T

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

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

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

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	**DP Barcode:** D383706
Decision No.: 440319	**Registration No.:** NA
Petition No.: NA	**Regulatory Action:** NA
Risk Assessment Type: NA	**Case No.:** NA
TXR No.: 0055521	**CAS No.:** NA
MRID No.: NA	**40 CFR:** NA

FROM: John Liccione
Toxicologist/Risk Assessor
RABV
Health Effects Division (7905P)

THROUGH: Jack Arthur
Branch Chief
RABV
Health Effects Division (7905P)

TO: Michael Metzger
Branch Chief
RABVII
Health Effects Division (7905P)

[illegible] RRC
12/29/[illegible]

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

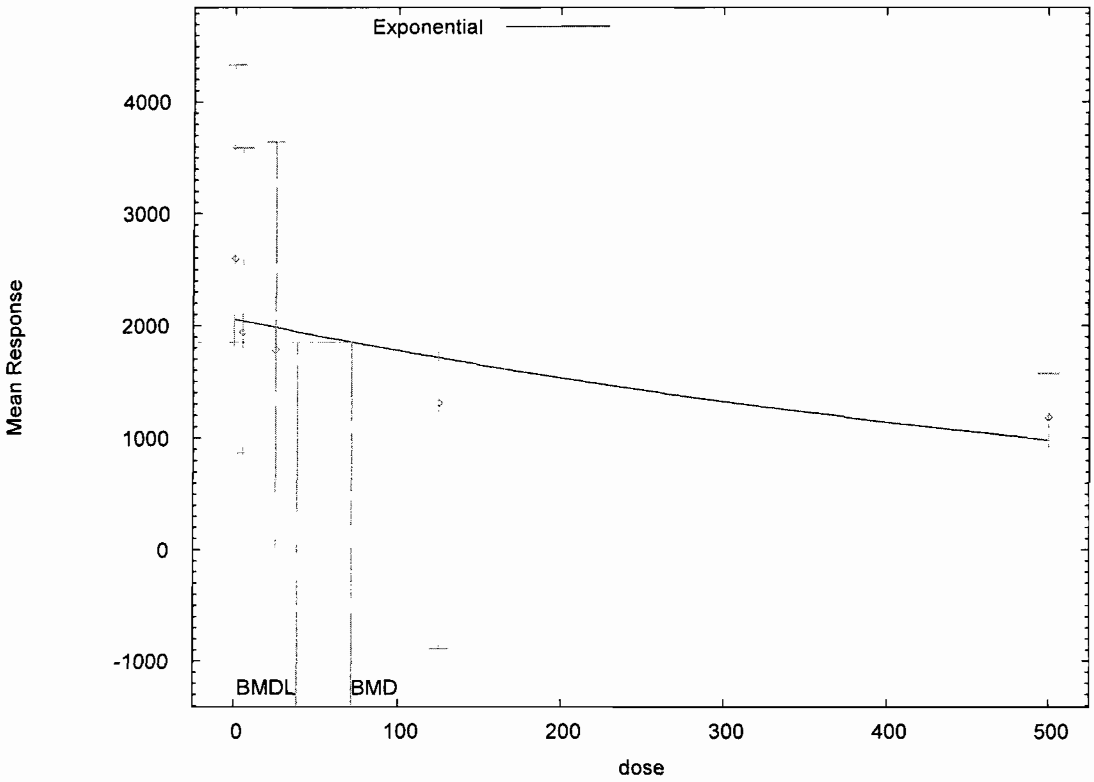
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                            Tue May 25 08:57:51 2010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

