156

0.5	10	4.382	1.412
1	10	5.386	1.392
2.5	10	4.545	1.516
10	10	3.17	0.9698

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	4.974	1.241	-0.3312
	0.5	4.869	1.241	-1.243
	1	4.767	1.241	1.578
	2.5	4.472	1.241	0.1867
	10	3.249	1.241	-0.2026
3	0	4.842	1.233	0.006185
	0.5	4.833	1.233	-1.157
	1	4.81	1.233	1.477
	2.5	4.678	1.233	-0.3397
	10	3.164	1.233	0.01387
4	0	4.974	1.241	-0.3312
	0.5	4.869	1.241	-1.243
	1	4.767	1.241	1.578
	2.5	4.472	1.241	0.1867
	10	3.249	1.241	-0.2026
5	0	4.871	1.23	-0.06815
	0.5	4.871	1.23	-1.258
	1	4.871	1.23	1.326
	2.5	4.545	1.23	-1.117e-007
	10	3.17	1.23	1.828e-009

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	-33.60184	6	79.20368
A2	-30.94339	10	81.88679
A3	-33.60184	6	79.20368
R	-41.66348	2	87.32697
2	-35.80666	3	77.61331
3	-35.48913	4	78.97826
4	-35.80666	3	77.61331
5	-35.33311	5	80.66622

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	21.44	8	0.006066
Test 2	5.317	4	0.2563
Test 3	5.317	4	0.2563
Test 4	4.41	3	0.2205
Test 5a	3.775	2	0.1515
Test 5b	0.6351	1	0.4255
Test 6a	4.41	3	0.2205
Test 6b	-1.421e-014	0	N/A
Test 7a	3.463	1	0.06277
Test 7b	0.312	1	0.5764
Test 7c	0.9471	2	0.6228

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 greater than .1. A homogeneous variance model appears to be appropriate here.

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.

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

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

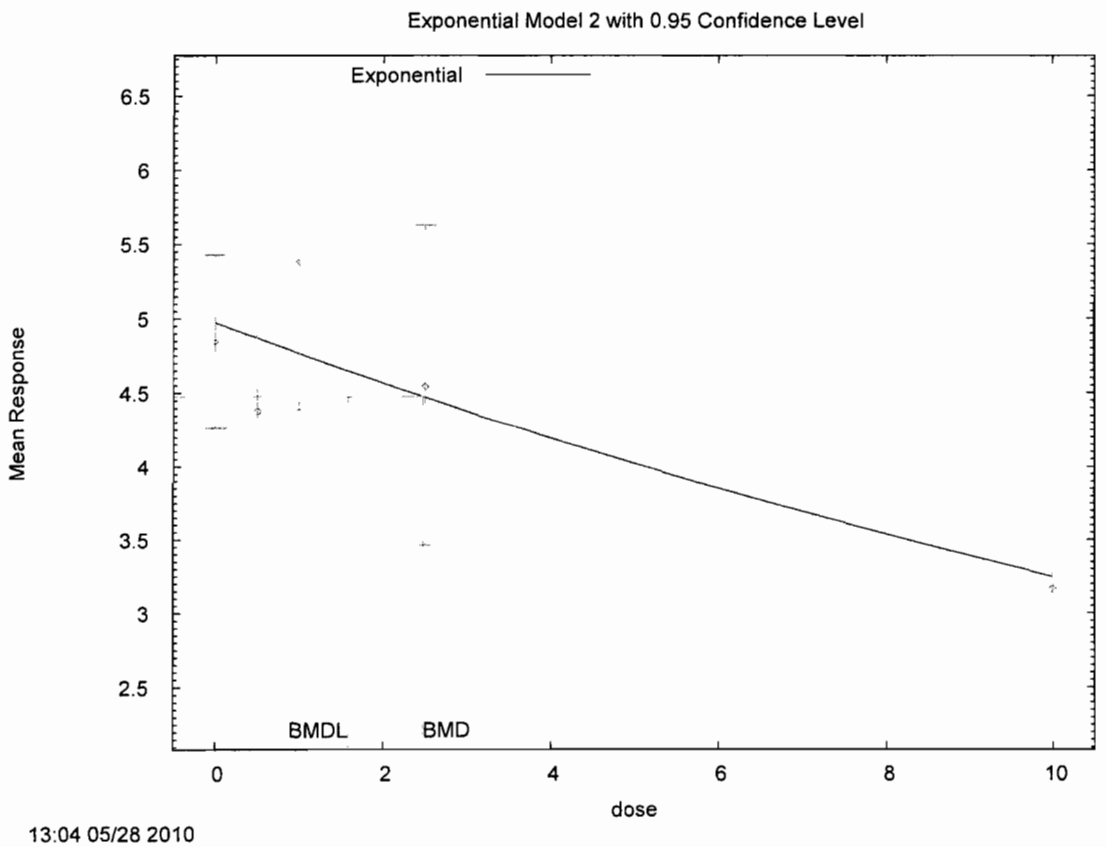
Specified Effect = 0.100000

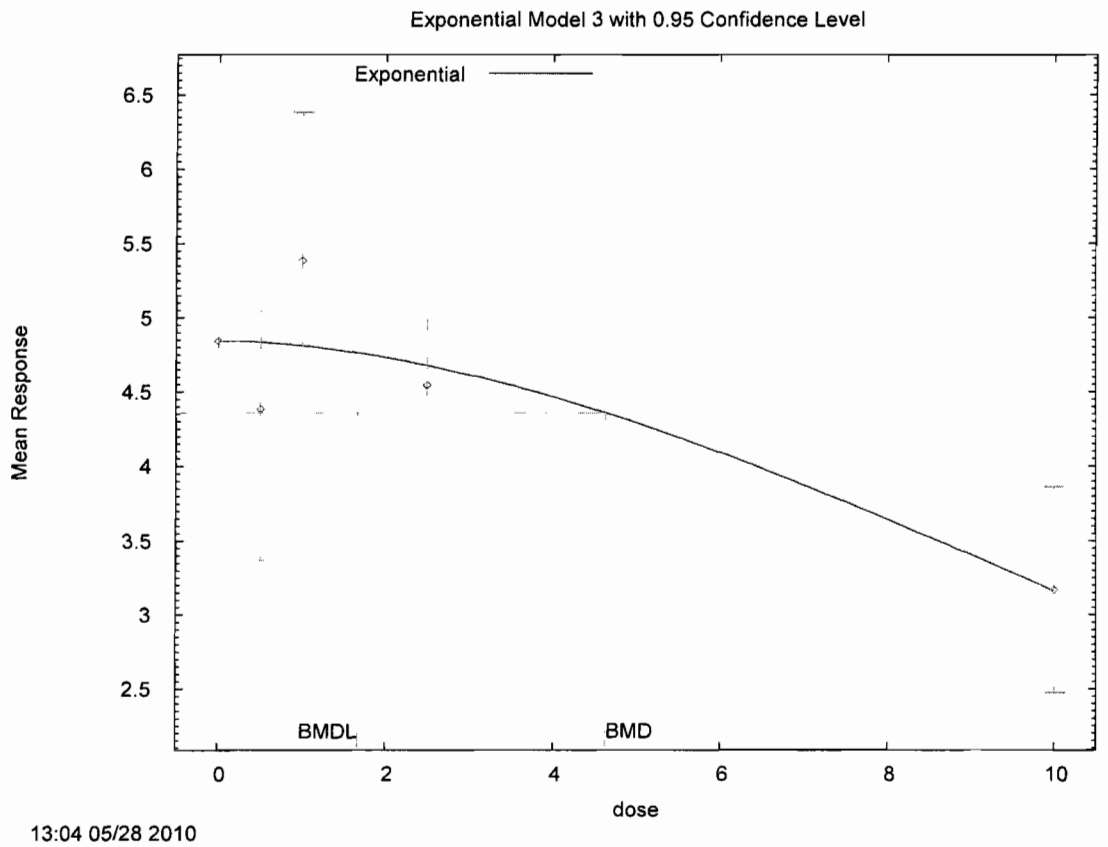
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	2.47396	1.5852
3	4.62946	1.66739
4	2.47396	1.01307
5	2.56504	1.23841




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
6.5
6
5.5
5
4.5
4
3.5
3
2.5
BMDL
BMD
0
2
4
6
8
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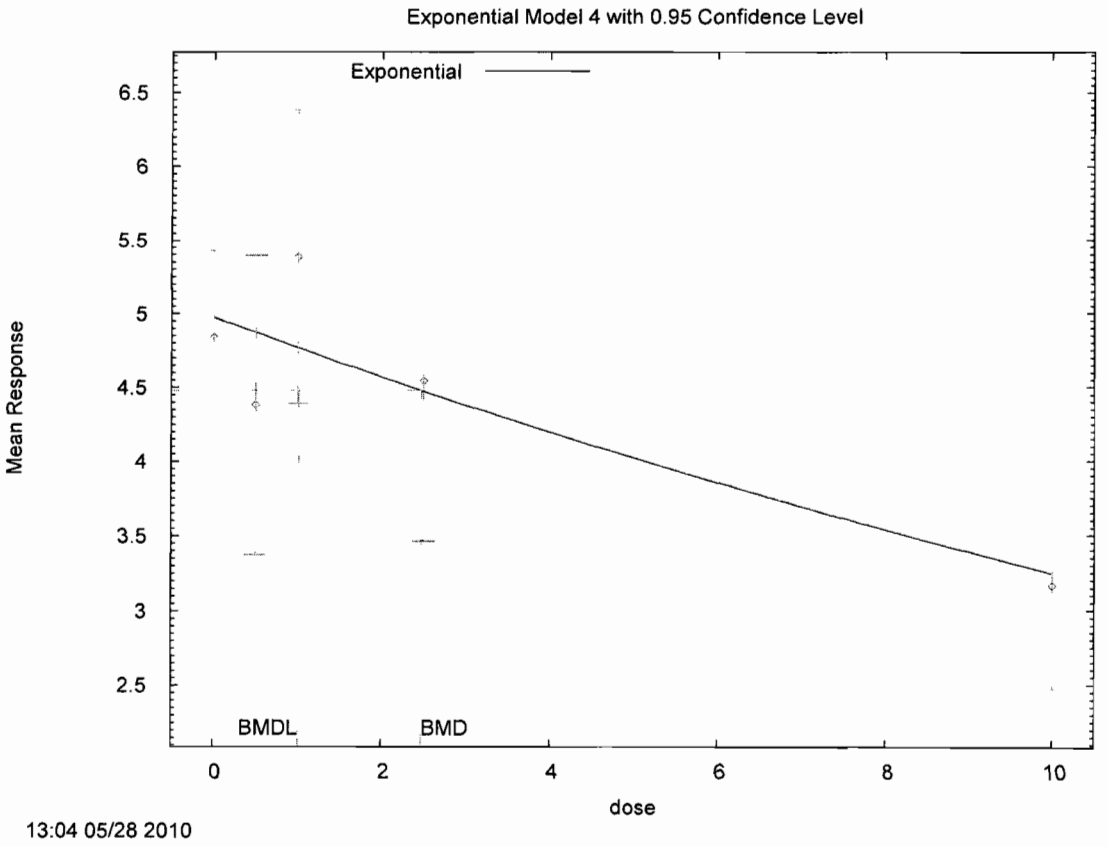
dose
13:04 05/28 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
6.5
6
5.5
5
4.5
4
3.5
3
2.5
BMDL
BMD
0
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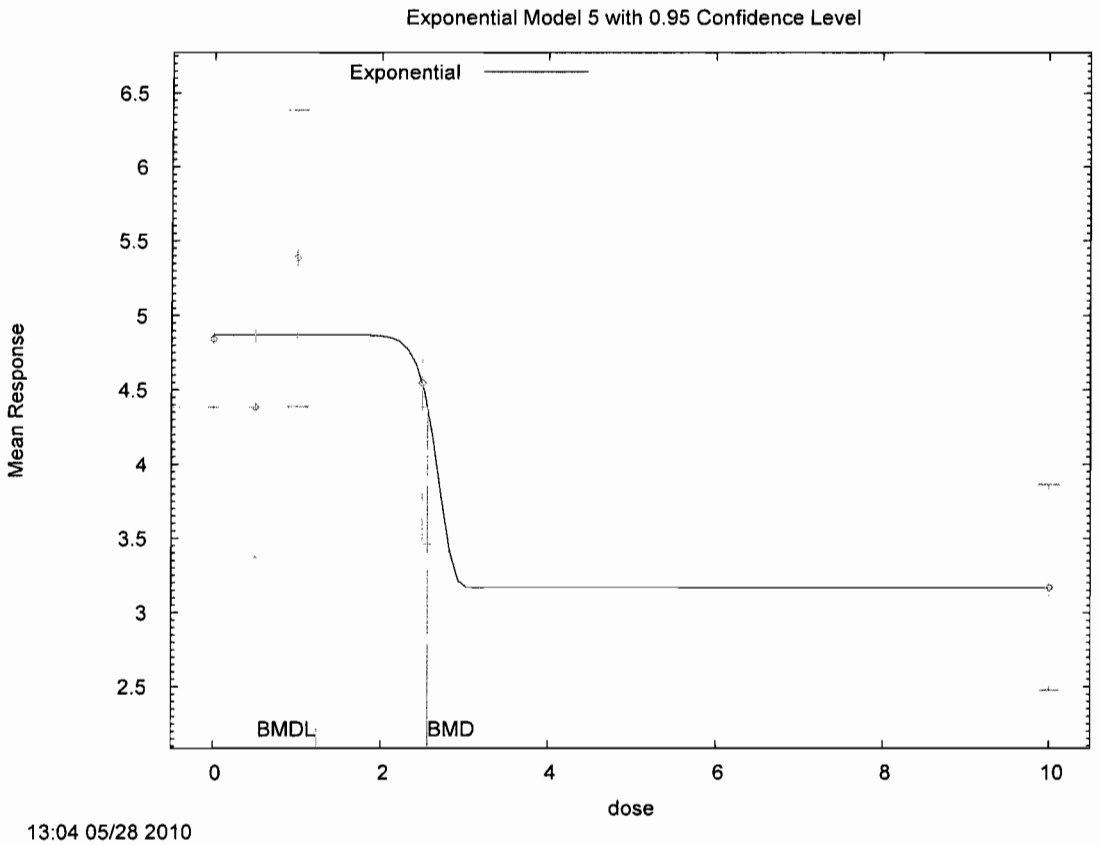
dose
13:04 05/28 2010



Acephate 46151801
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```
==============================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                  Fri May 28 12:54:49 2010
==============================================================================

 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-1.16404	-1.16404	-1.16404	-1.16404
rho(S)	0	0	0	0
a	3.45536	3.45536	5.21314	5.21314
b	0.043809	0.043809	0.299202	0.299202
c	--	--	0.535734	0.535734
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.8543	-0.8543	-1.10039	-1.10039
rho	0	0	0	0
a	4.47623	4.47623	4.91021	4.91021
b	0.0484152	0.0484152	0.574275	0.574275
c	--	--	0.608192	0.608192
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	4.965	0.7511
0.5	10	4.47	0.7346
1	10	3.836	0.3535

2.5	10	3.644	0.5343
10	10	2.933	0.4694

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	4.476	0.6524	2.369
	0.5	4.369	0.6524	0.4863
	1	4.265	0.6524	-2.078
	2.5	3.966	0.6524	-1.562
	10	2.758	0.6524	0.8442
3	0	4.476	0.6524	2.369
	0.5	4.369	0.6524	0.4863
	1	4.265	0.6524	-2.078
	2.5	3.966	0.6524	-1.562
	10	2.758	0.6524	0.8442
4	0	4.91	0.5768	0.2998
	0.5	4.43	0.5768	0.2164
	1	4.07	0.5768	-1.281
	2.5	3.444	0.5768	1.094
	10	2.993	0.5768	-0.329
5	0	4.91	0.5768	0.2998
	0.5	4.43	0.5768	0.2164
	1	4.07	0.5768	-1.281
	2.5	3.444	0.5768	1.094
	10	2.993	0.5768	-0.329

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	4.101066	6	3.797868
A2	7.810165	10	4.37967
A3	4.101066	6	3.797868
R	-19.42932	2	42.85863
2	-3.642492	3	13.28498
3	-3.642492	3	13.28498
4	2.509849	4	2.980302
5	2.509849	4	2.980302

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	54.48	8	< 0.0001
Test 2	7.418	4	0.1154
Test 3	7.418	4	0.1154
Test 4	15.49	3	0.001444
Test 5a	15.49	3	0.001444
Test 5b	-6.395e-014	0	N/A
Test 6a	3.182	2	0.2037
Test 6b	12.3	1	0.0004518
Test 7a	3.182	2	0.2037
Test 7b	12.3	1	0.0004518
Test 7c	-7.105e-015	0	N/A

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 greater than .1. A homogeneous variance model appears to be appropriate here.

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems

```
  to adequately describe the data.

  The p-value for Test 7b is less than .05.  Model 5 appears
  to fit the data better than Model 3.

  Degrees of freedom for Test 7c are less than or equal to 0.
  The Chi-Square test for fit is not valid.


Benchmark Dose Computations:

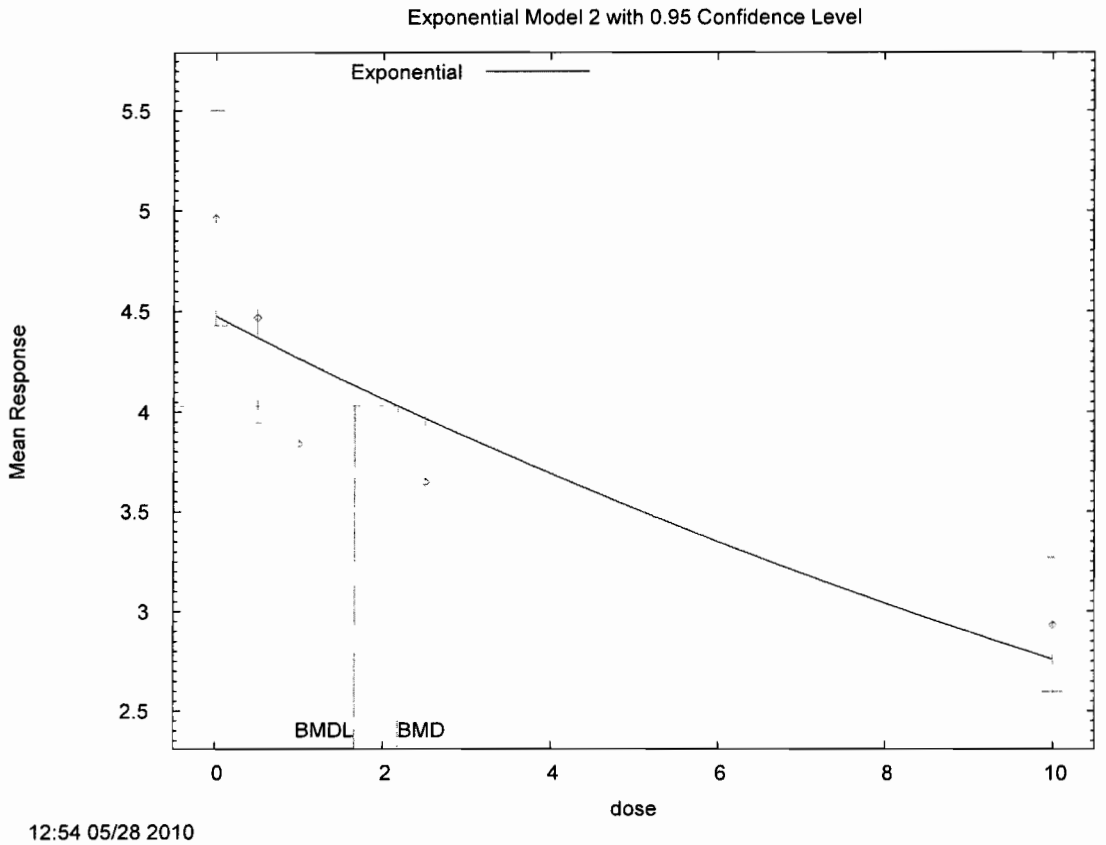
  Specified Effect = 0.100000

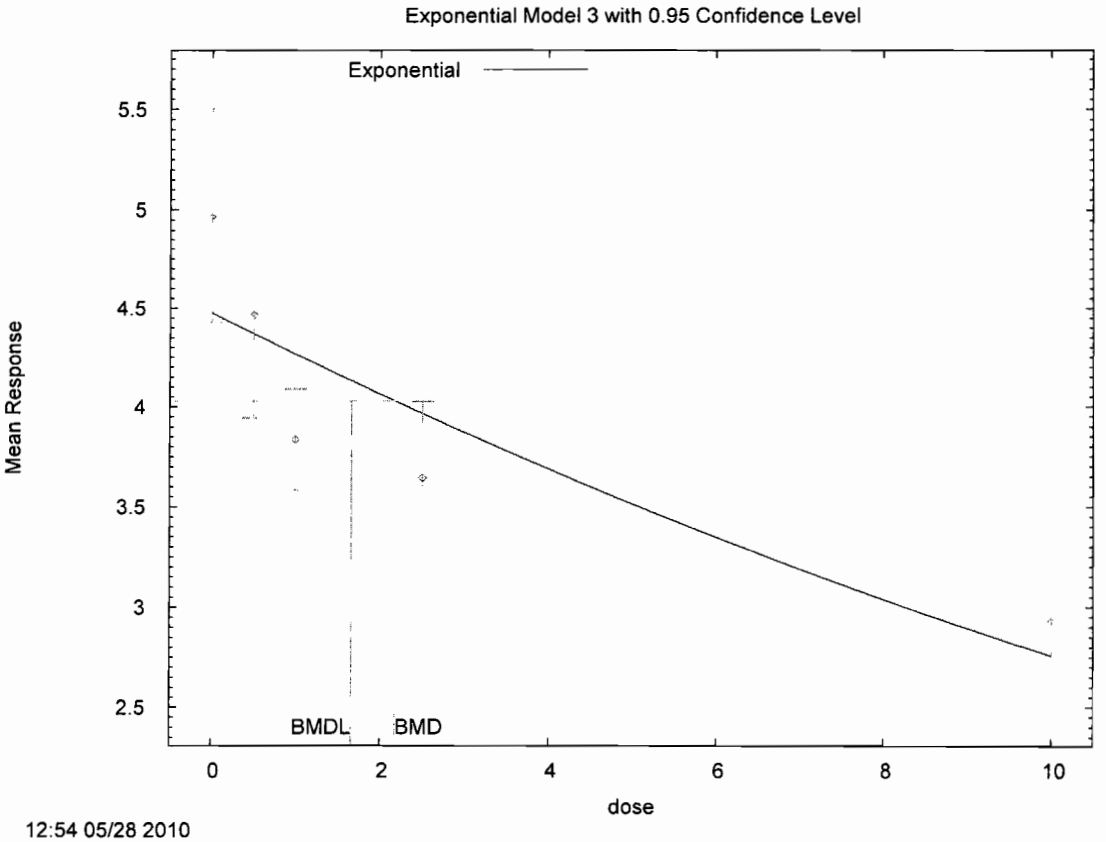
         Risk Type = Relative deviation

  Confidence Level = 0.950000


             BMD and BMDL by Model

   Model              BMD                 BMDL
  -------         ------------         ----------
     2              2.17618             1.66388
     3              2.17618             1.66388
     4             0.513127            0.303985
     5             0.513127            0.303985
```


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
5.5
5
4.5
4
3.5
3
2.5
BMDL
BMD
0
2
4
6
8
10
dose
12:54 05/28 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
5.5
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4.5
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3.5
3
2.5
BMDL
BMD
0
2
4
6
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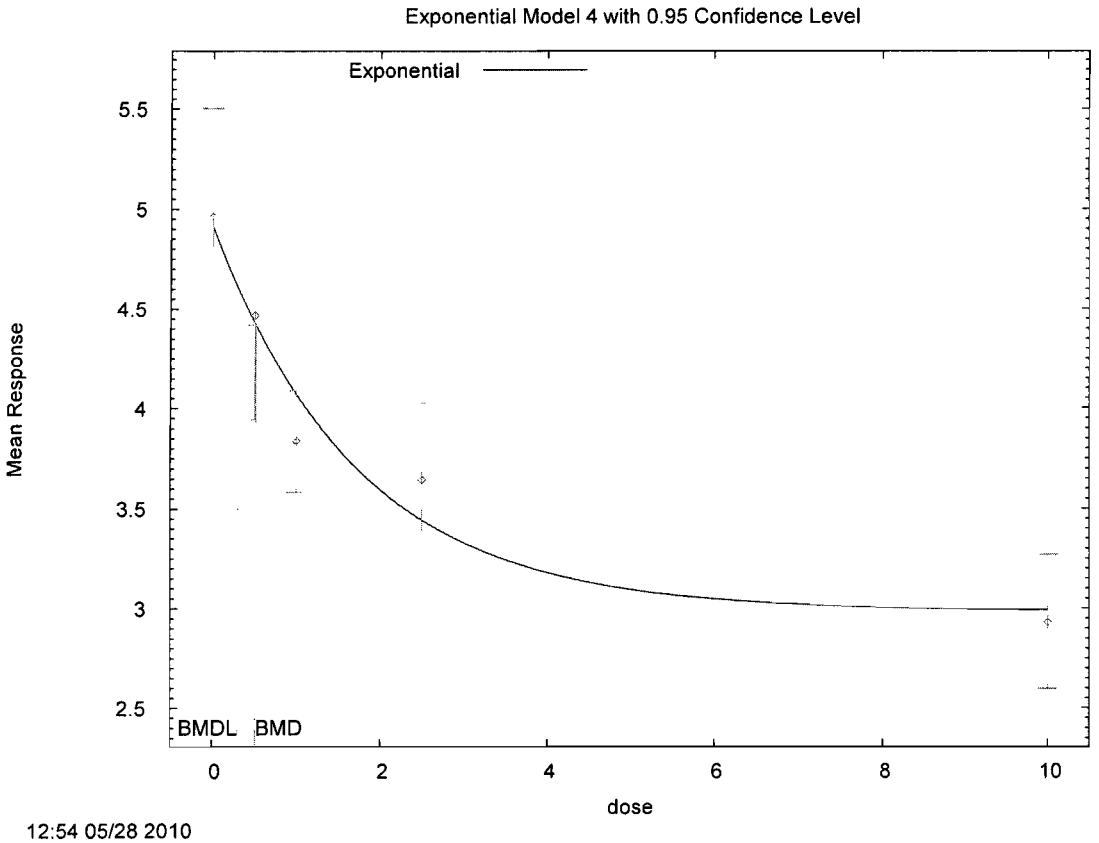
dose
12:54 05/28 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
5.5
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4.5
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3.5
3
2.5
BMDL
BMD
0
2
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dose
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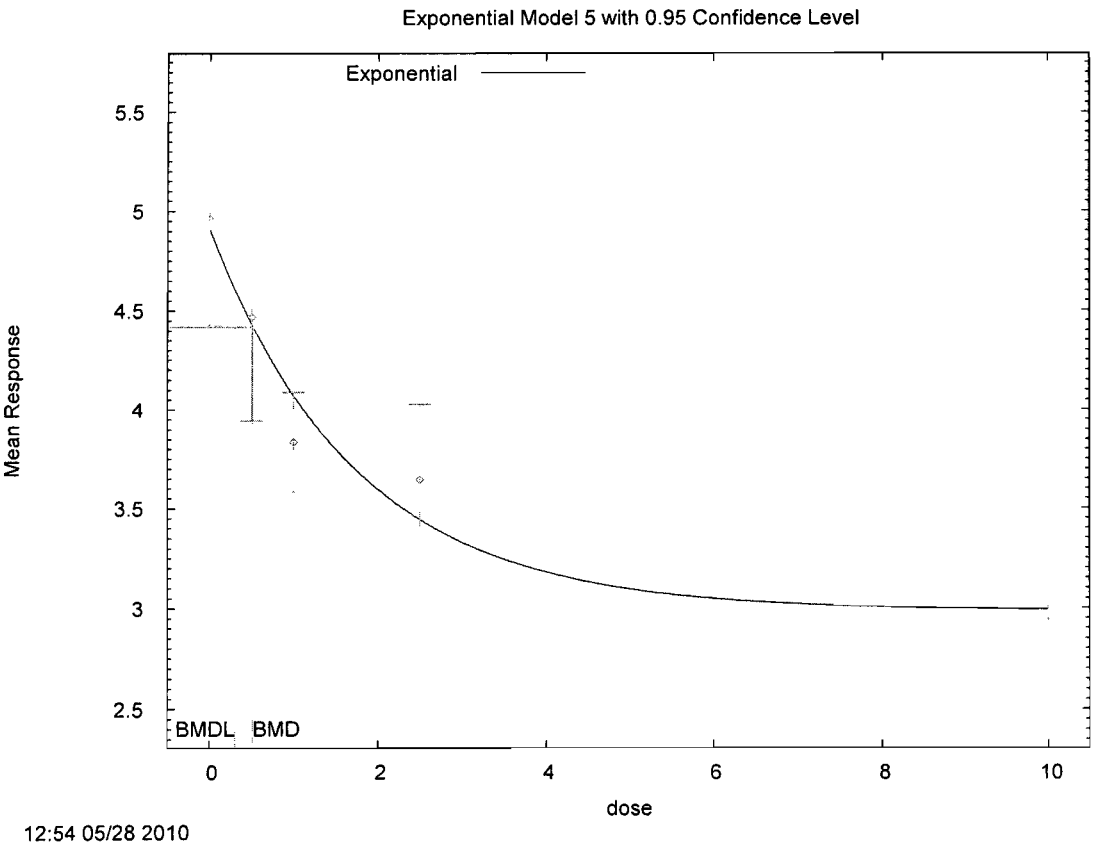
Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
5.5
5
4.5
4
3.5
3
2.5
BMDL
BMD
0
2
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dose
12:54 05/28 2010

Acephate
MRID 46151801
Female Brain

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Wed May 05 09:09:48 2010
 ================================================================