 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
```

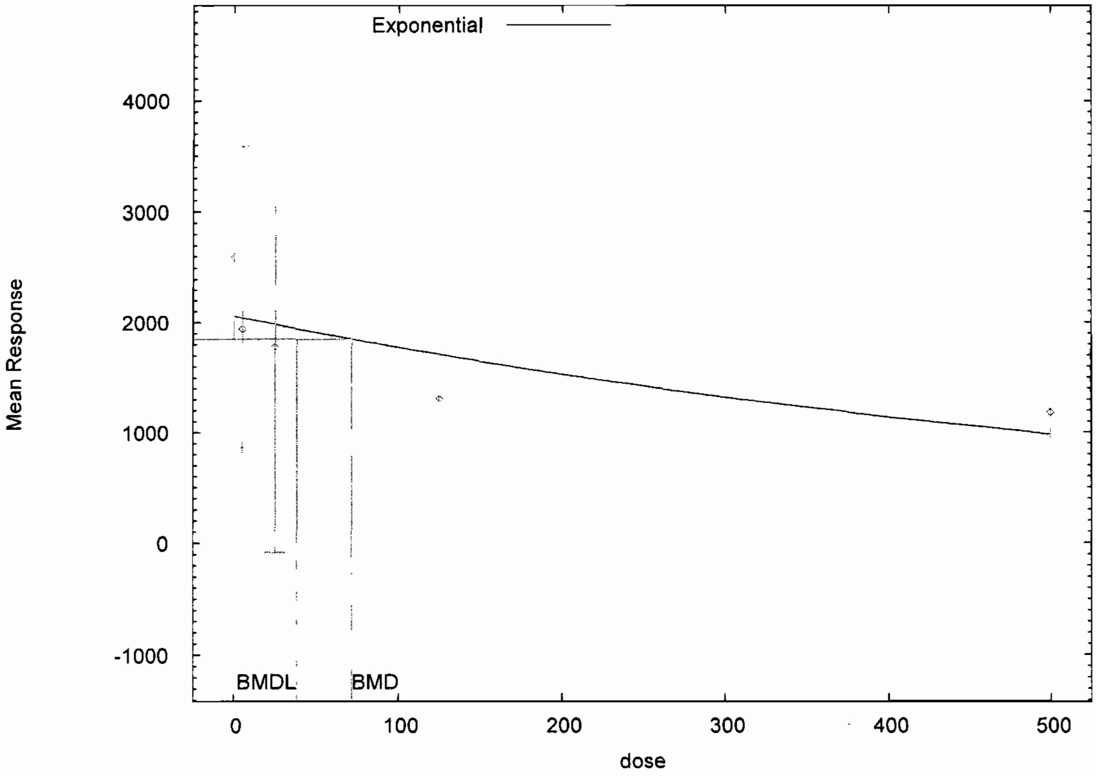
```
   Test 6a                        8.65          2         0.01324
   Test 6b                       11.09          1       0.0008668
   Test 7a                        8.65          2         0.01324
   Test 7b                       11.09          1       0.0008668
   Test 7c                  -5.684e-014          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



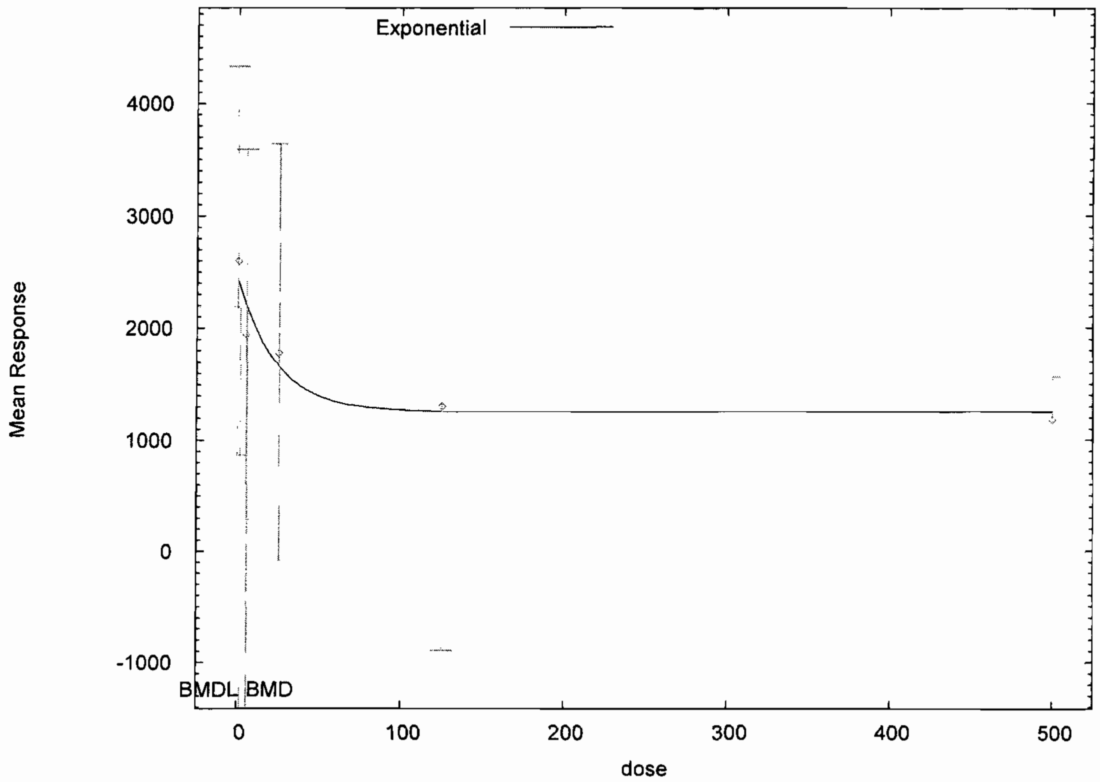
08:57 05/25 2010

Exponential Model 3 with 0.95 Confidence Level



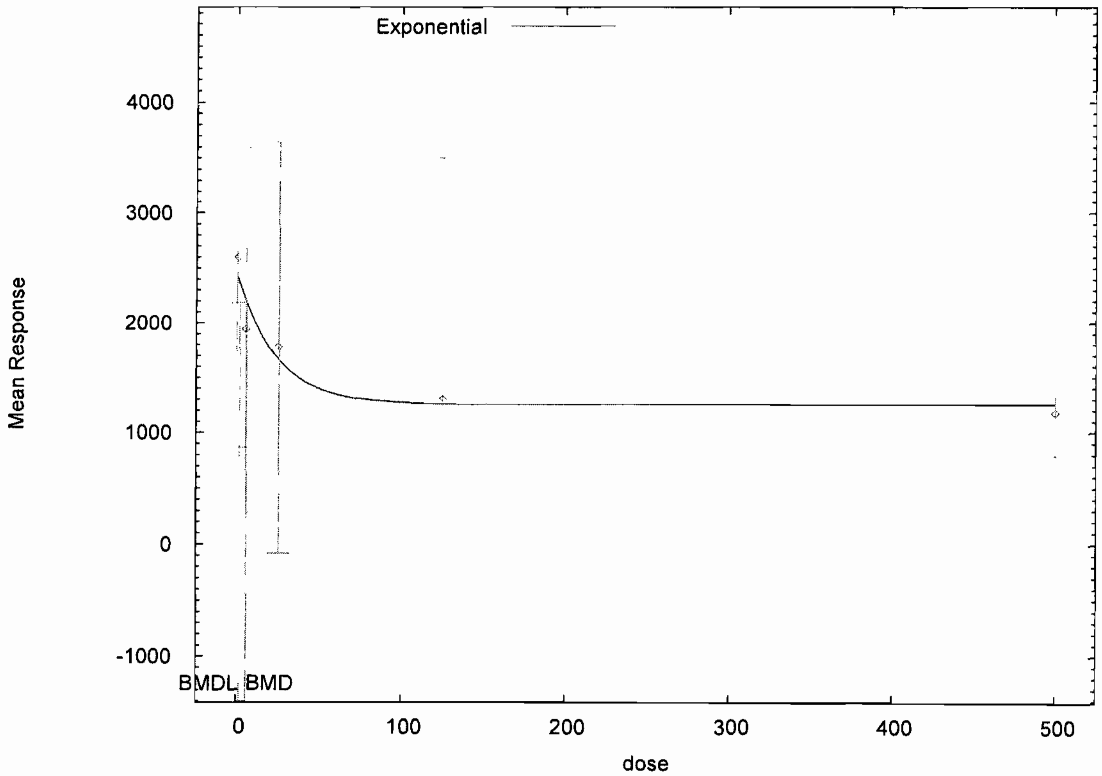
08:57 05/25 2010

Exponential Model 4 with 0.95 Confidence Level



08:57 05/25 2010

Exponential Model 5 with 0.95 Confidence Level



08:57 05/25 2010

Acephate; MRID 44203302
Male RBC ChE

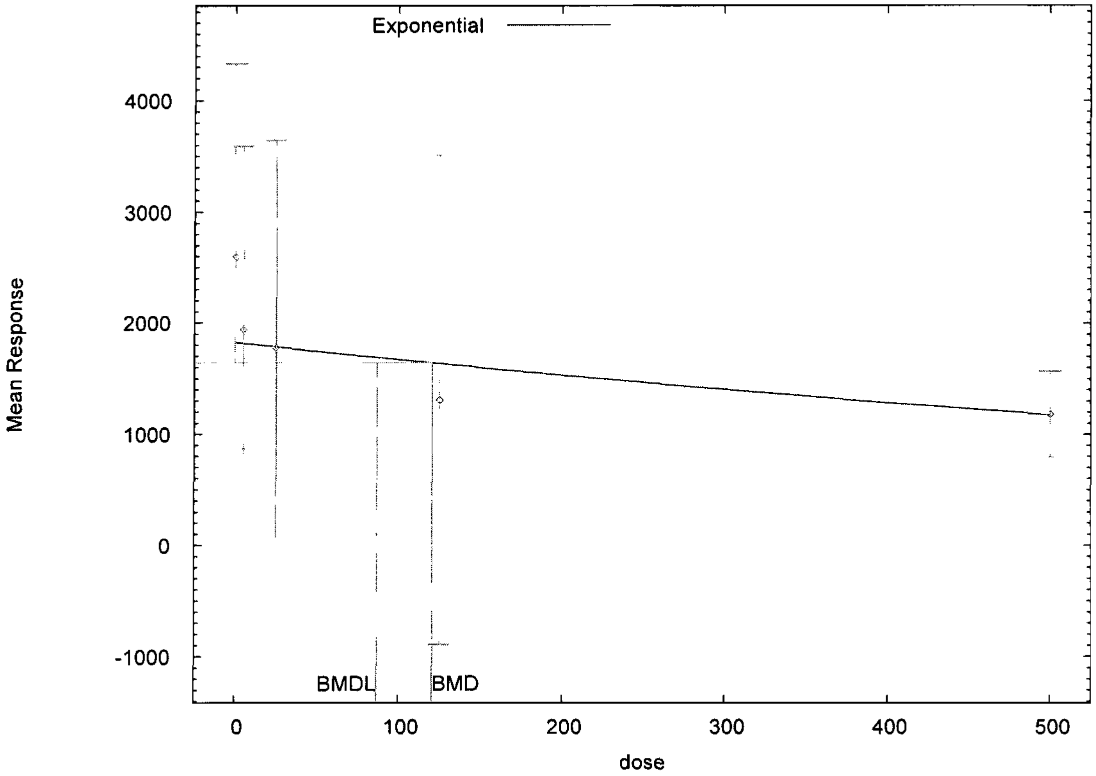
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                        Tue May 25 09:14:22 2010
 ====================================================================