 BMDS Model Run
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   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 = Mean
   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 = 250
   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          Model 3          Model 4          Model 5
     --------          -------          -------          -------          -------
      lnalpha          0.48874          0.48874          0.48874
0.48874
          rho(S)              0                0                0
0
            a          5.87086          5.87086           8.9565
8.9565
            b        0.0486709        0.0486709         0.298427
0.298427
            c               --               --         0.497643
0.497643
            d               --                1               --
1
```

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	0.854454	0.854454	0.854454	0.854454
rho	0	0	0	0
a	7.76399	7.76399	7.76399	7.76399
b	0.0483929	0.0483929	0.0483929	0.0483929
c	--	--	0	5.24625e-082
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	8.53	0.21
0.5	10	7.4	1.44
1	10	5.96	1.9
2.5	10	7.83	1.73
10	10	4.68	0.58

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	7.764	1.533	1.58
	0.5	7.578	1.533	-0.368
	1	7.397	1.533	-2.965
	2.5	6.879	1.533	1.961
	10	4.785	1.533	-0.2174
3	0	7.764	1.533	1.58
	0.5	7.578	1.533	-0.368
	1	7.397	1.533	-2.965
	2.5	6.879	1.533	1.961
	10	4.785	1.533	-0.2174
4	0	7.764	1.533	1.58
	0.5	7.578	1.533	-0.368
	1	7.397	1.533	-2.965
	2.5	6.879	1.533	1.961
	10	4.785	1.533	-0.2174
5	0	7.764	1.533	1.58
	0.5	7.578	1.533	-0.368
	1	7.397	1.533	-2.965
	2.5	6.879	1.533	1.961
	10	4.785	1.533	-0.2174

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	-37.21849	6	86.43698
A2	-16.85842	10	53.71684
A3	-37.21849	6	86.43698
R	-56.64988	2	117.2998
2	-46.36134	3	98.72268
3	-46.36134	3	98.72268
4	-46.36134	3	98.72268
5	-46.36134	4	100.7227

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	79.58	8	< 0.0001
Test 2	40.72	4	< 0.0001
Test 3	40.72	4	< 0.0001
Test 4	18.29	3	0.000384
Test 5a	18.29	3	0.000384
Test 5b	0	0	N/A
Test 6a	18.29	3	0.000384
Test 6b	0	0	N/A
Test 7a	18.29	2	0.000107
Test 7b	0	1	1
Test 7c	0	1	1

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

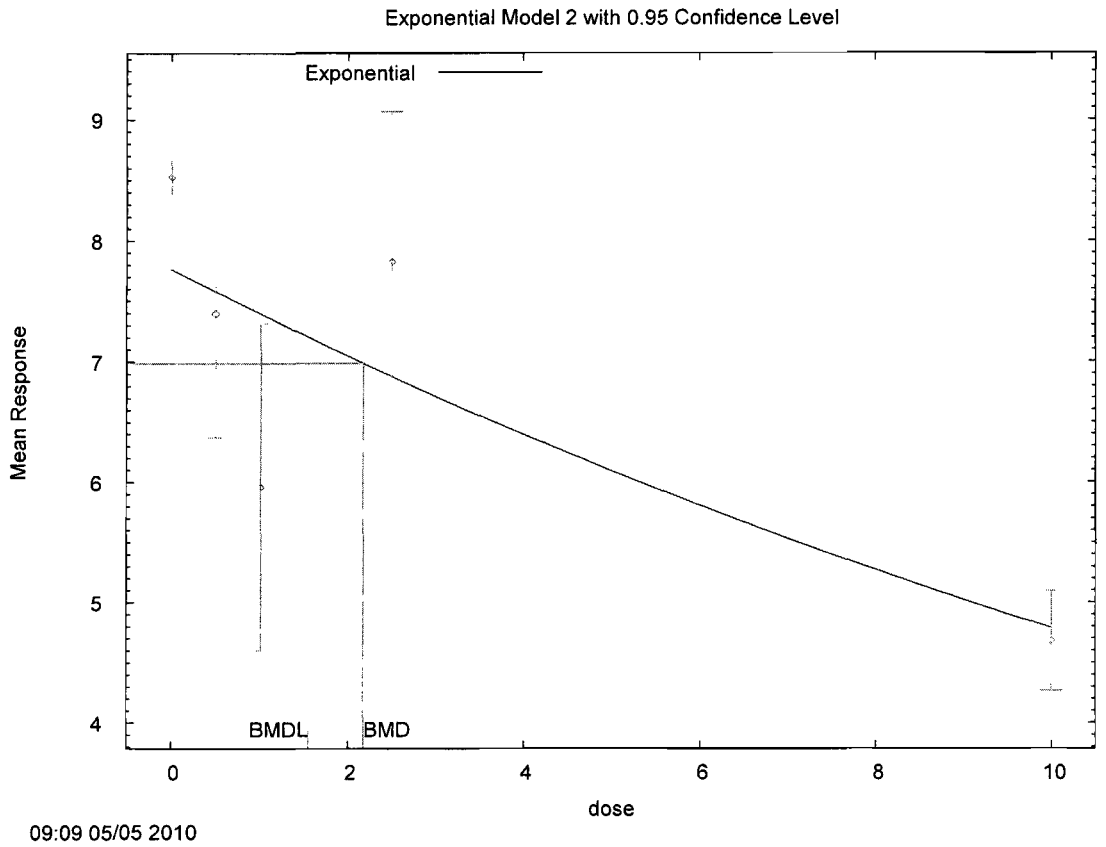
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	2.17719	1.54662
3	2.17719	1.54662
4	2.17719	0.847525
5	2.17719	1.54662


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
9
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7
6
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BMDL
BMD
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dose
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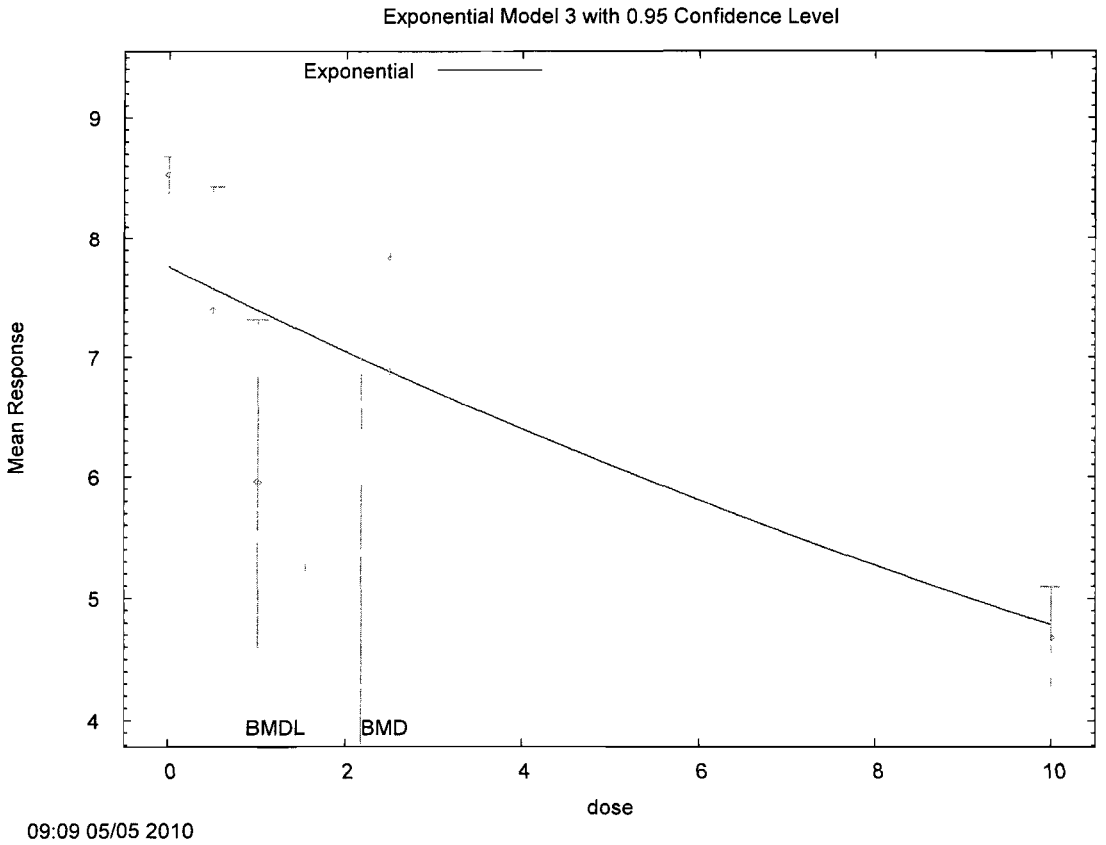
Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
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BMDL
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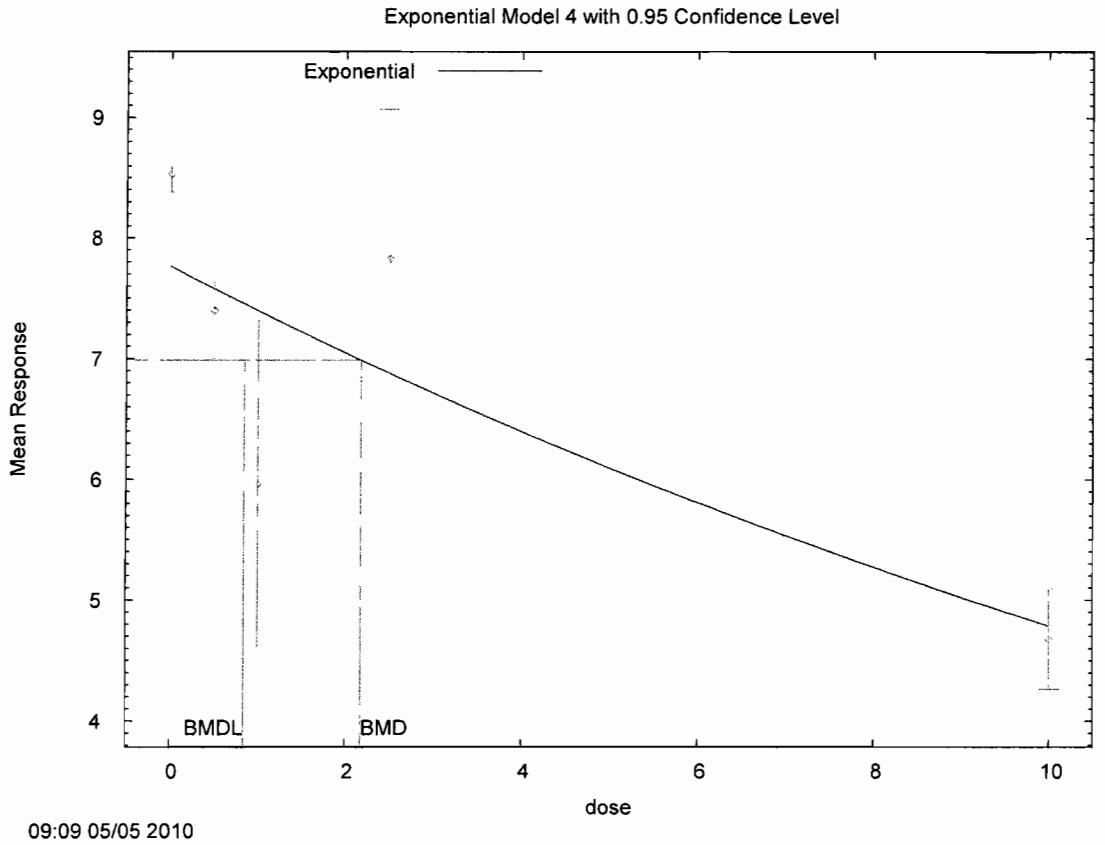
Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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BMDL
BMD
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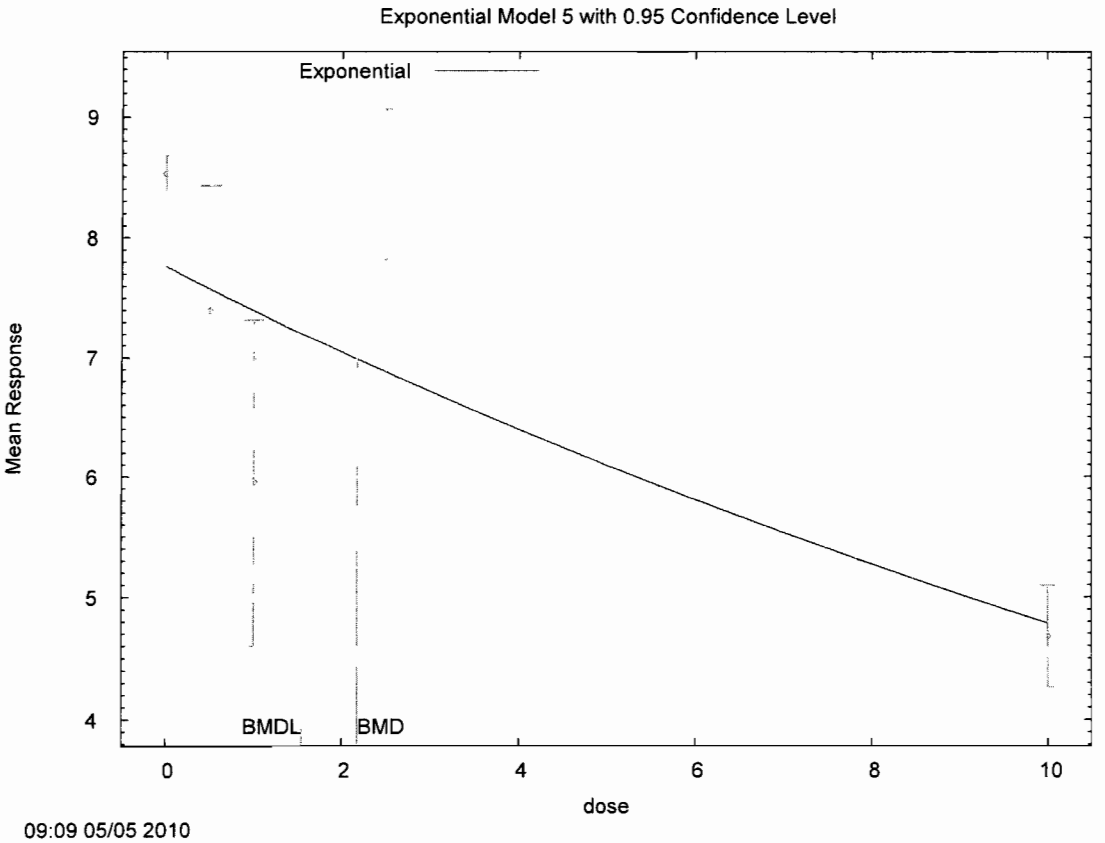
Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
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Acephate
MRID 46151801
Female Brain

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Thu May 06 08:30:20 2010
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 BMDS Model Run
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   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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha           1.93206           1.93206              1.93206
1.93206
          rho          -1.12909          -1.12909            -1.12909            -
1.12909
            a           5.87086           5.87086               8.9565
8.9565
            b         0.0486709         0.0486709             0.298427
0.298427
            c                --                --                0.497643
0.497643
            d                --                 1                  --
1
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-7.78191	-8.67515	-7.78191	-8.67515
rho	4.42293	4.84698	4.42293	4.84698
a	7.81678	7.43	7.81678	7.43
b	0.0506332	0.0958034	0.0506332	0.0957042
c	--	--	0	0
d	--	18	--	17.5751

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	8.53	0.21
0.5	10	7.4	1.44
1	10	5.96	1.9
2.5	10	7.83	1.73
10	10	4.68	0.58

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	7.817	1.928	1.17
	0.5	7.621	1.823	-0.384
	1	7.431	1.724	-2.698
	2.5	6.887	1.457	2.046
	10	4.711	0.6292	-0.1567
3	0	7.43	1.687	2.062
	0.5	7.43	1.687	-0.05624
	1	7.43	1.687	-2.756
	2.5	7.43	1.687	0.7499
	10	4.68	0.5502	-8.39e-010
4	0	7.817	1.928	1.17
	0.5	7.621	1.823	-0.384
	1	7.431	1.724	-2.698
	2.5	6.887	1.457	2.046
	10	4.711	0.6292	-0.1567
5	0	7.43	1.687	2.062
	0.5	7.43	1.687	-0.05624
	1	7.43	1.687	-2.756
	2.5	7.43	1.687	0.7499
	10	4.68	0.5502	1.138e-009

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	-37.21849	6	86.43698
A2	-16.85842	10	53.71684
A3	-37.04427	7	88.08855
R	-56.64988	2	117.2998
2	-42.14443	4	92.28886
3	-39.93778	5	89.87557
4	-42.14443	4	92.28886
5	-39.93778	5	89.87557

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	79.58	8	< 0.0001
Test 2	40.72	4	< 0.0001
Test 3	40.37	3	< 0.0001
Test 4	10.2	3	0.01694
Test 5a	5.787	2	0.05538
Test 5b	4.413	1	0.03566
Test 6a	10.2	3	0.01694
Test 6b	-2.132e-013	0	N/A
Test 7a	5.787	2	0.05538
Test 7b	-1.135e-010	0	N/A
Test 7c	4.413	1	0.03566

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 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.

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.

The p-value for Test 5b is less than .05. Model 3 appears
to fit the data better than Model 2.

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.

Degrees of freedom for Test 6b are less than or equal to 0.
The Chi-Square test for fit is not valid.

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.

Degrees of freedom for Test 7b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 7c is less than .05. Model 5 appears
to fit the data better than Model 4.

Benchmark Dose Computations:

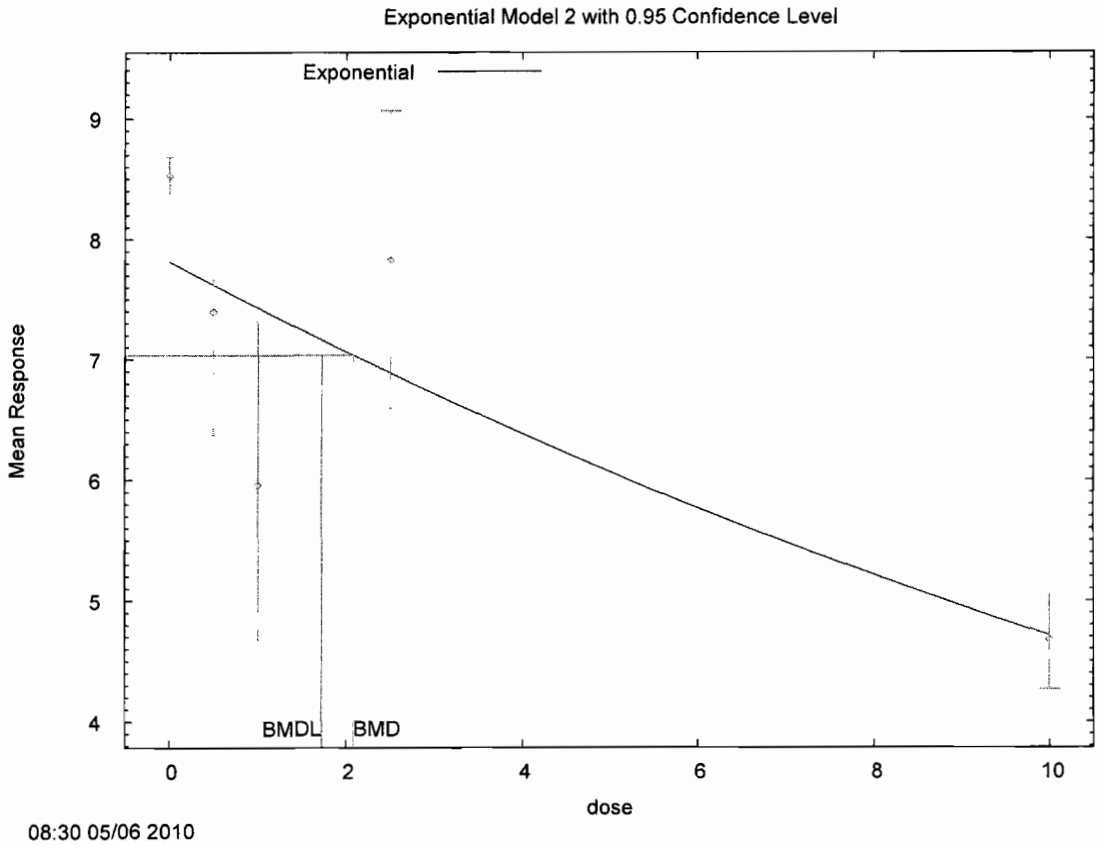
Specified Effect = 0.100000

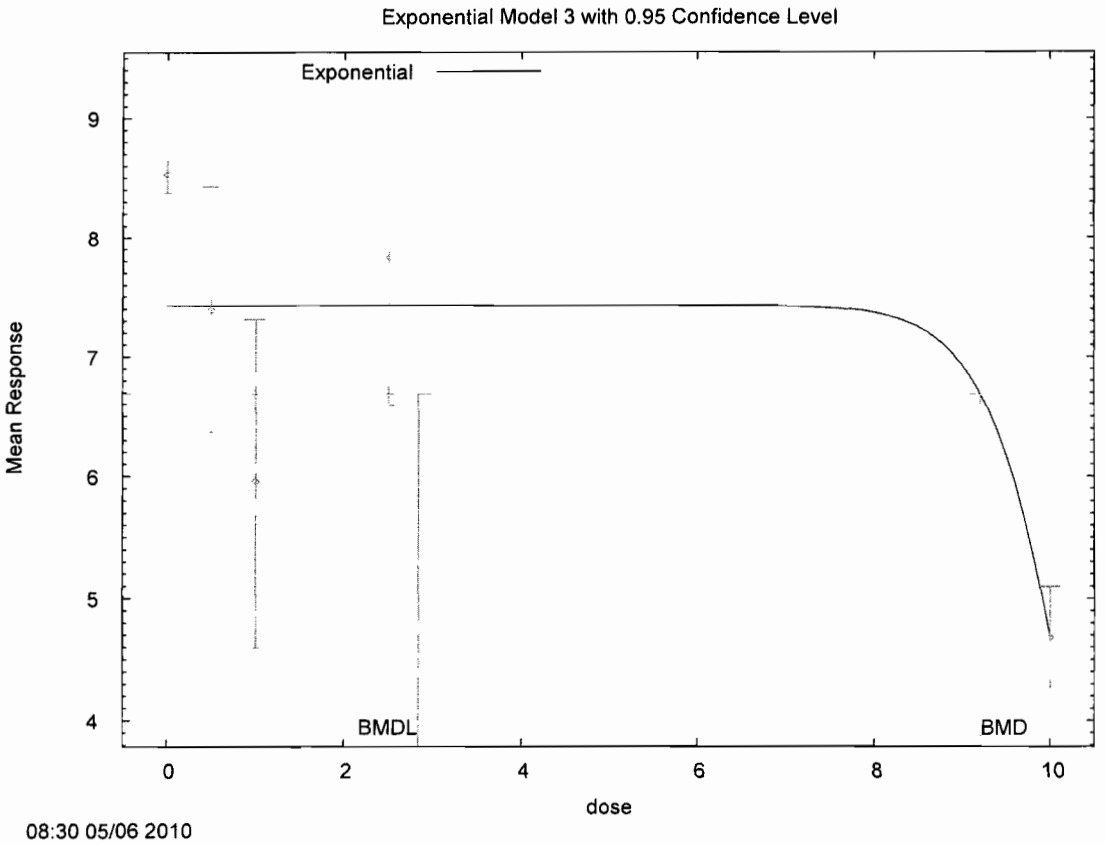
Risk Type = Relative deviation

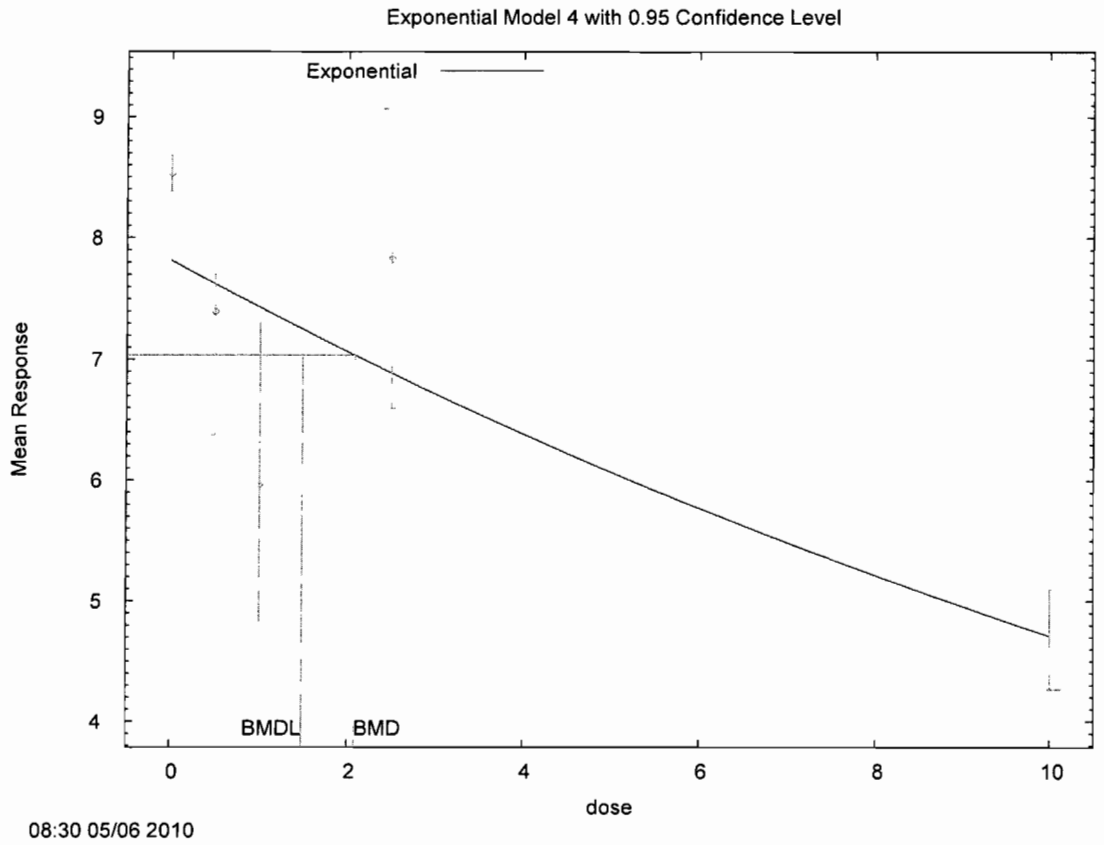
Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	2.08086	1.72587
3	9.21135	2.83442
4	2.08086	1.48553
5	9.19308	2.56793


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:30 05/06 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:30 05/06 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
9
8
7
6
5
4
BMDL
BMD
0
2
4
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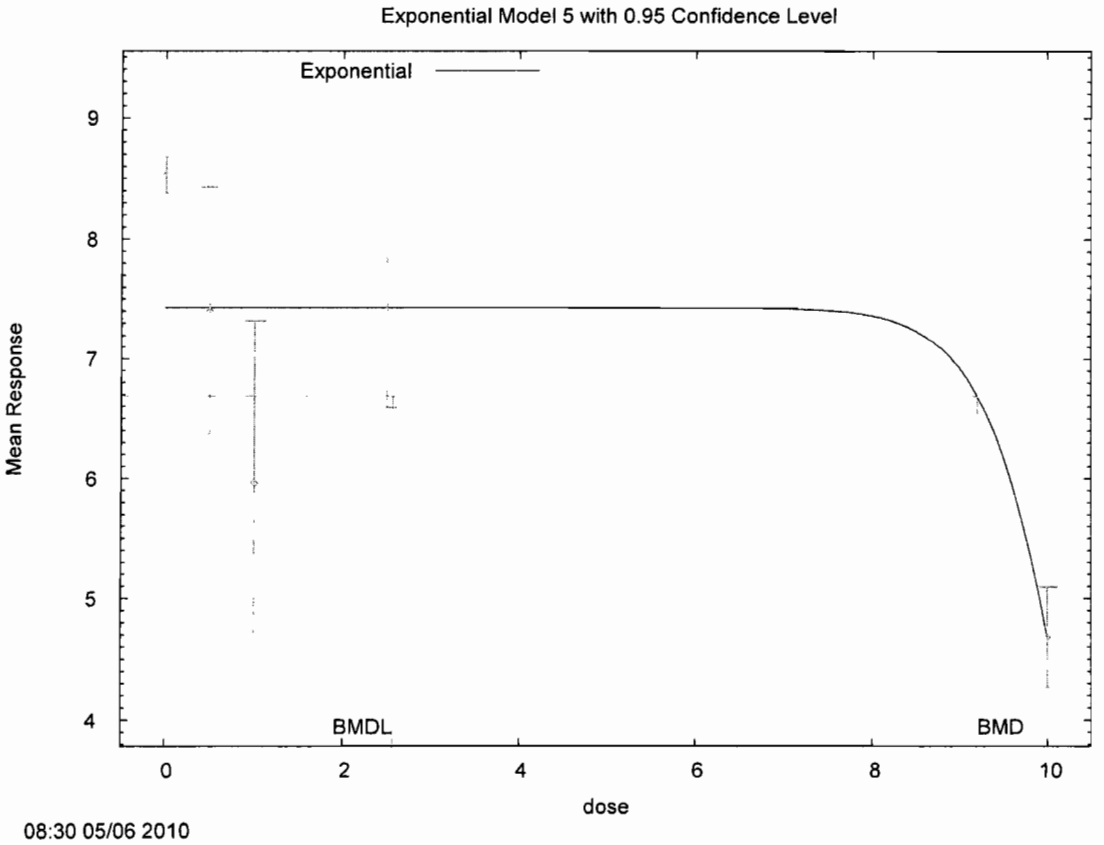
8
10
dose
08:30 05/06 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:30 05/06 2010

Acephate
MRID 46151801
Female RBC ChE

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Mon May 17 11:19:43 2010
 ================================================================

 BMDS Model Run
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   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 = Mean
   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 = 250
   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          Model 3          Model 4          Model 5
     --------          -------          -------          -------          -------
      lnalpha           -1.4068          -1.4068          -1.4068             -
1.4068
          rho(S)                0                0                0
0
            a           2.30416          2.30416           3.1185
3.1185
            b          0.027023         0.027023         0.253552
0.253552
            c                --               --         0.613848
0.613848
            d                --                1               --
1
```

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-1.22814	-1.25595	-1.22814	-1.25595
rho	0	0	0	0
a	2.6859	2.63	2.6859	2.63
b	0.0263442	0.0871575	0.0263442	0.0892311
c	--	--	0	0.046679
d	--	9.55671	--	11.0456

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	2.36	0.49
0.5	10	2.97	0.49
1	10	2.53	0.68
2.5	10	2.66	0.55
10	10	2.01	0.34

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2.686	0.5411	-1.904
	0.5	2.651	0.5411	1.866
	1	2.616	0.5411	-0.5029
	2.5	2.515	0.5411	0.8491
	10	2.064	0.5411	-0.3147
3	0	2.63	0.5337	-1.6
	0.5	2.63	0.5337	2.015
	1	2.63	0.5337	-0.5926
	2.5	2.63	0.5337	0.1778
	10	2.01	0.5337	-3.519e-007
4	0	2.686	0.5411	-1.904
	0.5	2.651	0.5411	1.866
	1	2.616	0.5411	-0.5029
	2.5	2.515	0.5411	0.8491
	10	2.064	0.5411	-0.3147
5	0	2.63	0.5337	-1.6
	0.5	2.63	0.5337	2.015
	1	2.63	0.5337	-0.5926
	2.5	2.63	0.5337	0.1778
	10	2.01	0.5337	-6.192e-008

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	10.16998	6	-8.339958
A2	12.5241	10	-5.048204
A3	10.16998	6	-8.339958
R	1.510524	2	0.9789524
2	5.703607	3	-5.407213
3	6.398674	4	-4.797349
4	5.703607	3	-5.407213
5	6.398676	5	-2.797351

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	22.03	8	0.004866
Test 2	4.708	4	0.3186
Test 3	4.708	4	0.3186
Test 4	8.933	3	0.0302
Test 5a	7.543	2	0.02302
Test 5b	1.39	1	0.2384
Test 6a	8.933	3	0.0302
Test 6b	1.901e-013	0	N/A
Test 7a	7.543	1	0.006026
Test 7b	2.289e-006	1	0.9988

Test 7c	1.39	2	0.499

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 greater than .1. A homogeneous variance model appears to be appropriate here.

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.

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.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