 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         -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
```

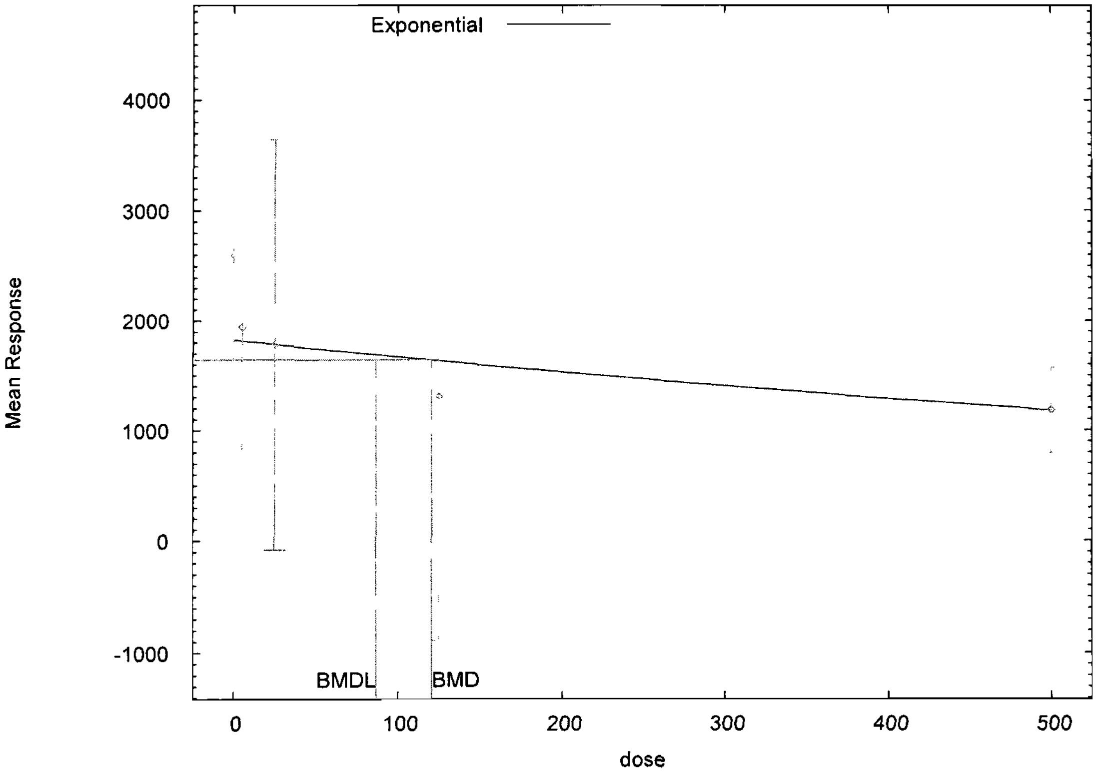
```
   difference between response and/or variances among the dose
   levels, it seems appropriate to model the data.

   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



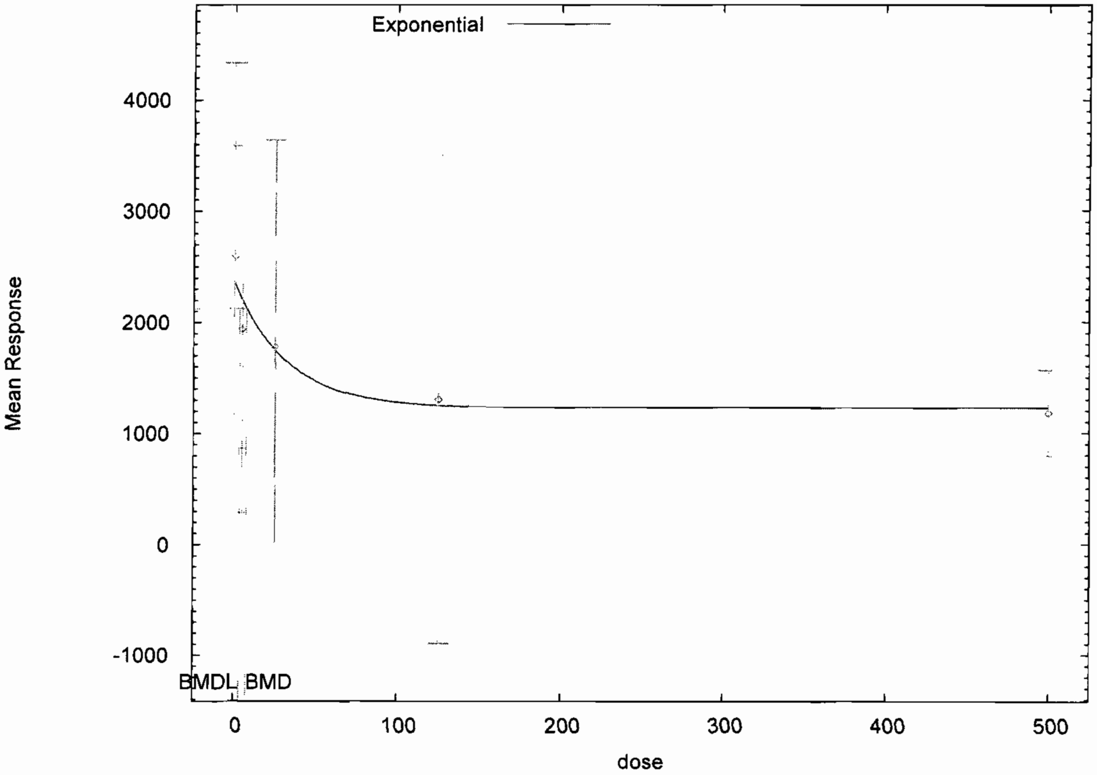
09:14 05/25 2010

Exponential Model 3 with 0.95 Confidence Level



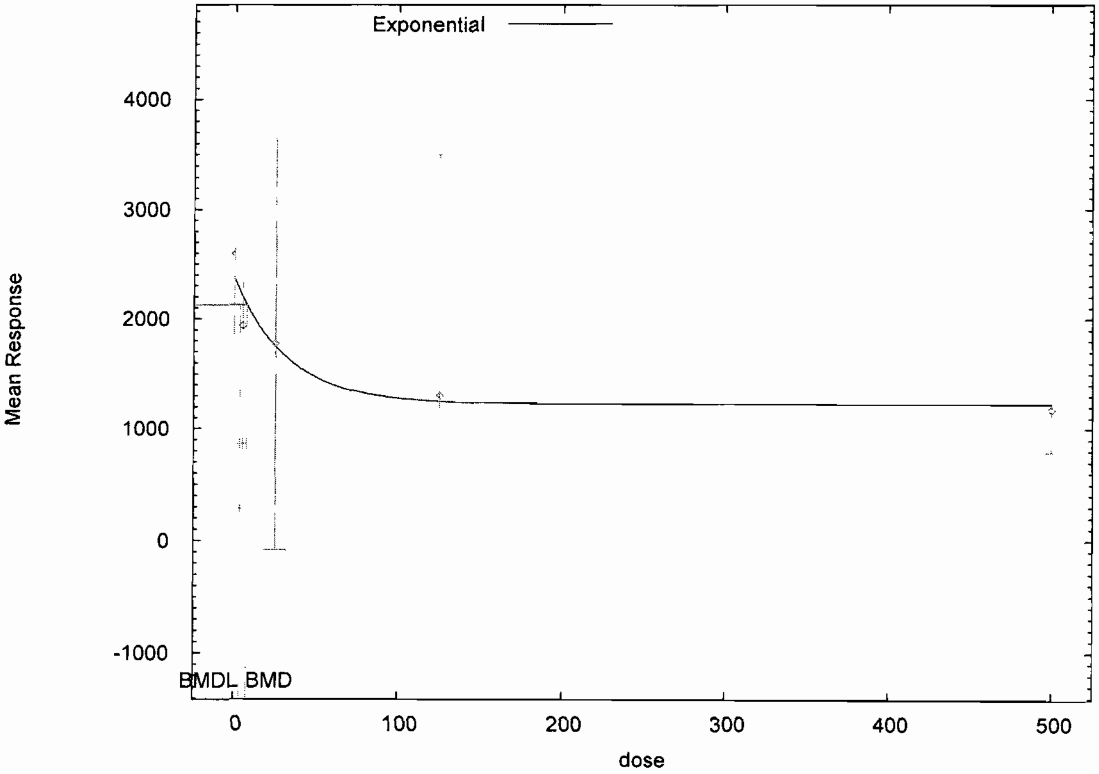
09:14 05/25 2010

Exponential Model 4 with 0.95 Confidence Level



09:14 05/25 2010

Exponential Model 5 with 0.95 Confidence Level



09:14 05/25 2010