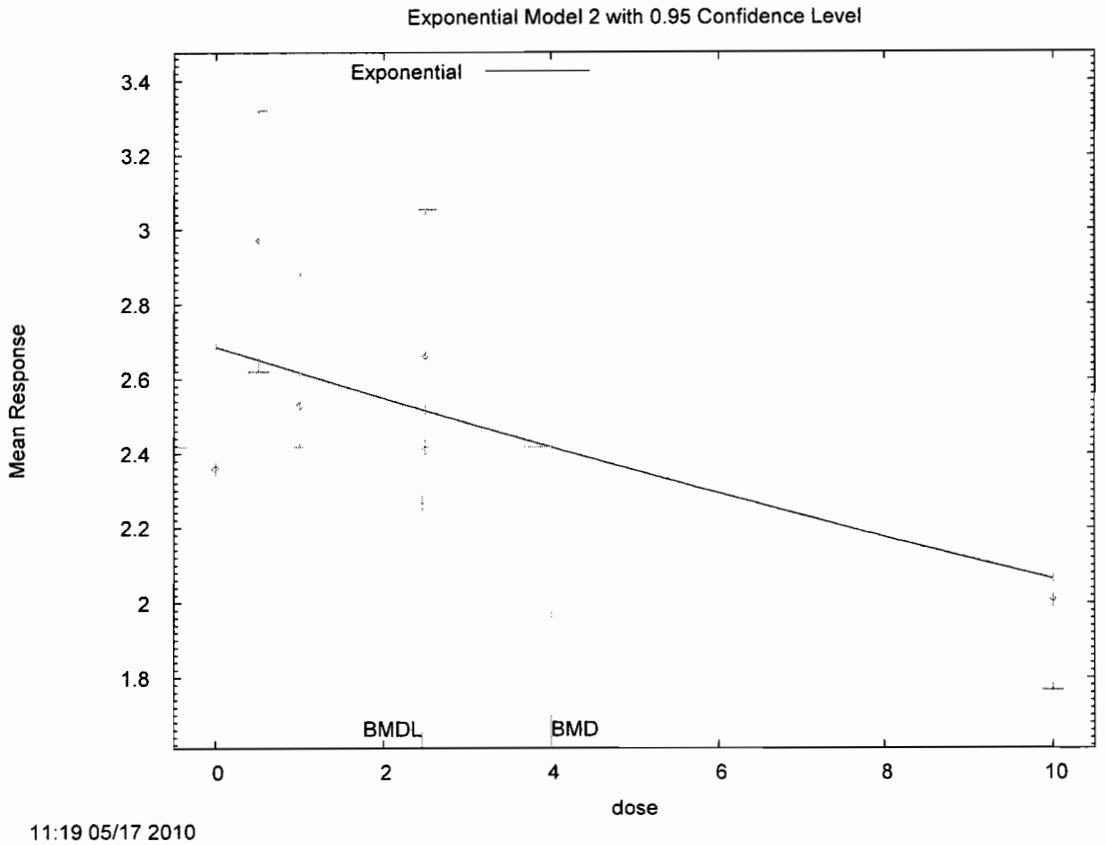
Specified Effect = 0.100000

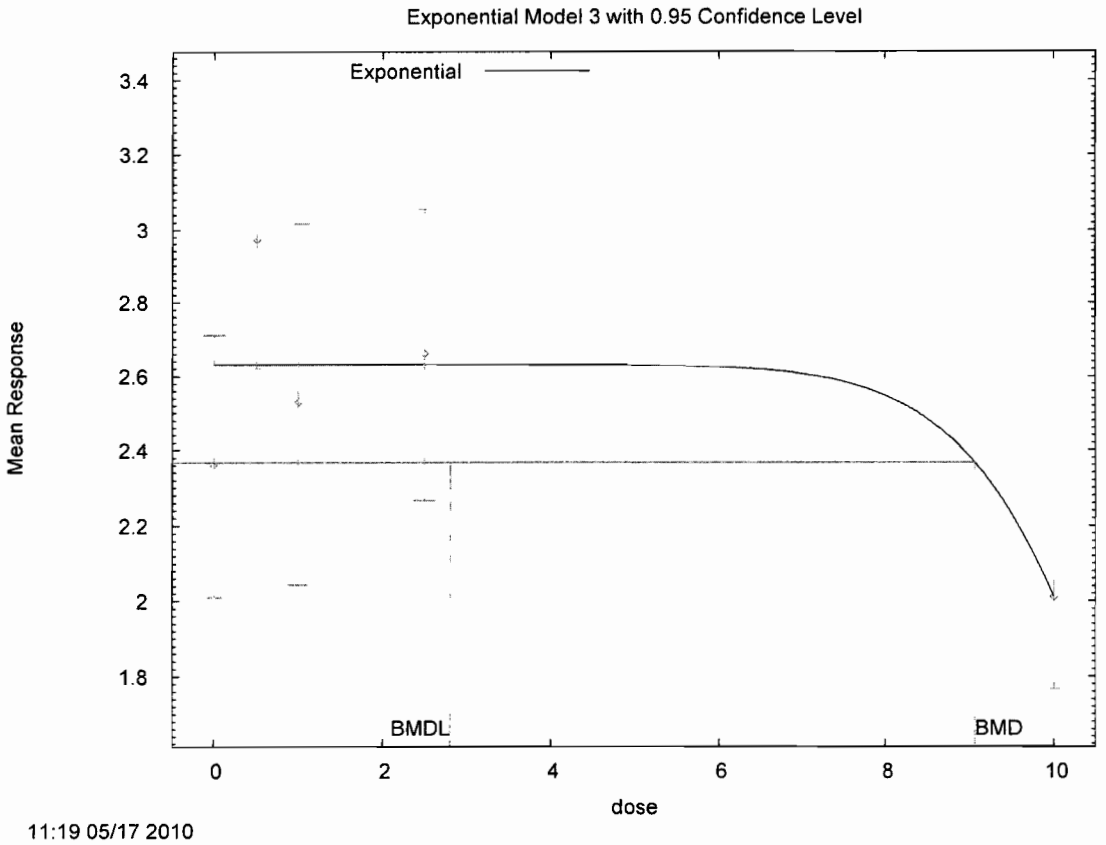
Risk Type = Relative deviation

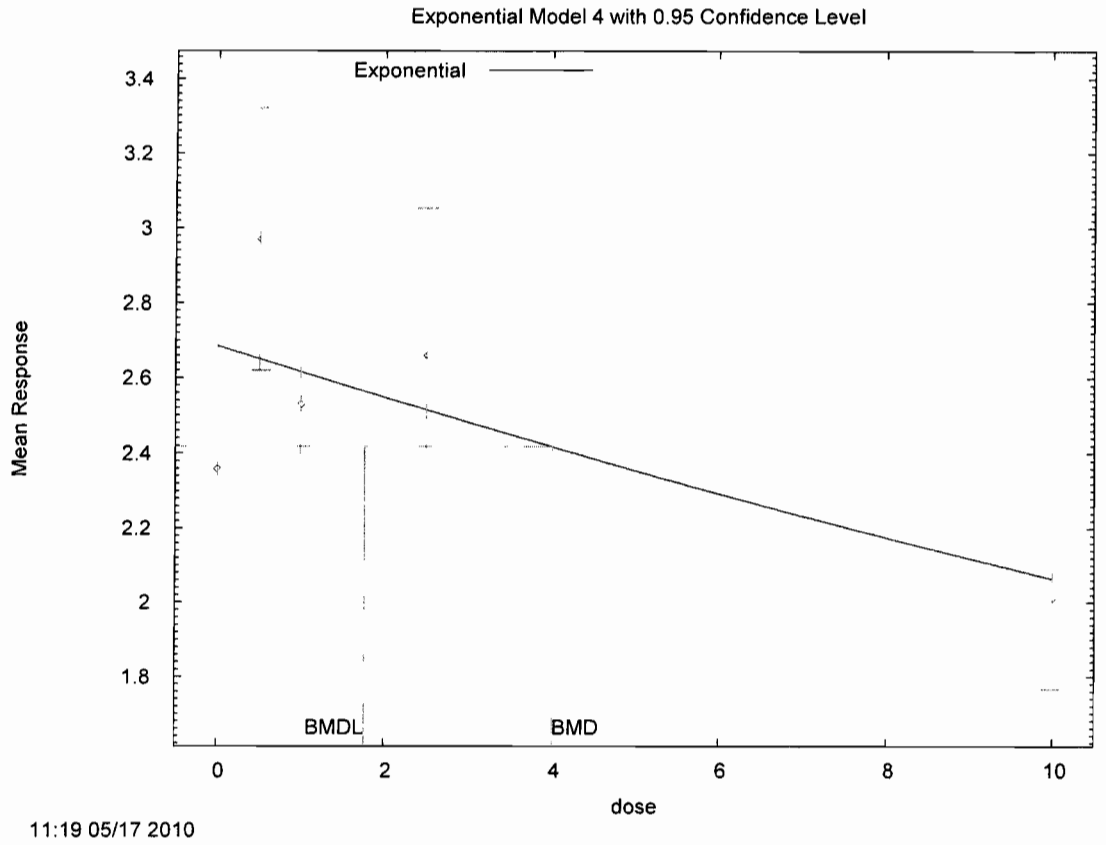
Confidence Level = 0.950000

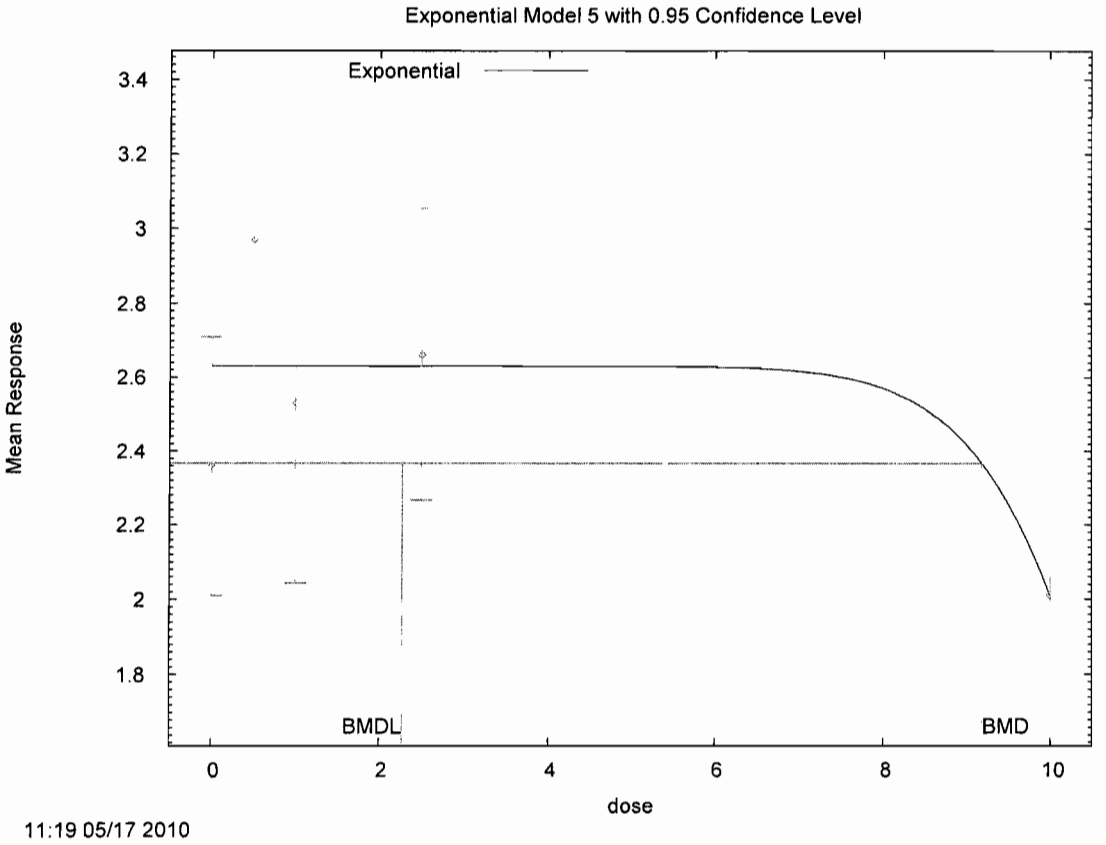
BMD and BMDL by Model

Model	BMD	BMDL
2	3.99939	2.46447
3	9.06629	2.80769
4	3.99939	1.76794
5	9.18307	2.27305


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
3.4
3.2
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
10
dose
11:19 05/17 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
3.4
3.2
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
10
dose
11:19 05/17 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
3.4
3.2
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
10
dose
11:19 05/17 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
3.4
3.2
3
2.8
2.6
2.4
2.2
2
1.8
BMDL
BMD
0
2
4
6
8
10
dose
11:19 05/17 2010

Acephate
MRID 46151801
Male Brain ChE

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Wed May 05 08:45:16 2010
 ================================================================

 BMDS Model Run
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   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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha          0.922736          0.922736            0.922736
0.922736
          rho(S)              0                 0                   0
0
            a           5.65468           5.65468              9.6495
9.6495
            b         0.0632749         0.0632749            0.330841
0.330841
            c                --                --            0.424399
0.424399
```

d	--	1	--
1			

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	1.19495	1.19495	1.17663	
1.17663				
rho	0	0	0	
0				
a	8.1811	8.1811	8.53035	
8.53035				
b	0.0668131	0.0668131	0.257991	
0.257991				
c	--	--	0.478782	
0.478782				
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	9.19	1.04
0.5	10	8.01	1.89
1	10	6.01	2.85
2.5	10	7.37	0.8
10	10	4.3	0.75

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	8.181	1.818	1.755
	0.5	7.912	1.818	0.17
	1	7.652	1.818	-2.858
	2.5	6.923	1.818	0.7784
	10	4.194	1.818	0.1841
3	0	8.181	1.818	1.755
	0.5	7.912	1.818	0.17
	1	7.652	1.818	-2.858
	2.5	6.923	1.818	0.7784
	10	4.194	1.818	0.1841
4	0	8.53	1.801	1.158
	0.5	7.992	1.801	0.03114
	1	7.519	1.801	-2.65
	2.5	6.417	1.801	1.673
	10	4.421	1.801	-0.2127
5	0	8.53	1.801	1.158
	0.5	7.992	1.801	0.03114
	1	7.519	1.801	-2.65
	2.5	6.417	1.801	1.673
	10	4.421	1.801	-0.2127

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	-48.06841	6	108.1368
A2	-34.4889	10	88.97779
A3	-48.06841	6	108.1368
R	-66.97517	2	137.9503
2	-54.87371	3	115.7474
3	-54.87371	3	115.7474
4	-54.41587	4	116.8317
5	-54.41587	4	116.8317

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	64.97	8	< 0.0001
Test 2	27.16	4	< 0.0001
Test 3	27.16	4	< 0.0001
Test 4	13.61	3	0.003486
Test 5a	13.61	3	0.003486
Test 5b	-2.842e-014	0	N/A
Test 6a	12.69	2	0.001751
Test 6b	0.9157	1	0.3386

Test 7a	12.69	2	0.001751
Test 7b	0.9157	1	0.3386
Test 7c	-3.283e-012	0	N/A

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

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.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

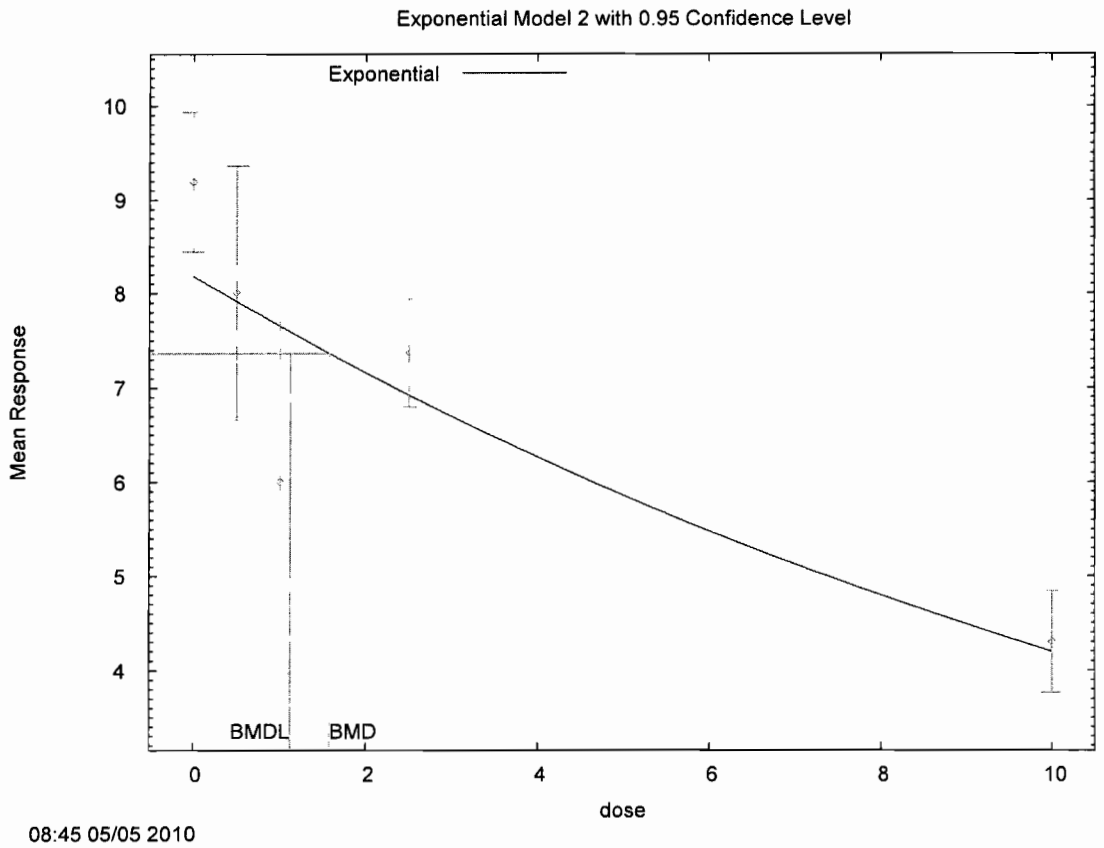
Specified Effect = 0.100000

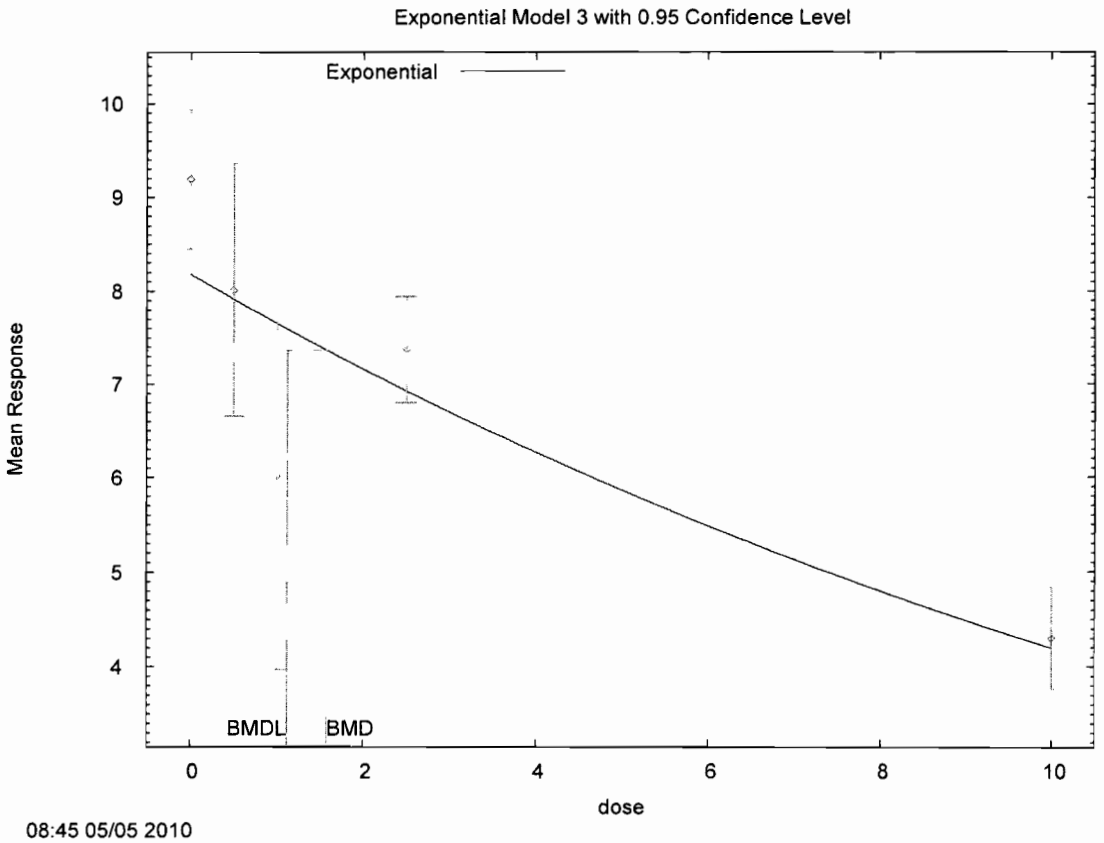
Risk Type = Relative deviation

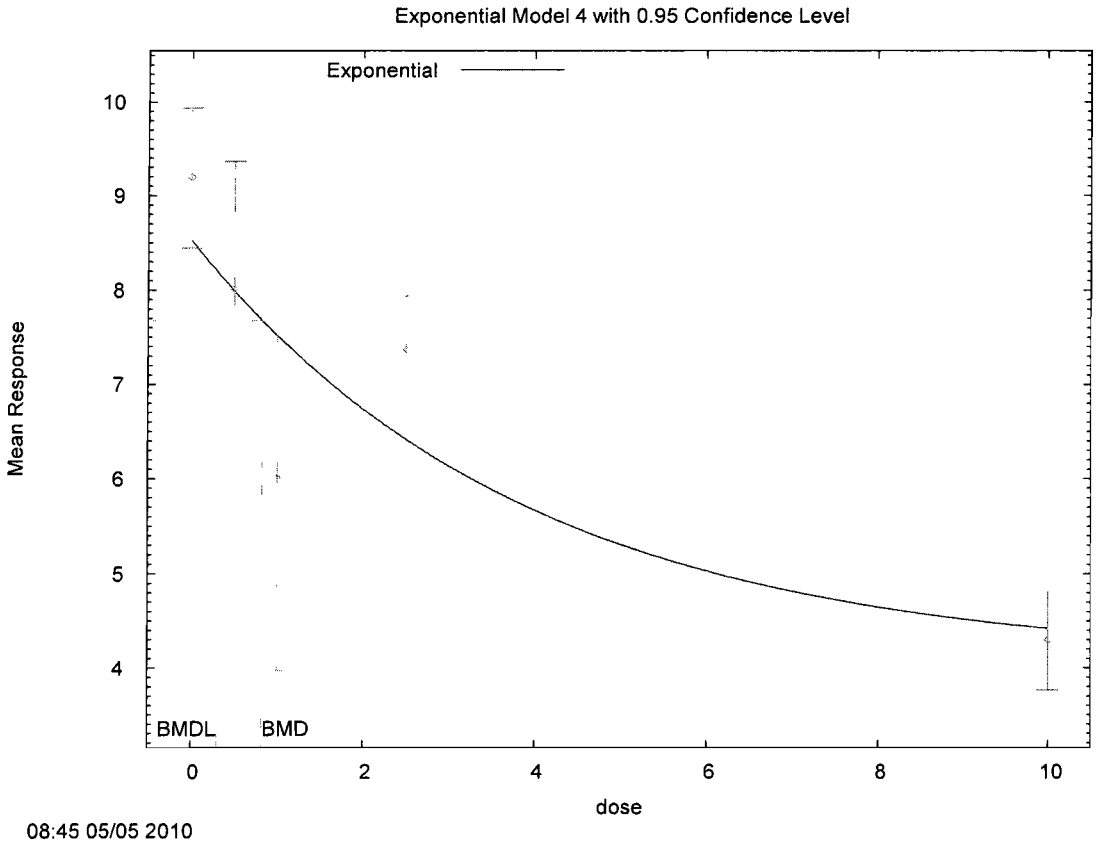
Confidence Level = 0.950000

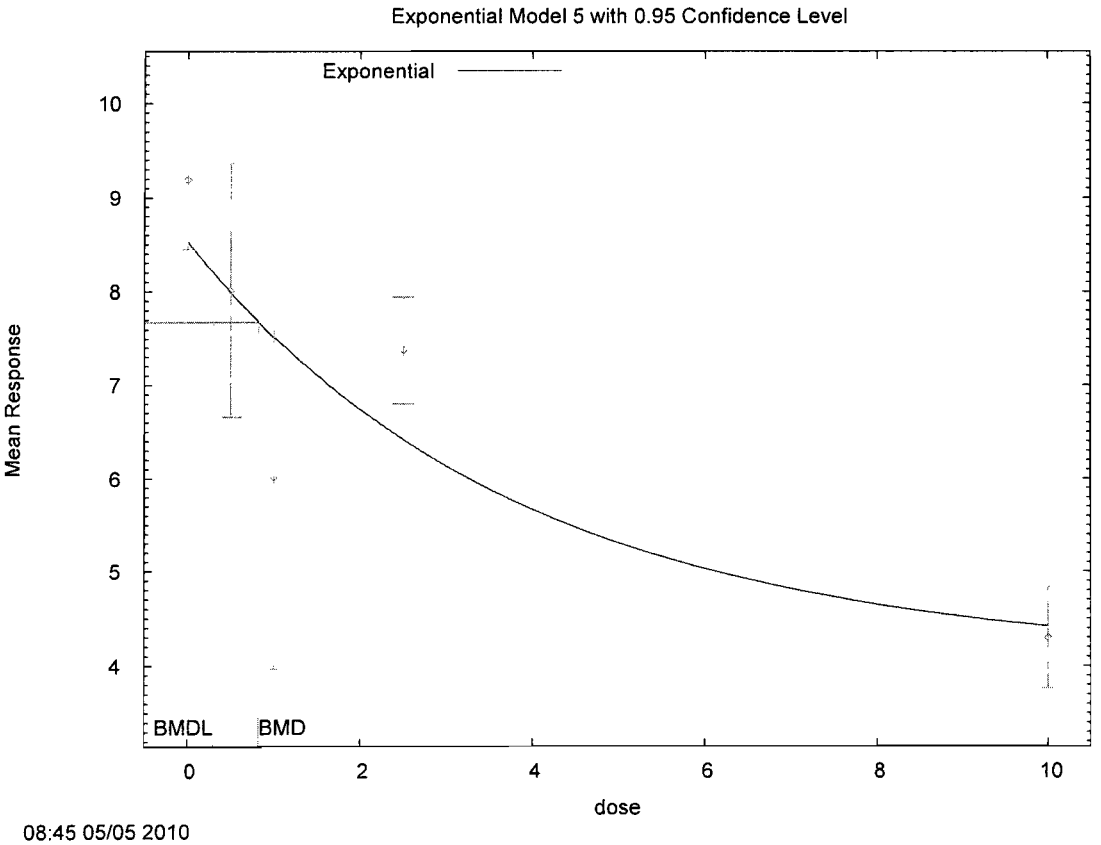
BMD and BMDL by Model

Model	BMD	BMDL
2	1.57695	1.12009
3	1.57695	1.12009
4	0.82568	0.303293
5	0.825679	0.303293


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:45 05/05 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:45 05/05 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:45 05/05 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:45 05/05 2010

Acephate
MRID 46151801
Male Brain

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                          Wed May 05 08:56:40 2010
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 BMDS Model Run
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   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 = Mean
   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 = 250
   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           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
      lnalpha         -0.712361         -0.712361          -0.712361          -
0.712361
          rho          0.626961          0.626961           0.626961
0.626961
            a           5.65468           5.65468              9.6495
9.6495
            b         0.0632749         0.0632749           0.330841
0.330841
            c                --                --           0.424399
0.424399
            d                --                 1                 --
1
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-6.03898	-6.03898	-5.99878	-5.99878
rho	3.64713	3.64713	3.62486	3.62486
a	8.12352	8.12352	8.21573	8.21573
b	0.0636783	0.0636784	0.107549	0.107549
c	--	--	0.277846	0.277846
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	9.19	1.04
0.5	10	8.01	1.89
1	10	6.01	2.85
2.5	10	7.37	0.8
10	10	4.3	0.75

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	8.124	2.227	1.515
	0.5	7.869	2.101	0.2123
	1	7.622	1.982	-2.572
	2.5	6.928	1.666	0.8393
	10	4.297	0.6971	0.01239
3	0	8.124	2.227	1.515
	0.5	7.869	2.101	0.2123
	1	7.622	1.982	-2.572
	2.5	6.928	1.666	0.8393
	10	4.297	0.6971	0.01239
4	0	8.216	2.265	1.36
	0.5	7.905	2.112	0.157
	1	7.611	1.972	-2.567
	2.5	6.817	1.615	1.083
	10	4.307	0.7026	-0.02994
5	0	8.216	2.265	1.36
	0.5	7.905	2.112	0.157
	1	7.611	1.972	-2.567
	2.5	6.817	1.615	1.083
	10	4.307	0.7026	-0.02994

Other models for which likelihoods are calculated:

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

Model A2: $Y_{ij} = Mu(i) + e(ij)$