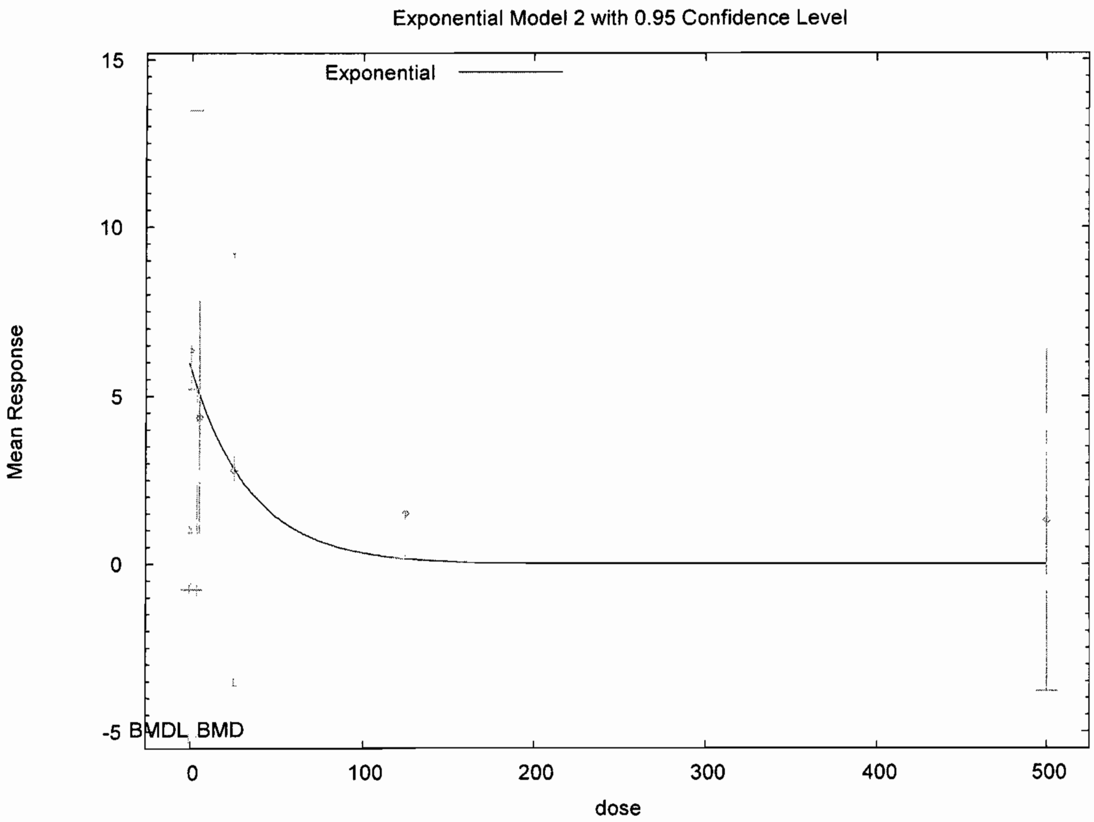
Acephate; MRID 44203302
Male Hippocampus ChE

```
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
```

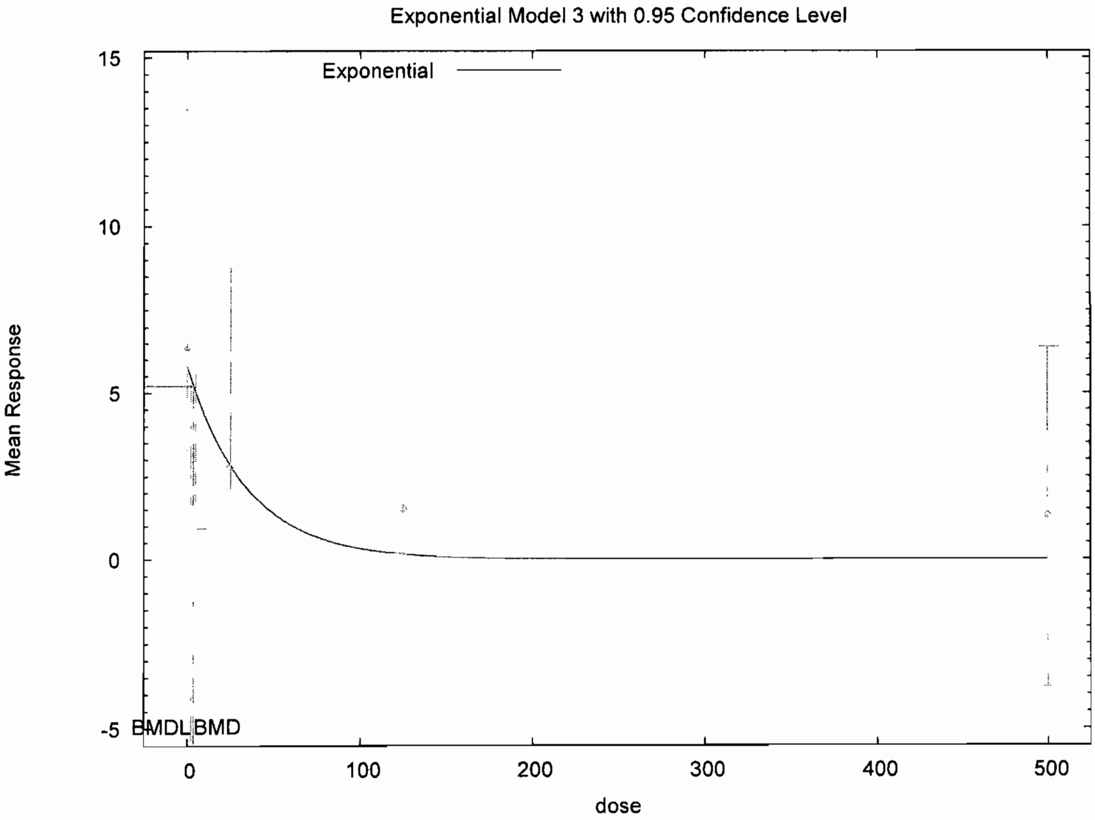
```
            d               --                   1                   --
1


                              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
```

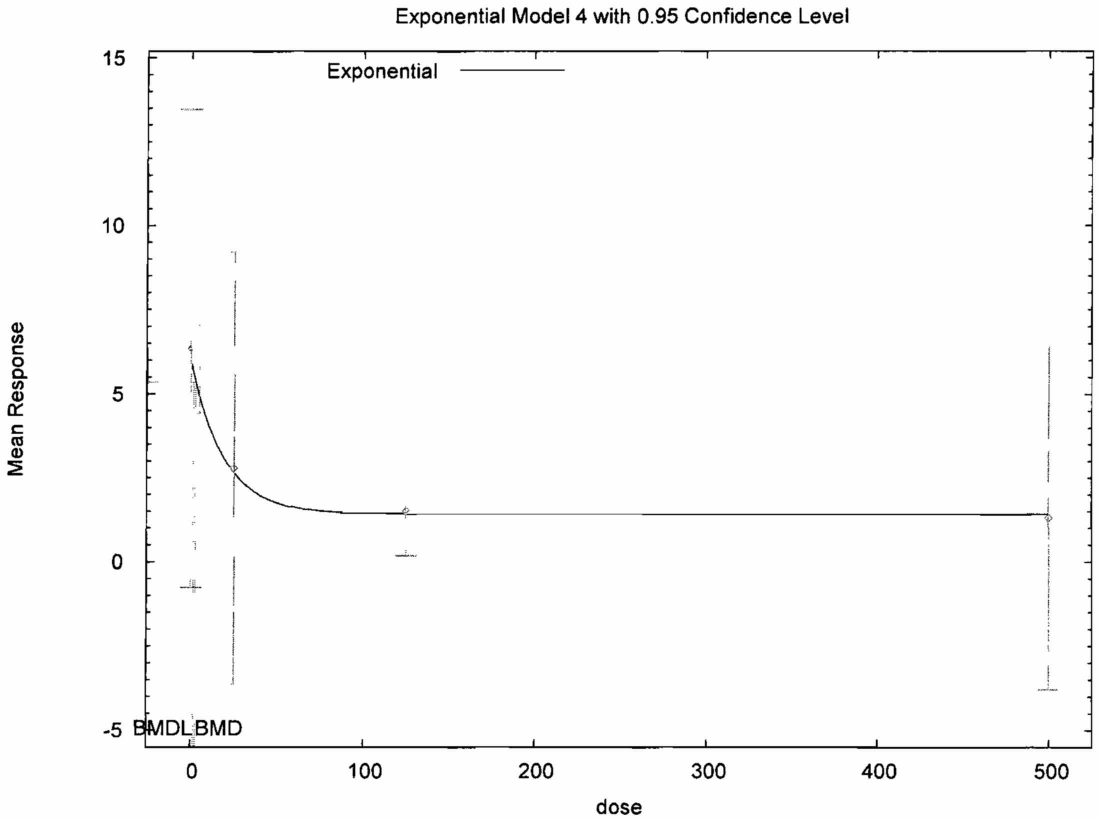
```
   Test 7c                      -2.629e-013          0                 N/A

     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
```