```
            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	-48.06841	6	108.1368
A2	-34.4889	10	88.97779
A3	-47.19034	7	108.3807
R	-66.97517	2	137.9503
2	-48.7652	4	105.5304
3	-48.7652	4	105.5304
4	-48.71019	5	107.4204
5	-48.71019	5	107.4204

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)
```

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	64.97	8	< 0.0001
Test 2	27.16	4	< 0.0001
Test 3	25.4	3	< 0.0001
Test 4	3.15	3	0.3691
Test 5a	3.15	3	0.3691
Test 5b	-5.684e-013	0	N/A
Test 6a	3.04	2	0.2187
Test 6b	0.11	1	0.7401
Test 7a	3.04	2	0.2187
Test 7b	0.11	1	0.7401
Test 7c	0	0	N/A

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 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.

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

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

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

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

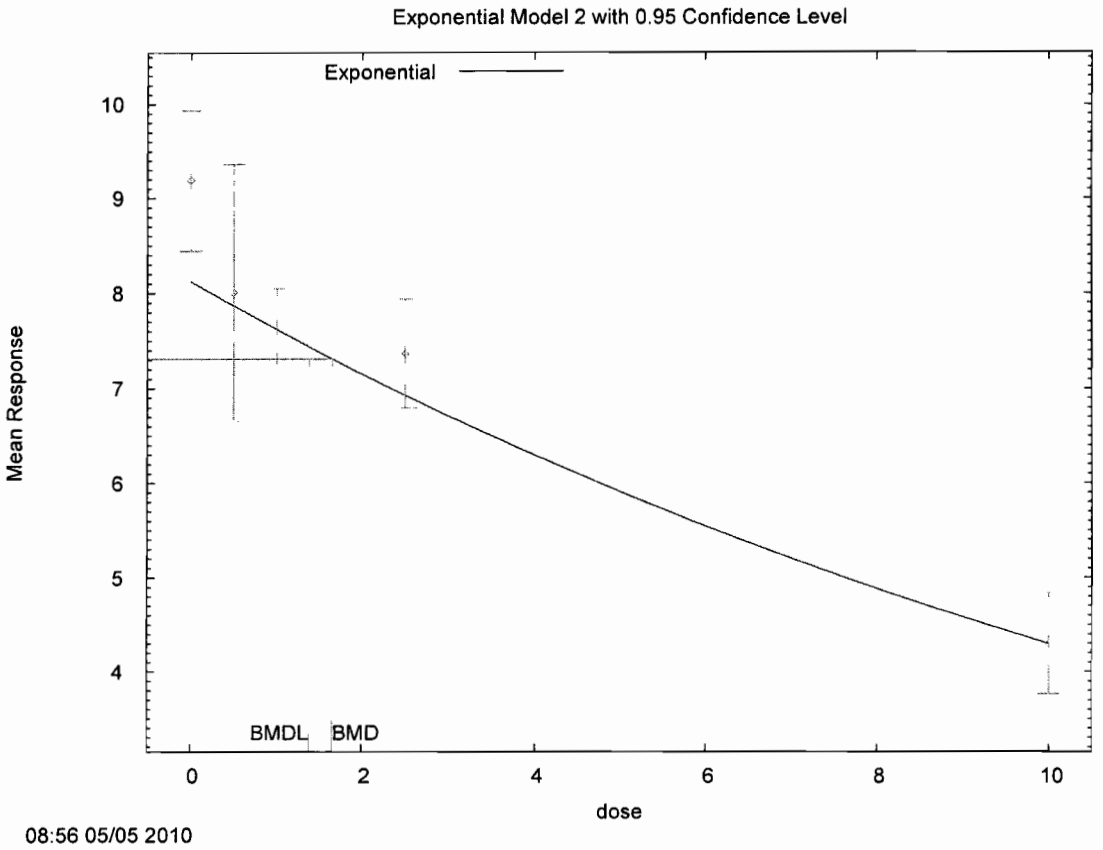
Specified Effect = 0.100000

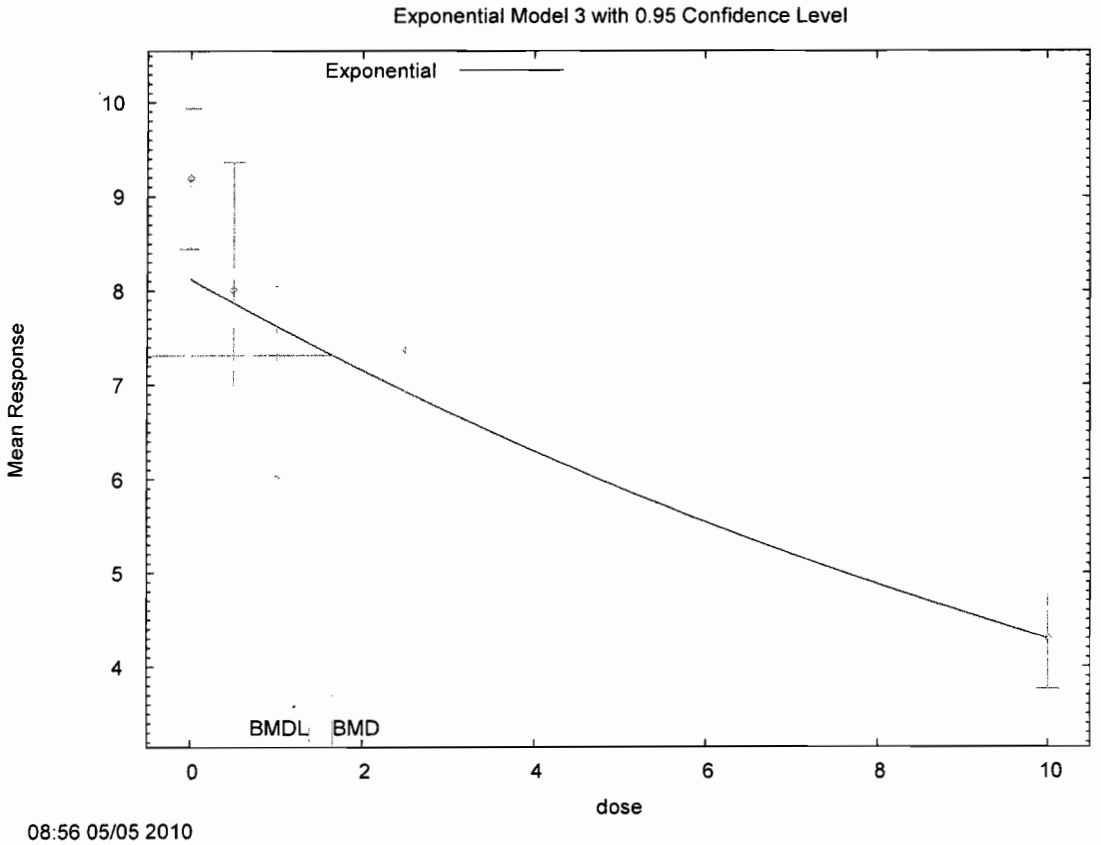
Risk Type = Relative deviation

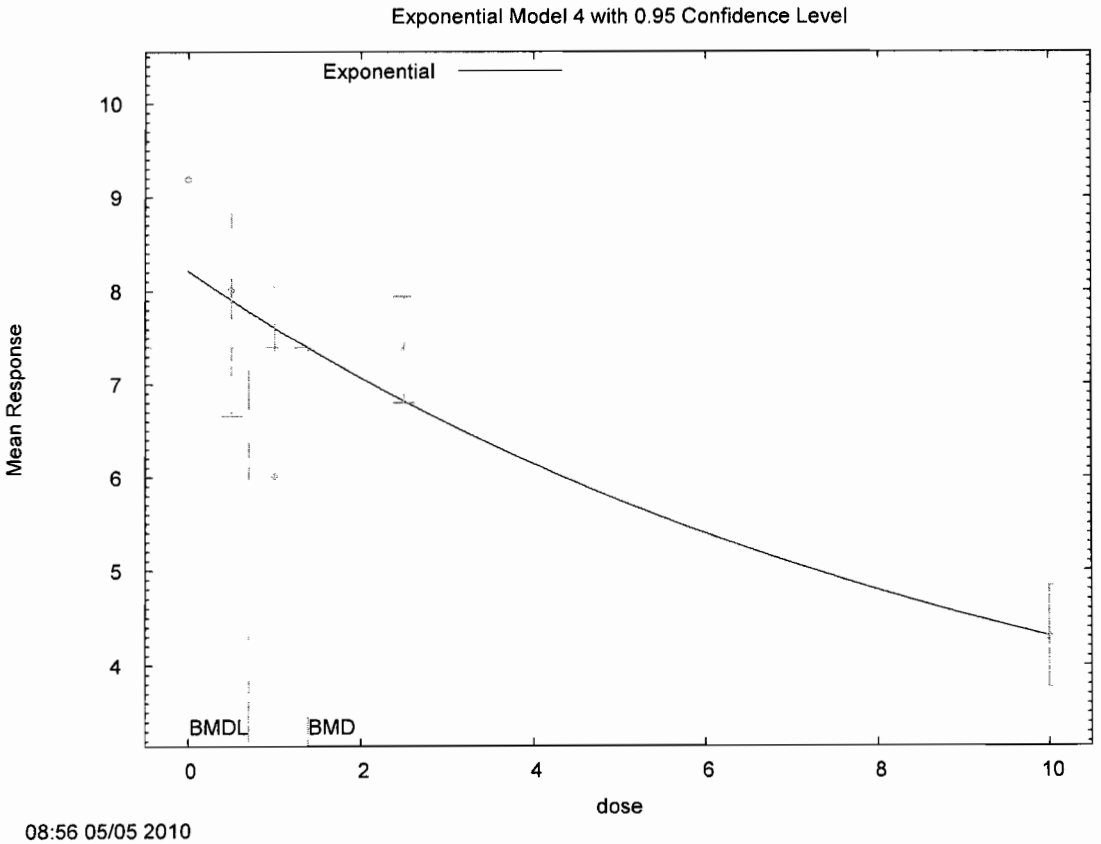
Confidence Level = 0.950000

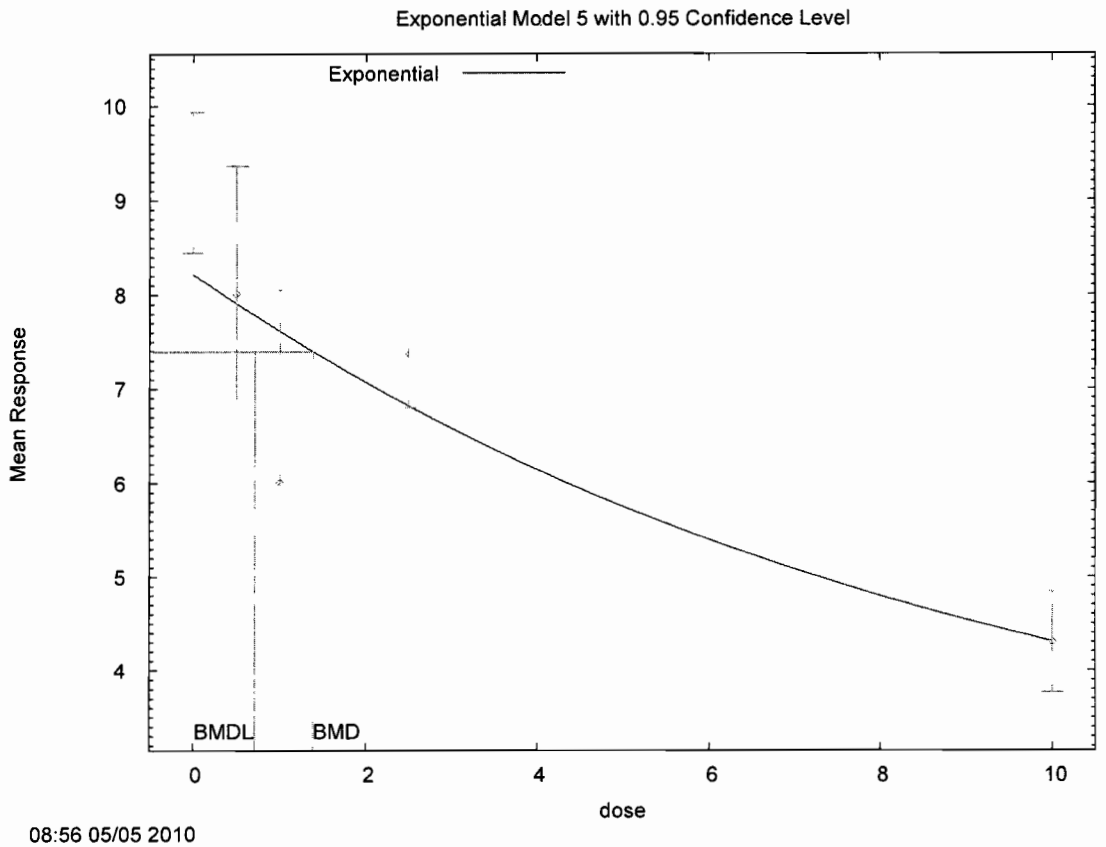
BMD and BMDL by Model

Model	BMD	BMDL
2	1.65457	1.38198
3	1.65457	1.38198
4	1.38589	0.703295
5	1.38589	0.703295


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:56 05/05 2010


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:56 05/05 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
08:56 05/05 2010



Acephate
MRID 46151801
Male RBC ChE

```
==============================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                  Thu May 06 10:07:27 2010
 ==============================================================================

 BMDS Model Run
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   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 = Mean
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 = 250
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	Model 3	Model 4	Model 5
lnalpha	-2.00488	-2.00488	-2.00488	-2.00488
rho(S)	0	0	0	0
a	2.22082	2.22082	2.688	2.688
b	0.00804937	0.00804937	0.136697	0.136697
c	--	--	0.690901	0.690901
d	--	1	--	1

(S) = Specified

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-1.68135	-1.71875	-1.68135	-1.71875
rho	0	0	0	0
a	2.33505	2.3375	2.33505	2.3375
b	0.00804446	0.0851304	0.00804446	0.0952119
c	--	--	0	0.714461
d	--	13.0916	--	13.6387

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.95	0.28
0.5	10	2.49	0.42
1	10	2.35	0.19

2.5	10	2.56	0.53
10	10	2.07	0.42

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2.335	0.4314	-2.822
	0.5	2.326	0.4314	1.204
	1	2.316	0.4314	0.2467
	2.5	2.289	0.4314	1.99
	10	2.155	0.4314	-0.6199
3	0	2.337	0.4234	-2.894
	0.5	2.337	0.4234	1.139
	1	2.337	0.4234	0.09335
	2.5	2.337	0.4234	1.662
	10	2.07	0.4234	-2.504e-008
4	0	2.335	0.4314	-2.822
	0.5	2.326	0.4314	1.204
	1	2.316	0.4314	0.2467
	2.5	2.289	0.4314	1.99
	10	2.155	0.4314	-0.6199
5	0	2.337	0.4234	-2.894
	0.5	2.337	0.4234	1.139
	1	2.337	0.4234	0.09335
	2.5	2.337	0.4234	1.662
	10	2.07	0.4234	-2.137e-008

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	25.12208	6	-38.24417
A2	30.66978	10	-41.33955
A3	25.12208	6	-38.24417
R	16.4211	2	-28.8422
2	17.03382	3	-28.06763
3	17.96863	4	-27.93725
4	17.03382	3	-28.06763
5	17.96863	5	-25.93725

Additive constant for all log-likelihoods = -45.95. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	28.5	8	0.0003884
Test 2	11.1	4	0.02551
Test 3	11.1	4	0.02551
Test 4	16.18	3	0.001043
Test 5a	14.31	2	0.0007822
Test 5b	1.87	1	0.1715
Test 6a	16.18	3	0.001043
Test 6b	-3.553e-014	0	N/A
Test 7a	14.31	1	0.0001553
Test 7b	4.039e-008	1	0.9998
Test 7c	1.87	2	0.3927

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.

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.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

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.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

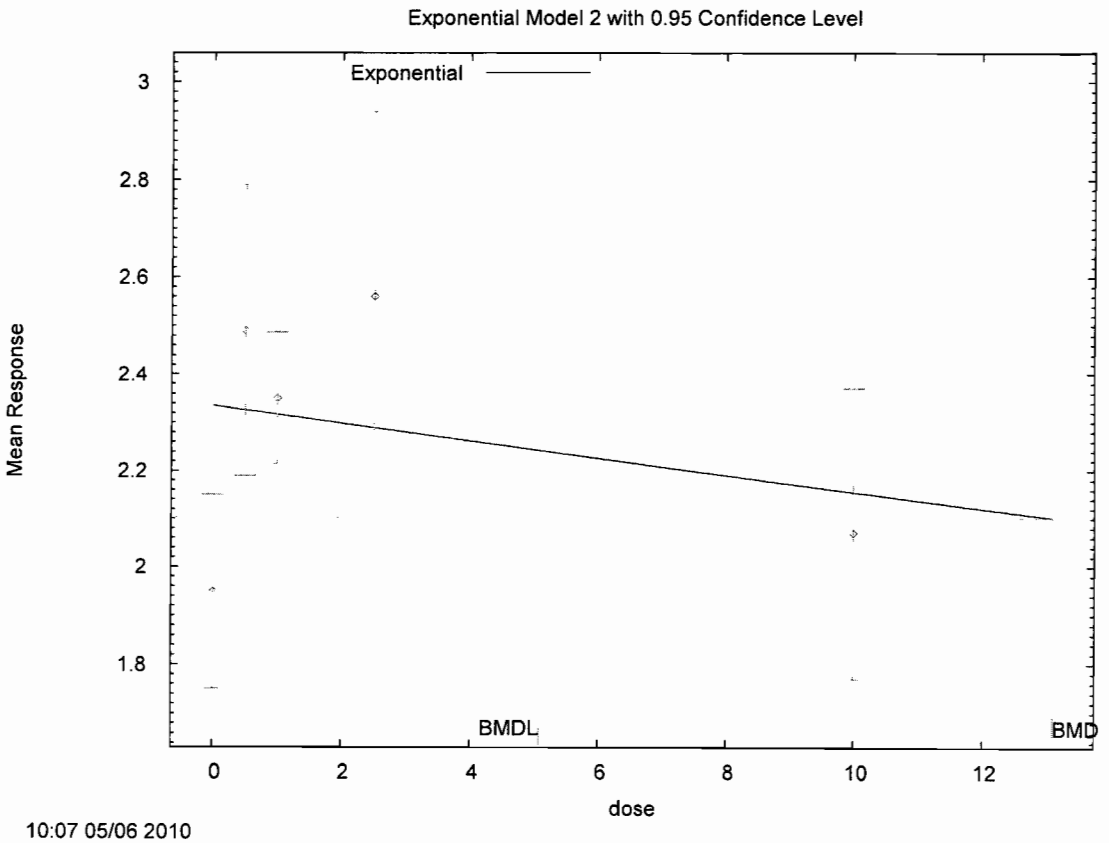
Specified Effect = 0.100000

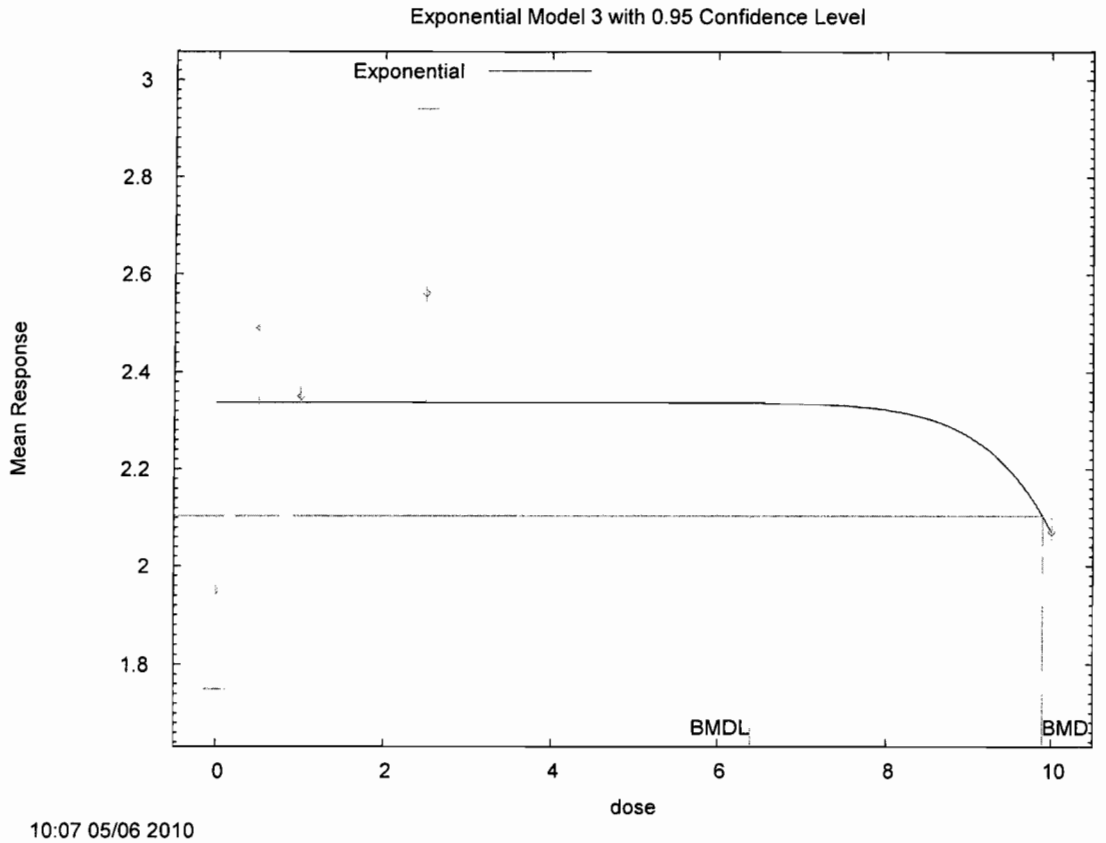
Risk Type = Relative deviation

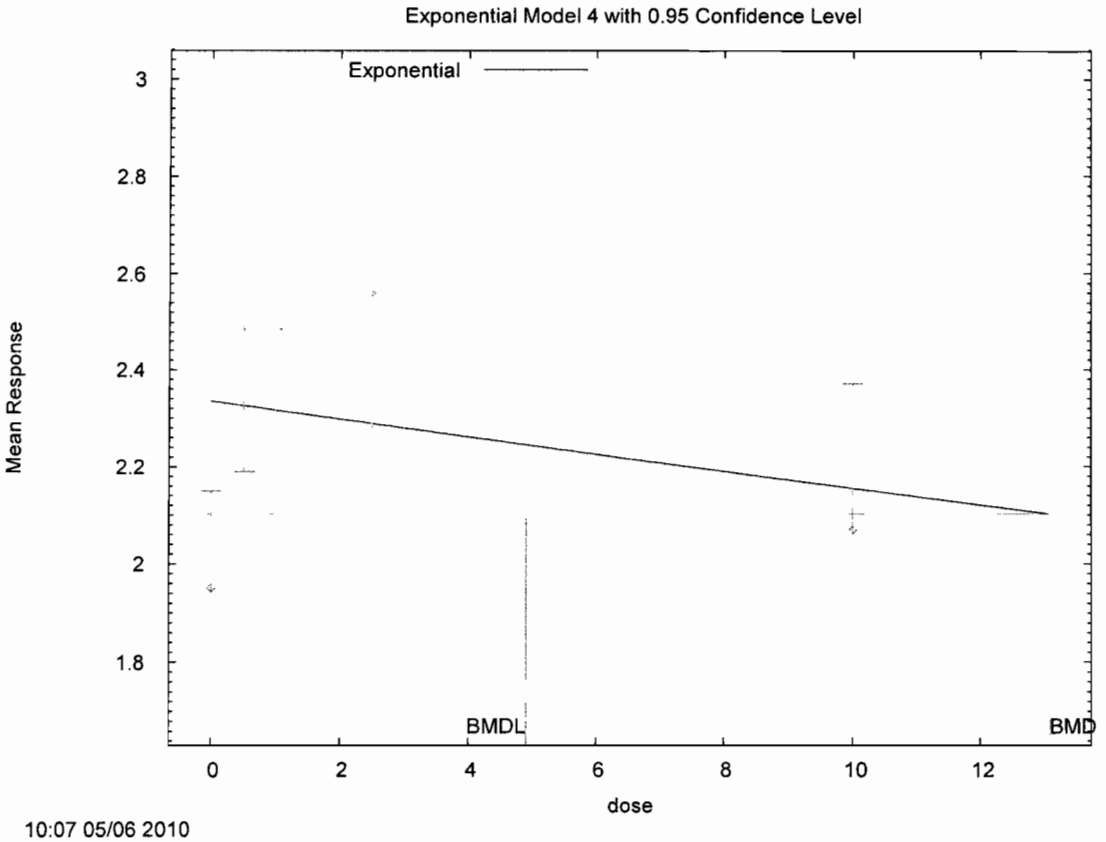
Confidence Level = 0.950000

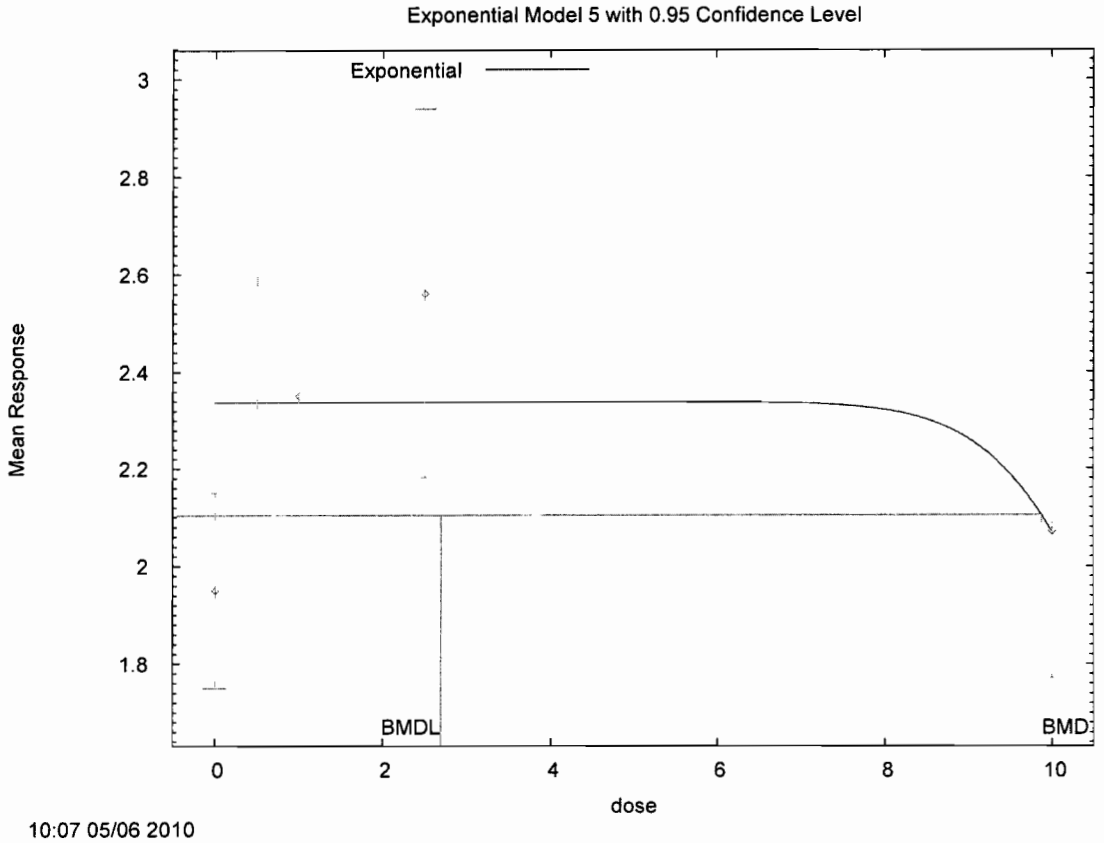
BMD and BMDL by Model

Model	BMD	BMDL
2	13.0973	5.07802
3	9.89151	6.38326
4	13.0973	4.90191
5	9.87453	2.68962




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
10:07 05/06 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
10:07 05/06 2010



Methamidophos; MRID 43025001
Male Brain ChE

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 ================================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                  Mon May 17 12:38:57 2010
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 BMDS Model Run
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   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 = Mean
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 = 4
Total number of records with missing values = 0
Maximum number of iterations = 250
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	Model 3	Model 4	Model 5
lnalpha	-3.94478	-3.94478	-3.94478	-3.94478
rho	1.28991	1.28991	1.28991	1.28991
a	3.62196	3.62196	15.855	15.855
b	0.180037	0.180037	0.524481	0.524481
c	--	--	0.162184	0.162184
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	0.897785	-7.56854	-3.9526	-3.95213
rho	-0.713709	4.48401	1.27891	1.27839
a	14.9343	10.3159	15.1009	15.0866
b	0.392077	0.150242	0.570022	0.569054
c	--	--	0.173225	0.173797
d	--	1	--	1.00762

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	6	15.1	0.6
0.9	6	10.1	0.8
3.3	6	4.5	0.5
9	6	2.7	0.2

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	14.93	0.597	0.6799
	0.9	10.49	0.6771	-1.425
	3.3	4.095	0.9472	1.047
	9	0.4382	2.103	2.635
3	0	10.32	4.254	2.755
	0.9	9.011	3.142	0.849
	3.3	6.283	1.4	-3.121
	9	2.668	0.2052	0.3763
4	0	15.1	0.7864	-0.002733
	0.9	10.09	0.6077	0.0385
	3.3	4.519	0.3636	-0.1274
	9	2.69	0.2609	0.09664
5	0	15.09	0.7855	0.04186
	0.9	10.11	0.6082	-0.04164
	3.3	4.511	0.3631	-0.07325
	9	2.692	0.261	0.0774

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	3.767684	5	2.464631
A2	8.407184	8	-0.8143686
A3	6.569476	6	-1.138953
R	-50.161	2	104.322
2	-10.69912	4	29.39824
3	-20.07085	4	48.14171
4	6.563596	5	-3.127191
5	6.569476	6	-1.138953

Additive constant for all log-likelihoods = -22.05. 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)

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

Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	117.1	6	< 0.0001
Test 2	9.279	3	0.0258
Test 3	3.675	2	0.1592
Test 4	34.54	2	< 0.0001
Test 5a	53.28	2	< 0.0001
Test 5b	-18.74	0	N/A
Test 6a	0.01176	1	0.9136
Test 6b	34.53	1	< 0.0001
Test 7a	-3.446e-011	0	N/A
Test 7b	53.28	2	< 0.0001
Test 7c	0.01176	1	0.9136

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.

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.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

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

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

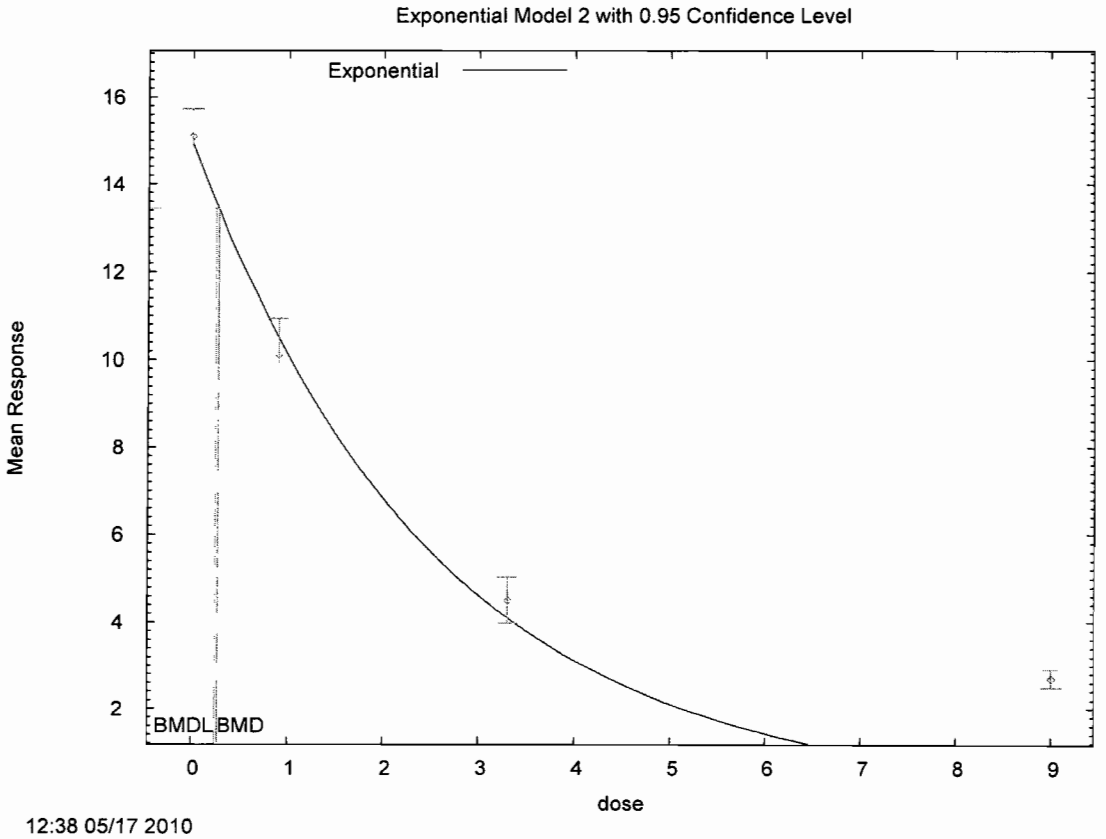
Specified Effect = 0.100000

Risk Type = Relative deviation

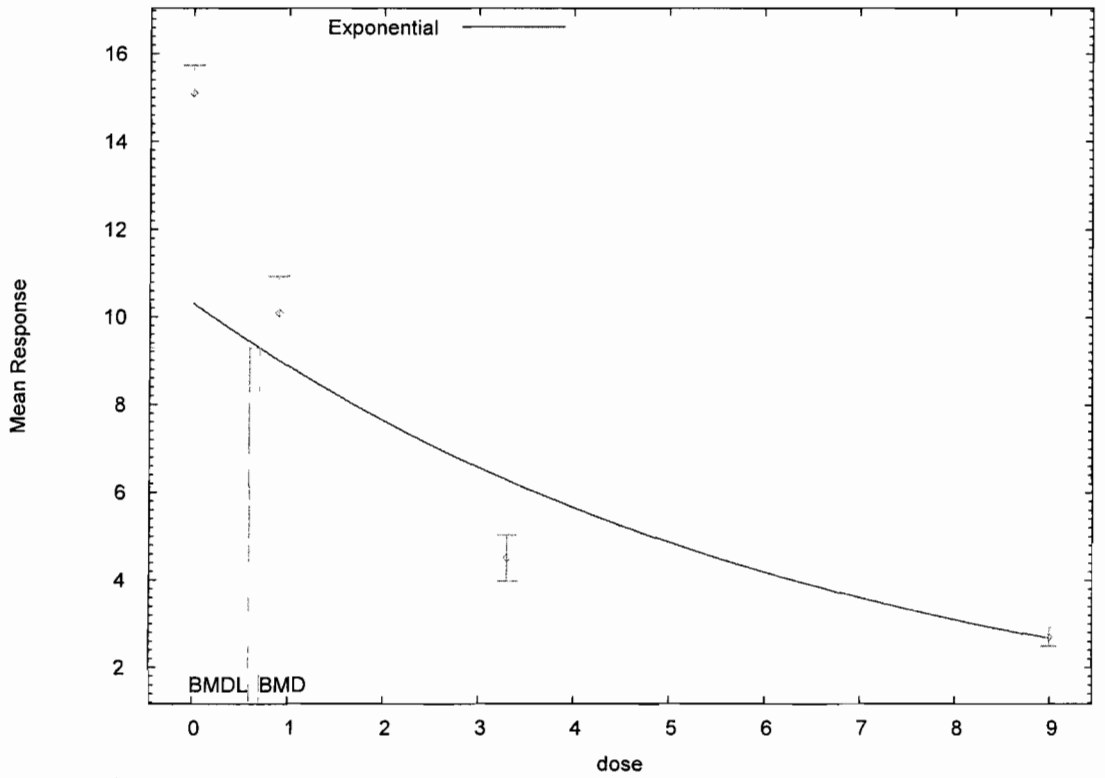
Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	0.268724	0.241661
3	0.701273	0.592691
4	0.226159	0.208557
5	0.23025	0.208596

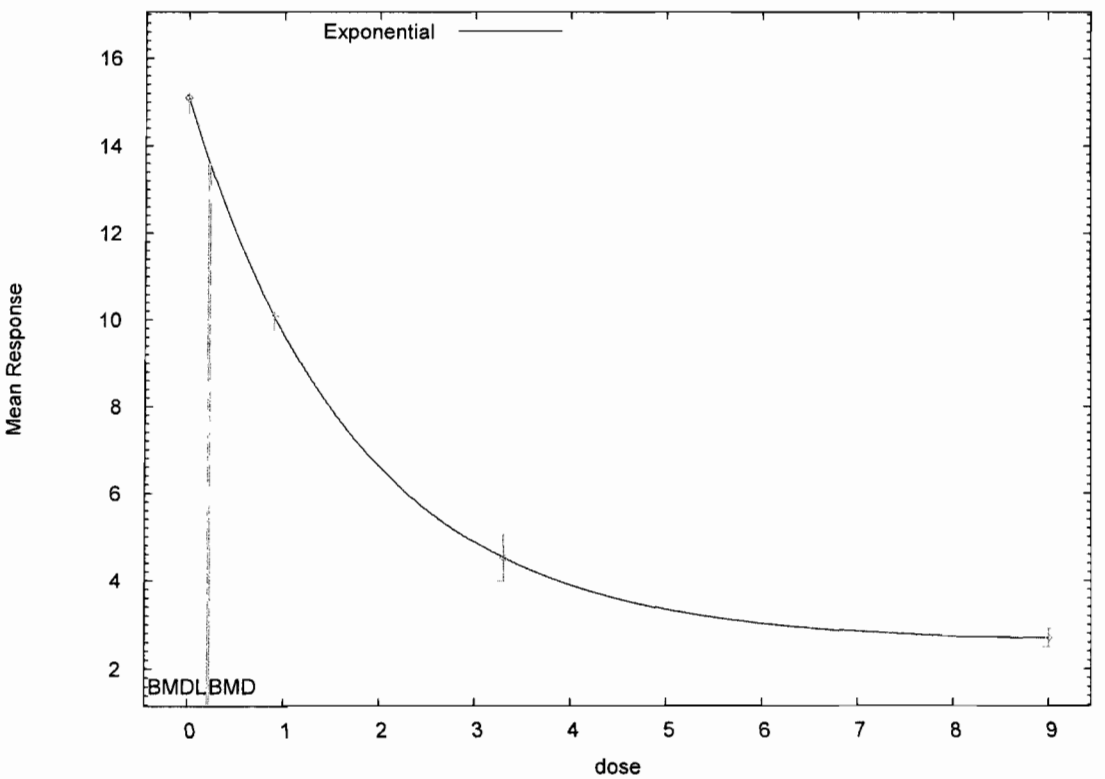


Exponential Model 3 with 0.95 Confidence Level



12:38 05/17 2010

Exponential Model 4 with 0.95 Confidence Level



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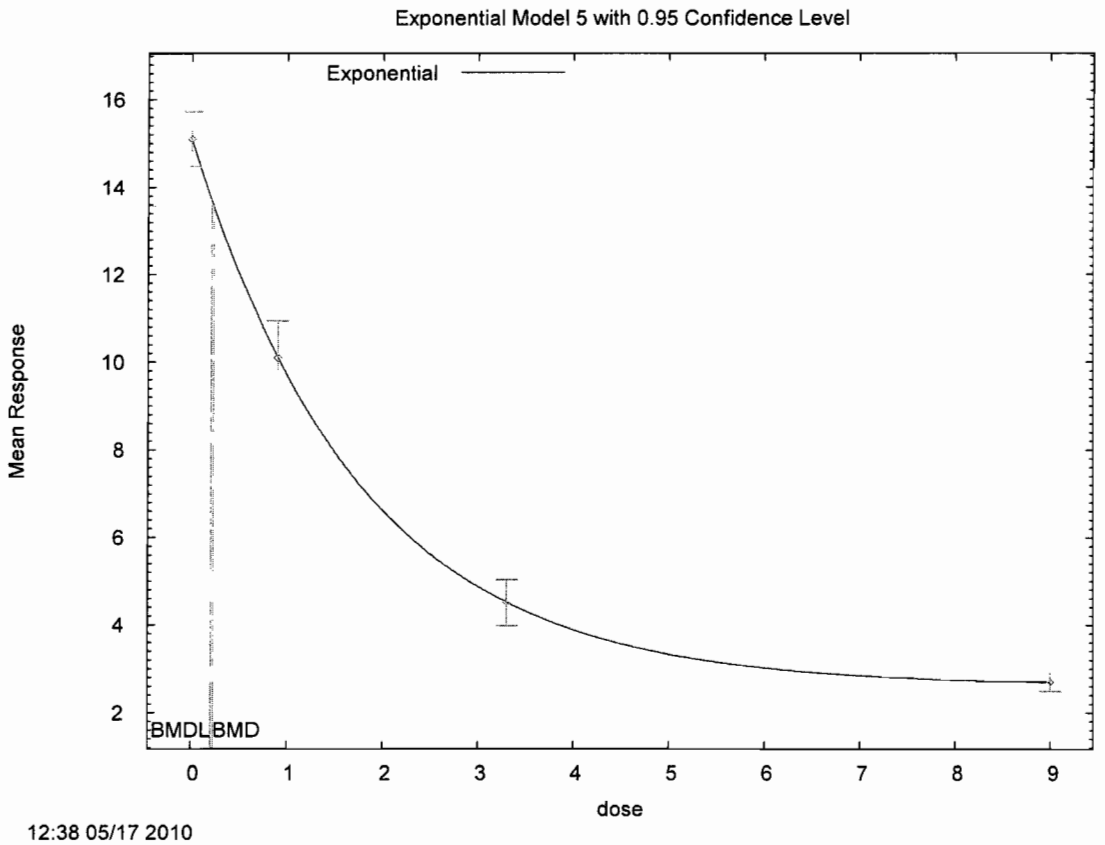

Methamidophos; MRID 46594003
Adult Male Brain ChE

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 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                Mon May 10 11:45:51 2010
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 BMDS Model Run
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   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 = Mean
  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 = 4
  Total number of records with missing values = 0
  Maximum number of iterations = 250
  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	Model 3	Model 4	Model 5
lnalpha	-1.82989	-1.82989	-1.82989	-1.82989
rho	0.470024	0.470024	0.470024	0.470024
a	8.00203	8.00203	12.159	12.159
b	0.359864	0.359864	0.665422	0.665422
c	--	--	0.312114	0.312114
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.659936	-0.42347	-0.659937	-0.686277
rho	0.0129101	-0.0935775	0.0129103	0.011815
a	11.6699	11.6153	11.6699	11.5801
b	0.358493	0.380847	0.358493	1.37083
c	--	--	0	0.616891
d	--	1.07208	--	1.67

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev

0	6	11.58	0.92
0.3	6	10.68	0.81
0.6	6	9.3	0.31
1.2	6	7.59	0.94

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	11.67	0.7304	-0.3015
	0.3	10.48	0.7299	0.6713
	0.6	9.411	0.7294	-0.3739
	1.2	7.59	0.7284	0.0002693
3	0	11.62	0.7215	-0.1198
	0.3	10.53	0.7248	0.4935
	0.6	9.458	0.7284	-0.5319
	1.2	7.541	0.7362	0.1623
4	0	11.67	0.7304	-0.3015
	0.3	10.48	0.7299	0.6713
	0.6	9.411	0.7294	-0.3739
	1.2	7.59	0.7284	0.0002692
5	0	11.58	0.7199	-0.0003249
	0.3	10.68	0.7195	-5.47e-005
	0.6	9.3	0.7189	0.0009453
	1.2	7.59	0.7181	-0.0005859

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	-4.086352	5	18.1727
A2	-0.6491752	8	17.29835
A3	-4.086324	6	20.17265
R	-24.29612	2	52.59223
2	-4.43225	4	16.8645
3	-4.370936	5	18.74187
4	-4.43225	4	16.8645
5	-4.086324	6	20.17265

Additive constant for all log-likelihoods = -22.05. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	47.29	6	< 0.0001
Test 2	6.874	3	0.07601
Test 3	6.874	2	0.03216
Test 4	0.6919	2	0.7076
Test 5a	0.5692	1	0.4506
Test 5b	0.1226	1	0.7262
Test 6a	0.6919	2	0.7076
Test 6b	3.73e-014	0	N/A
Test 7a	-2.508e-012	0	N/A
Test 7b	0.5692	1	0.4506
Test 7c	0.6919	2	0.7076

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 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.

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

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

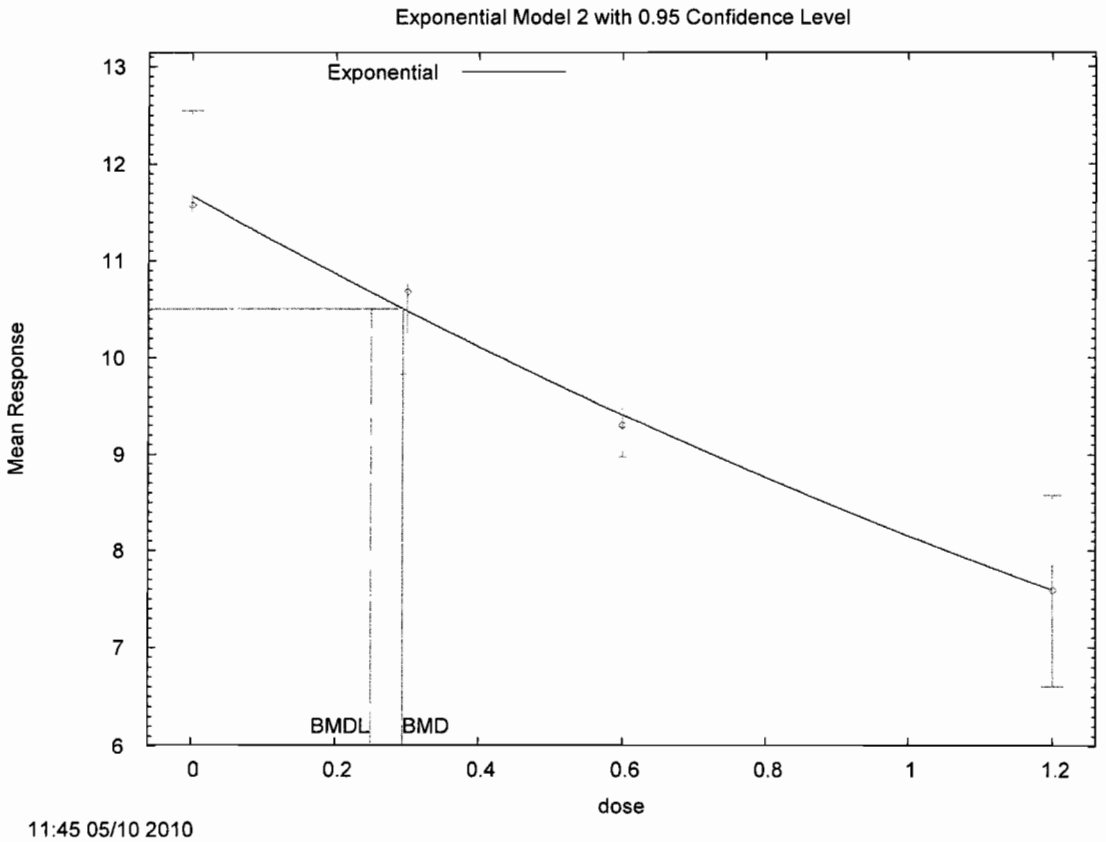
Specified Effect = 0.100000

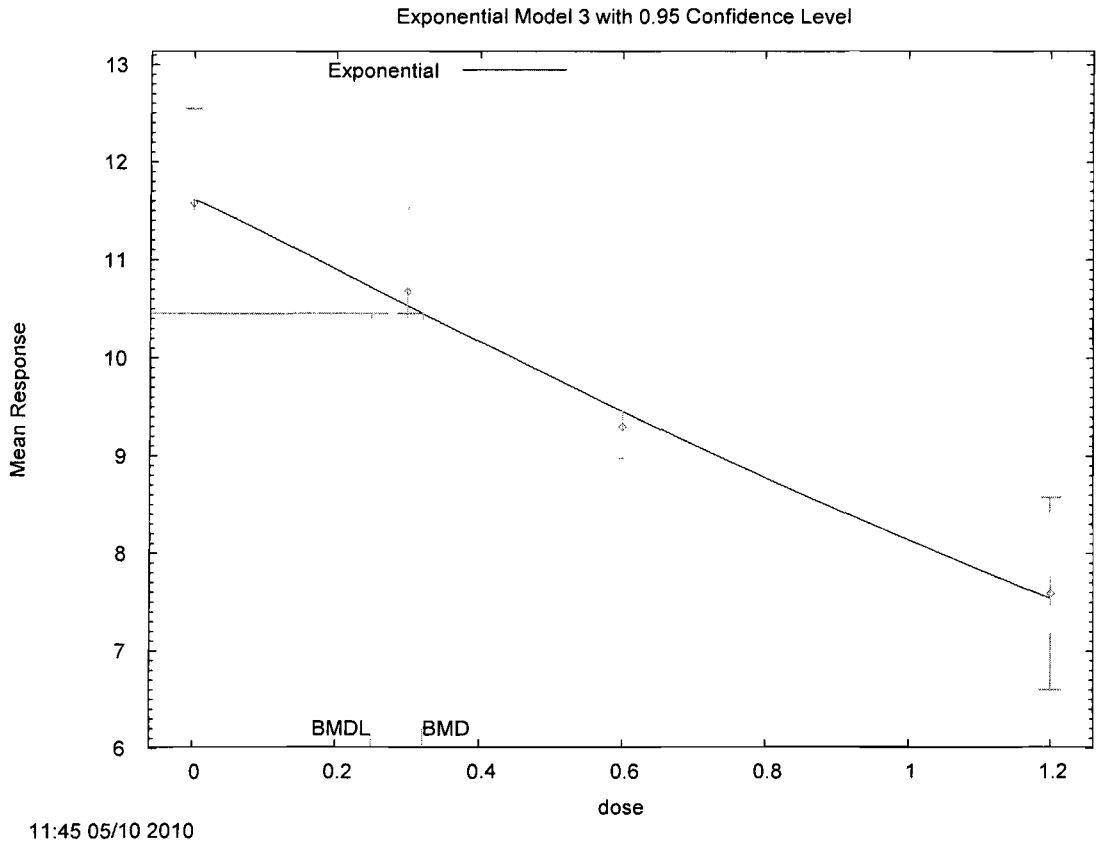
Risk Type = Relative deviation

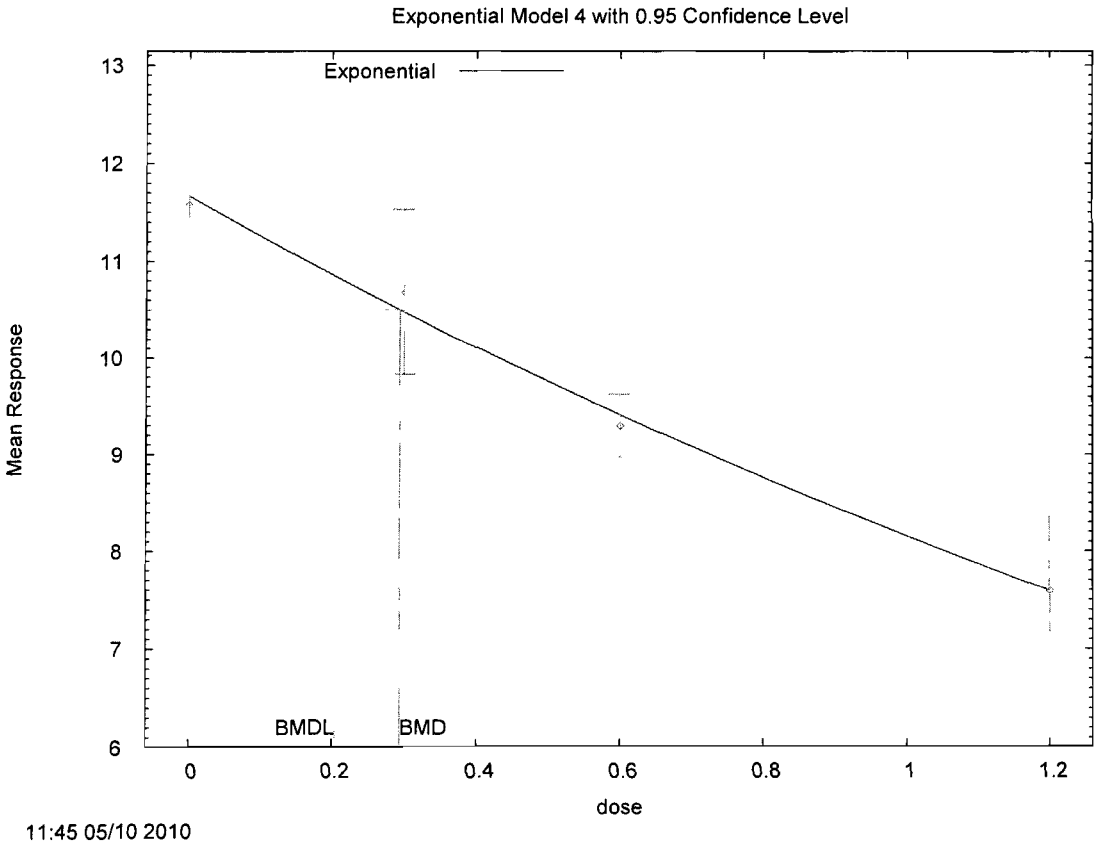
Confidence Level = 0.950000

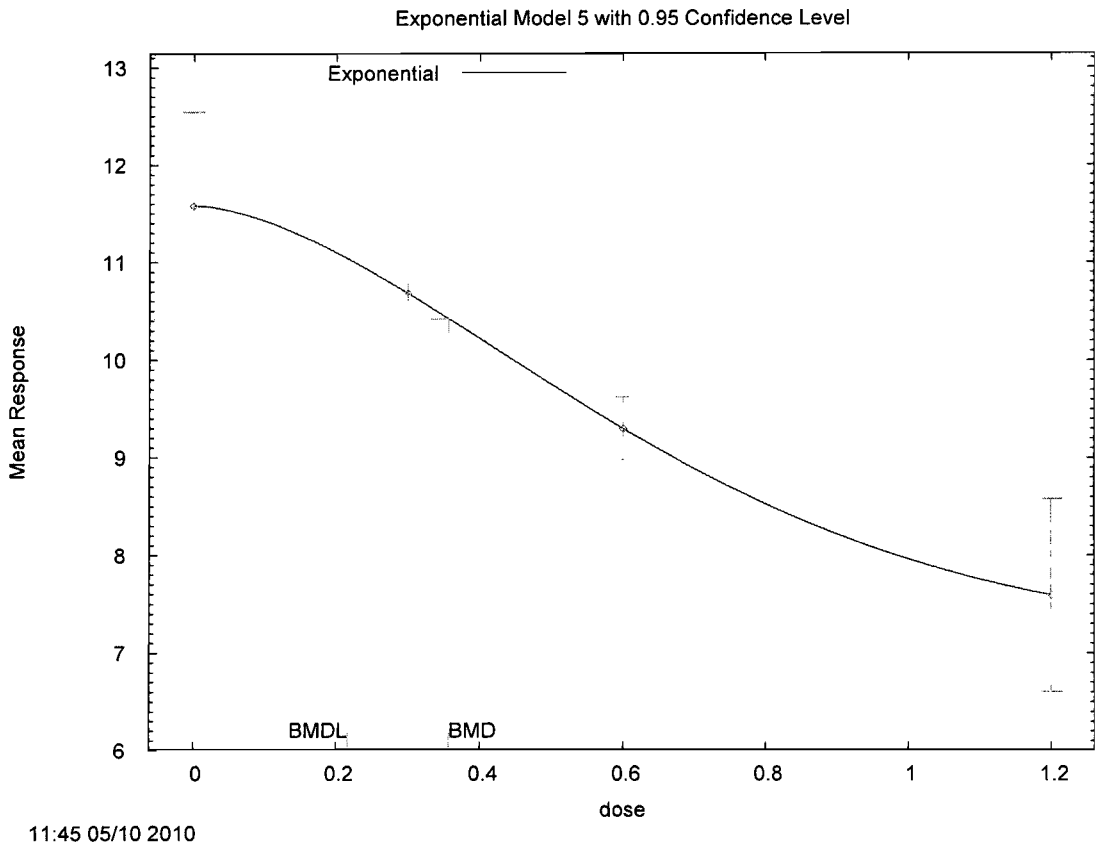
BMD and BMDL by Model

Model	BMD	BMDL
2	0.293899	0.249326
3	0.321838	0.250261
4	0.293899	0.204274
5	0.356502	0.216039




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
13
12
11
10
9
8
7
6
BMDL
BMD
0
0.2
0.4
0.6
0.8
1
1.2
dose
11:45 05/10 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
13
12
11
10
9
8
7
6
BMDL
BMD
0
0.2
0.4
0.6
0.8
1
1.2
dose
11:45 05/10 2010



Methamidophos; MRID 46594003
Pup Male Brain ChE

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        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Tue May 11 12:34:02 2010
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 BMDS Model Run
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   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 = Mean
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 = 4
Total number of records with missing values = 0
Maximum number of iterations = 250
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	Model 3	Model 4	Model 5
lnalpha	-9.58899	-9.58899	-9.58899	-9.58899
rho	4.0595	4.0595	4.0595	4.0595
a	4.56642	4.56642	6.111	6.111
b	0.748572	0.748572	0.883176	0.883176
c	--	--	0.0357552	0.0357552
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-10.2992	-10.7815	-10.2992	-9.36951
rho	4.65271	4.90347	4.65271	4.03617
a	5.95389	5.82961	5.95389	5.81087
b	0.764802	0.98288	0.764802	3.77943
c	--	--	0	0.727142
d	--	1.32336	--	2.16856

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	5.82	0.293
0.1	10	5.65	0.196
0.2	10	5.11	0.409
0.4	10	4.37	0.131

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	5.954	0.3681	-1.15
	0.1	5.516	0.3081	1.38
	0.2	5.109	0.2579	0.007219
	0.4	4.385	0.1807	-0.2575
3	0	5.83	0.3435	-0.08847
	0.1	5.565	0.3066	0.8749
	0.2	5.19	0.2584	-0.9821
	0.4	4.359	0.1684	0.2066
4	0	5.954	0.3681	-1.15
	0.1	5.516	0.3081	1.38
	0.2	5.109	0.2579	0.007219
	0.4	4.385	0.1807	-0.2575
5	0	5.811	0.3219	0.08966
	0.1	5.63	0.302	0.211
	0.2	5.145	0.2518	-0.4353
	0.4	4.362	0.1805	0.1383

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	33.34035	5	-56.6807
A2	39.94542	8	-63.89085
A3	34.22224	6	-56.44449
R	-1.117912	2	6.235824
2	32.42609	4	-56.85217
3	33.85266	5	-57.70533
4	32.42609	4	-56.85217
5	34.22224	6	-56.44449

Additive constant for all log-likelihoods = -36.76. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	82.13	6	< 0.0001
Test 2	13.21	3	0.004204
Test 3	11.45	2	0.003269
Test 4	3.592	2	0.1659
Test 5a	0.7392	1	0.3899
Test 5b	2.853	1	0.09119
Test 6a	3.592	2	0.1659
Test 6b	0	0	N/A
Test 7a	0	0	N/A
Test 7b	0.7392	1	0.3899
Test 7c	3.592	2	0.1659

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 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.

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

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

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

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

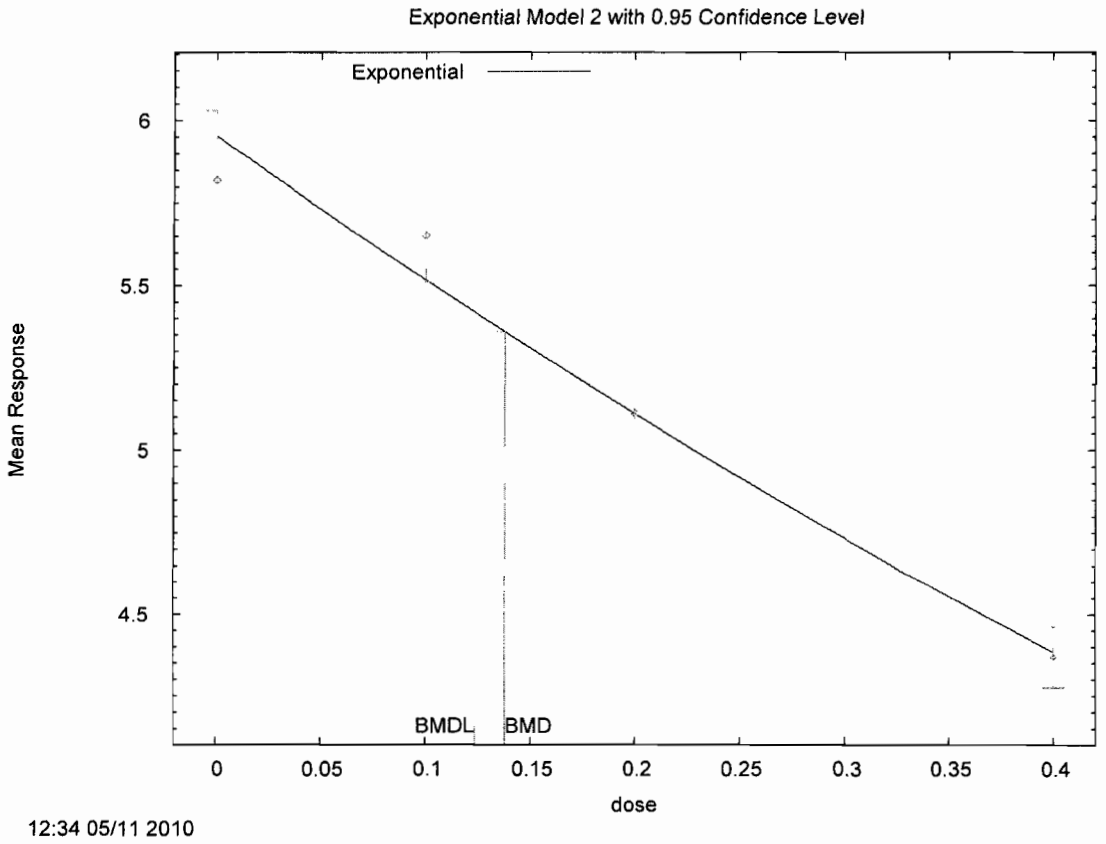
Specified Effect = 0.100000

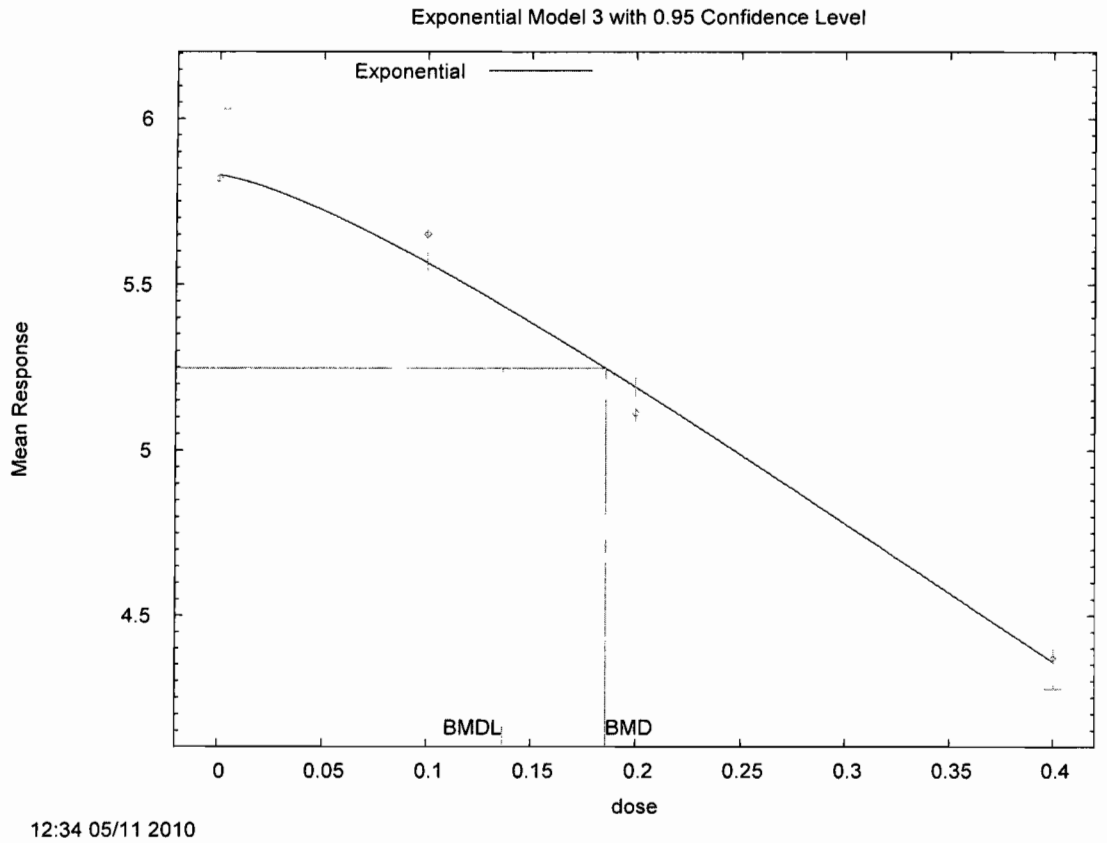
Risk Type = Relative deviation

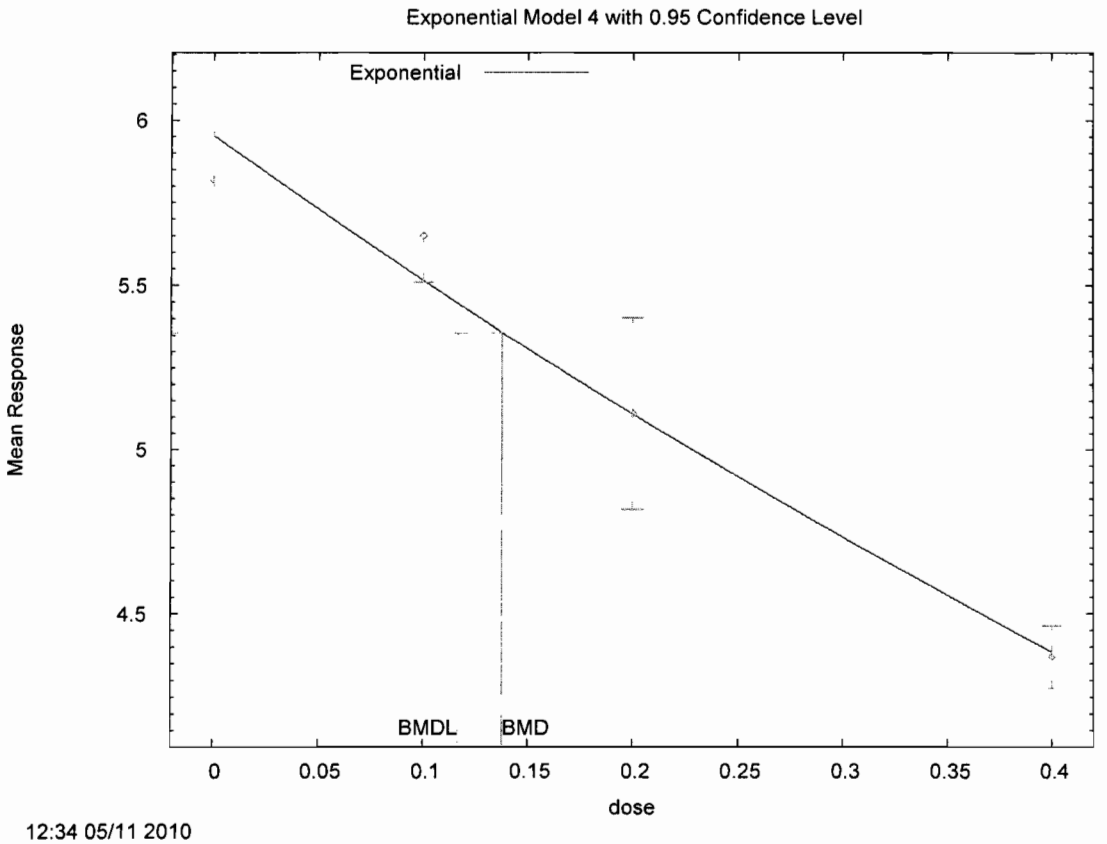
Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	0.137762	0.123473
3	0.185773	0.136508
4	0.137762	0.116722
5	0.184299	0.142706




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
6
5.5
5
4.5
BMDL
BMD
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
dose
12:34 05/11 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
6
5.5
5
4.5
BMDL
BMD
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
dose
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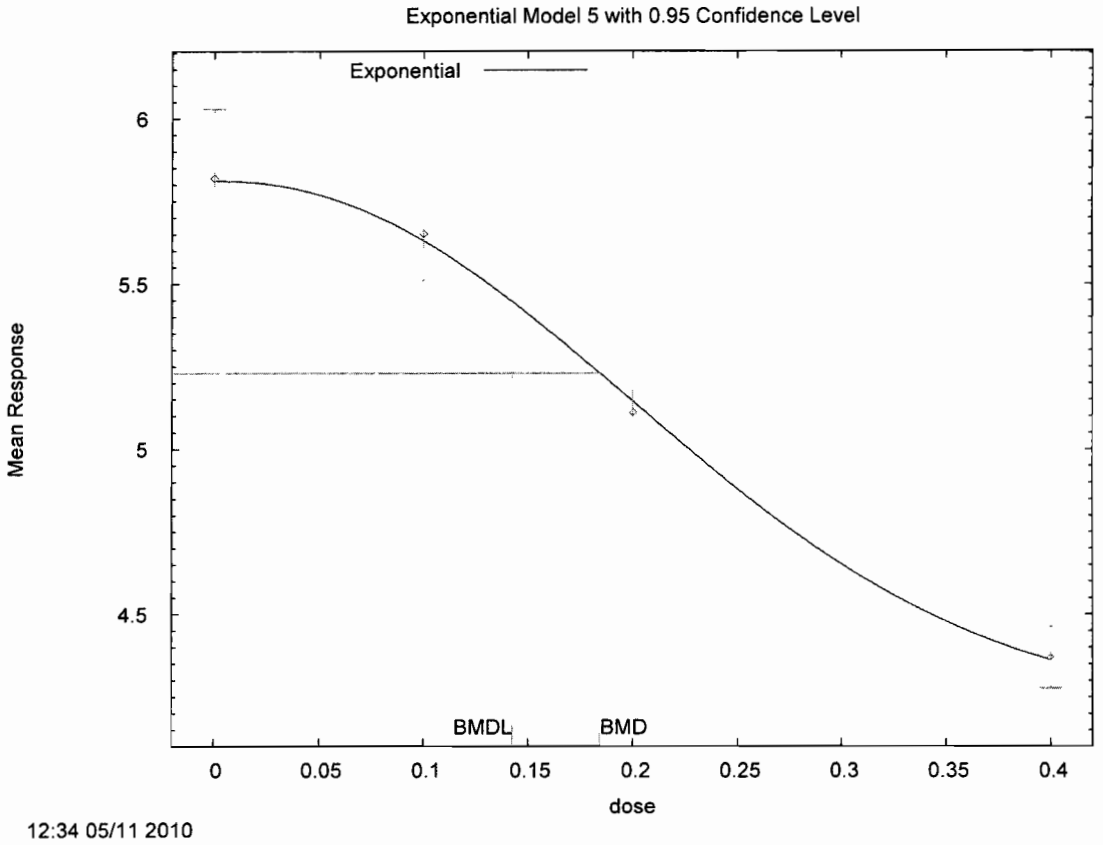


Methamidophos; MRID 46594003
Pup Female Brain ChE

```
 ================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Tue May 11 13:02:10 2010
 ================================================================

 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 = Mean
   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 = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   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	Model 3	Model 4	Model 5
lnalpha	-5.16111	-5.16111	-5.16111	-5.16111
rho	1.82977	1.82977	1.82977	1.82977
a	4.49747	4.49747	6.174	6.174
b	0.864179	0.864179	0.912821	0.912821
c	--	--	0.000683511	0.000683511
d	--	1	--	1

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-6.311	-5.96168	-6.311	-6.2369
rho	2.63667	2.32678	2.63667	2.48497
a	6.10263	5.89787	6.10263	5.86351
b	0.877212	1.2799	0.877212	3.78443
c	--	--	0	0.709514
d	--	1.62996	--	2.89803

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	5.88	0.299
0.1	10	5.74	0.543
0.2	10	5.26	0.299
0.4	10	4.22	0.289

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.103	0.4625	-1.522
	0.1	5.59	0.412	1.15
	0.2	5.121	0.367	1.201
	0.4	4.297	0.2912	-0.8322
3	0	5.898	0.4	-0.1413
	0.1	5.695	0.384	0.3729
	0.2	5.291	0.3526	-0.2824
	0.4	4.216	0.2706	0.05086
4	0	6.103	0.4625	-1.522
	0.1	5.59	0.412	1.15
	0.2	5.121	0.367	1.201
	0.4	4.297	0.2912	-0.8322
5	0	5.864	0.3982	0.131
	0.1	5.765	0.3899	-0.1993
	0.2	5.251	0.3471	0.08614
	0.4	4.221	0.2647	-0.01789

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	21.53072	5	-33.06145
A2	24.77319	8	-33.54638
A3	22.49798	6	-32.99597
R	-8.015557	2	20.03111
2	18.93527	4	-29.87055
3	22.22825	5	-34.4565
4	18.93527	4	-29.87055
5	22.49798	6	-32.99597

Additive constant for all log-likelihoods = -36.76. 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)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	65.58	6	< 0.0001
Test 2	6.485	3	0.09026
Test 3	4.55	2	0.1028
Test 4	7.125	2	0.02836
Test 5a	0.5395	1	0.4627
Test 5b	6.586	1	0.01028
Test 6a	7.125	2	0.02836
Test 6b	1.421e-014	0	N/A
Test 7a	-7.105e-015	0	N/A
Test 7b	0.5395	1	0.4627
Test 7c	7.125	2	0.02836

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.

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

The p-value for Test 5b is less than .05. Model 3 appears to fit the data better than Model 2.

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.

Degrees of freedom for Test 6b are less than or equal to 0.
The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is less than .05. Model 5 appears to fit the data better than Model 4.

Benchmark Dose Computations:

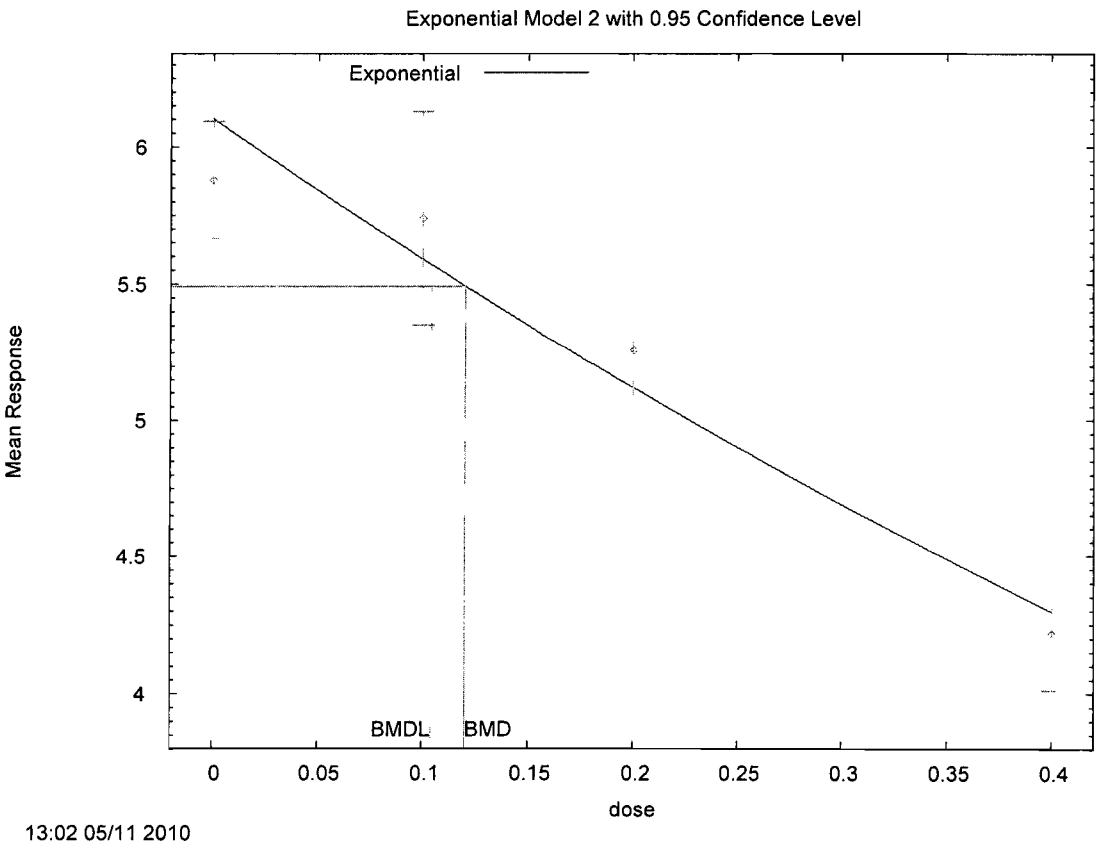
Specified Effect = 0.100000

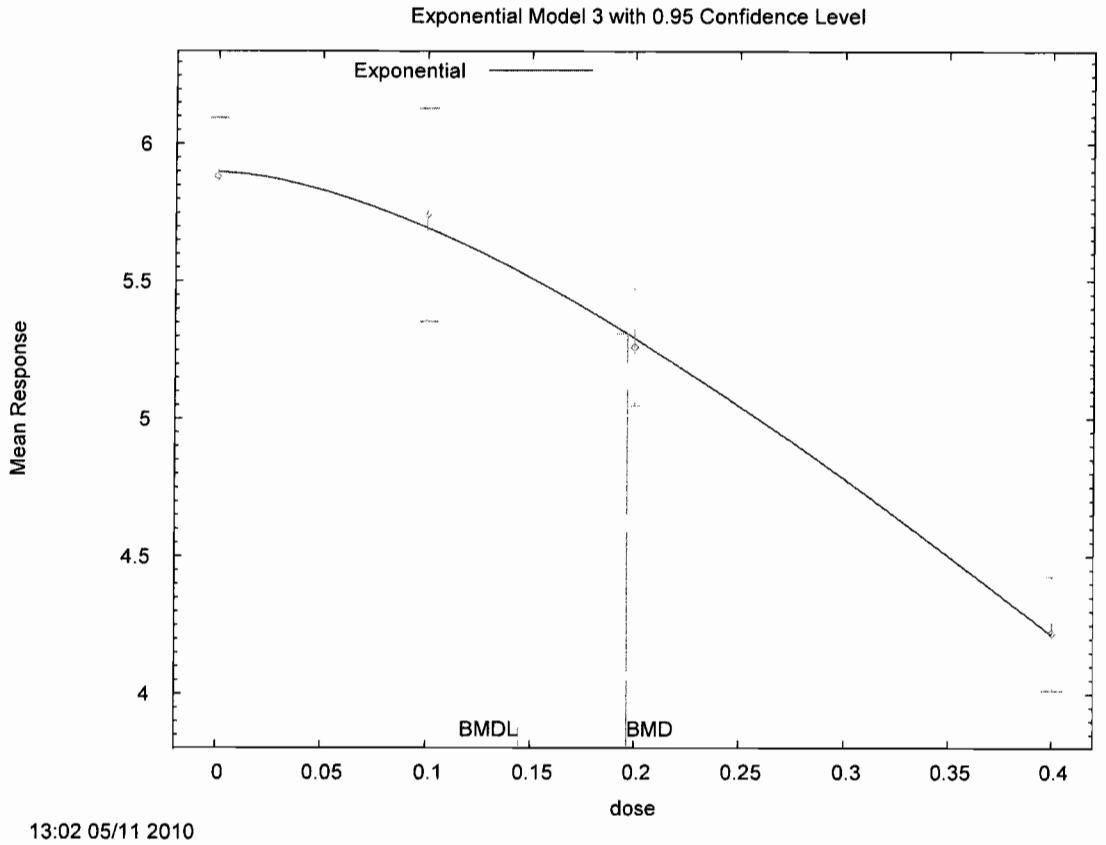
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	0.120108	0.104143
3	0.196438	0.144398
4	0.120108	0.101836
5	0.196201	0.149676




Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
6
5.5
5
4.5
4
BMDL
BMD
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0.05
0.1
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0.2
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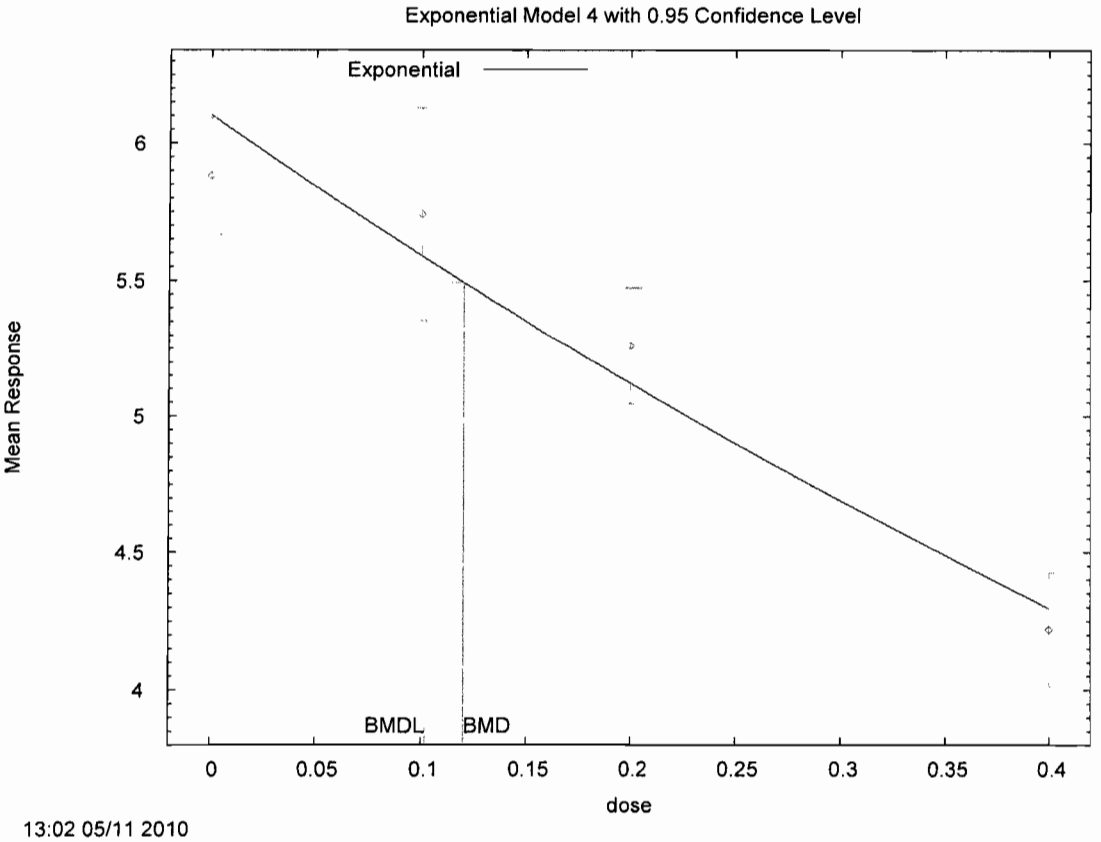
0.3
0.35
0.4
dose
13:02 05/11 2010


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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5.5
5
4.5
4
BMDL
BMD
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0.1
0.15
0.2
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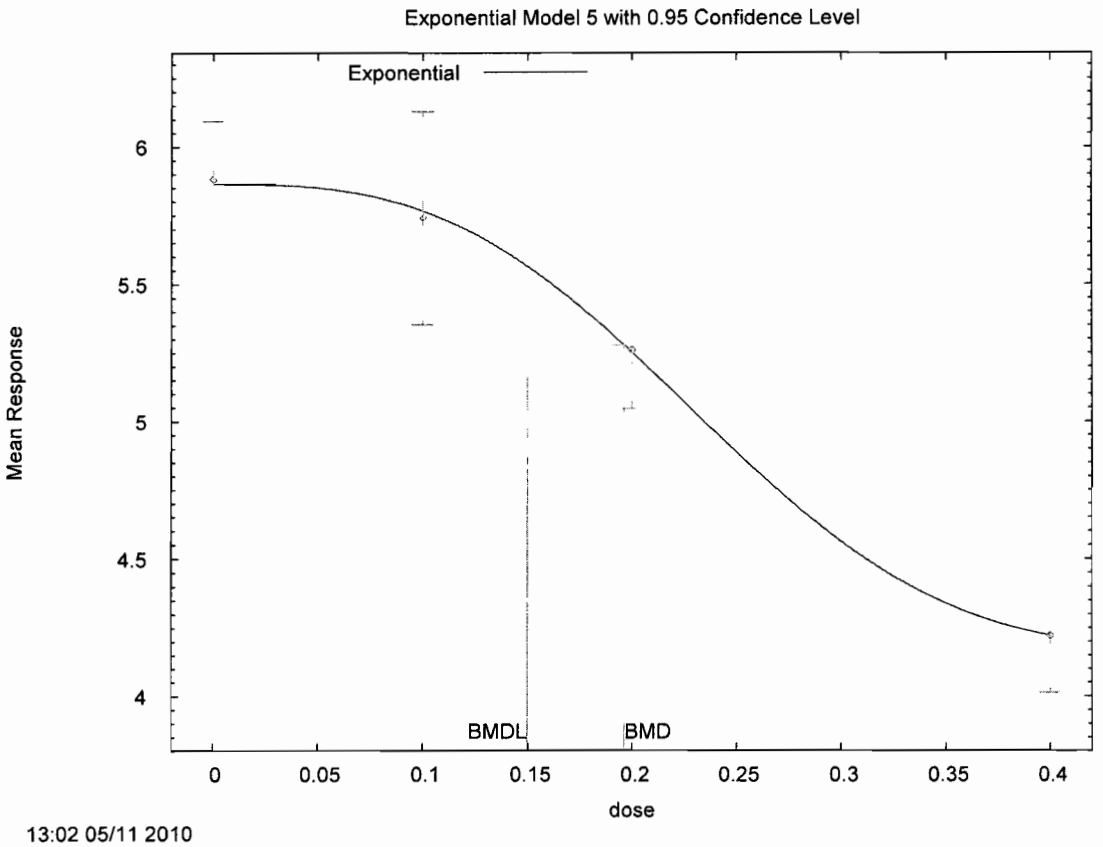
0.3
0.35
0.4
dose
13:02 05/11 2010


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
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5
4.5
4
BMDL
BMD
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0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
dose
13:02 05/11 2010

13544

R189123

Chemical Name: Acephate

PC Code: 103301
HED File Code: 13000 Tox Reviews
Memo Date: 9/9/2010
File ID: 00000000
Accession #: 000-00-0137

HED Records Reference Center
12/30/2010