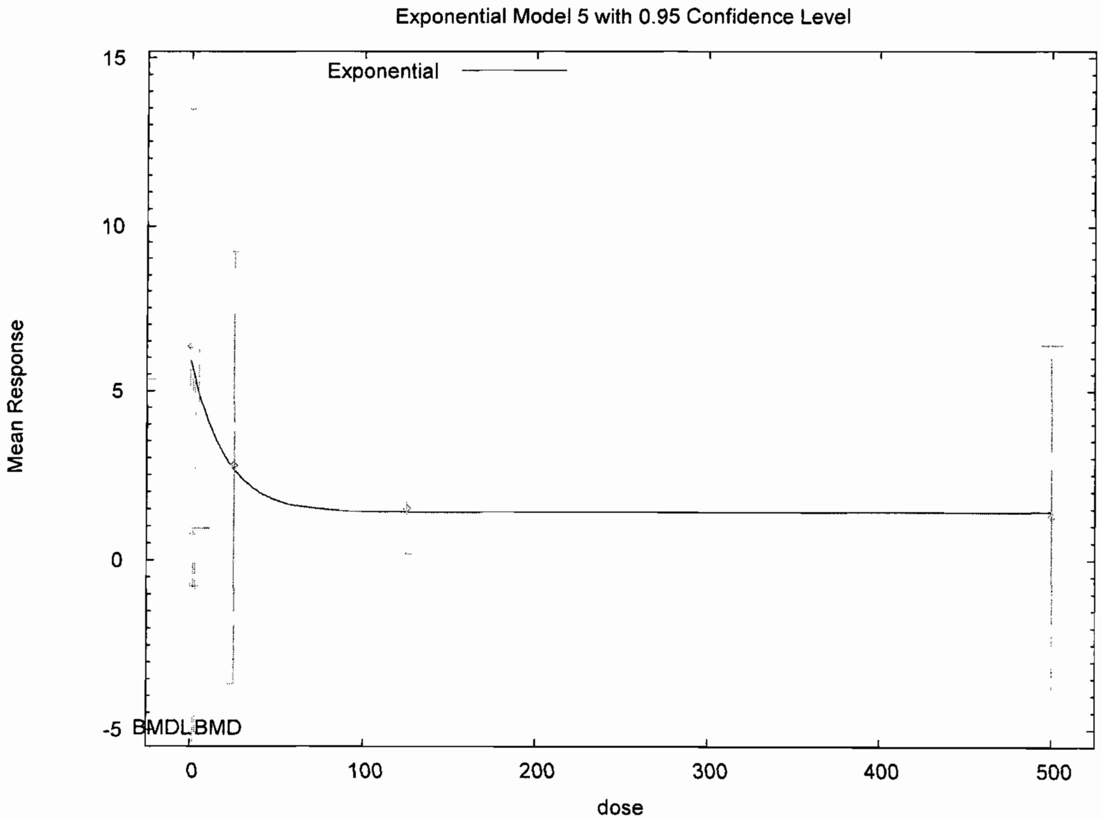
09:40 05/24 2010



09:40 05/24 2010



09:40 05/24 2010



09:40 05/24 2010

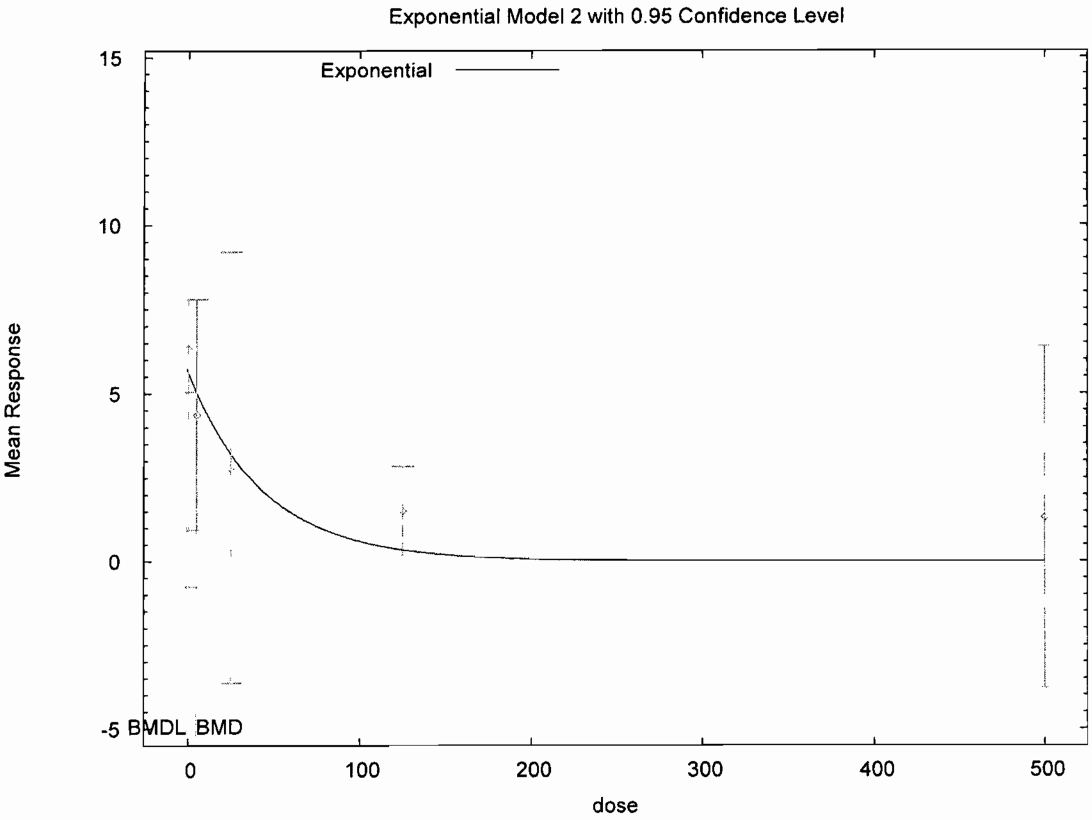
Acephate; MRID 44203302
Male Hippocampus ChE

```
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
```

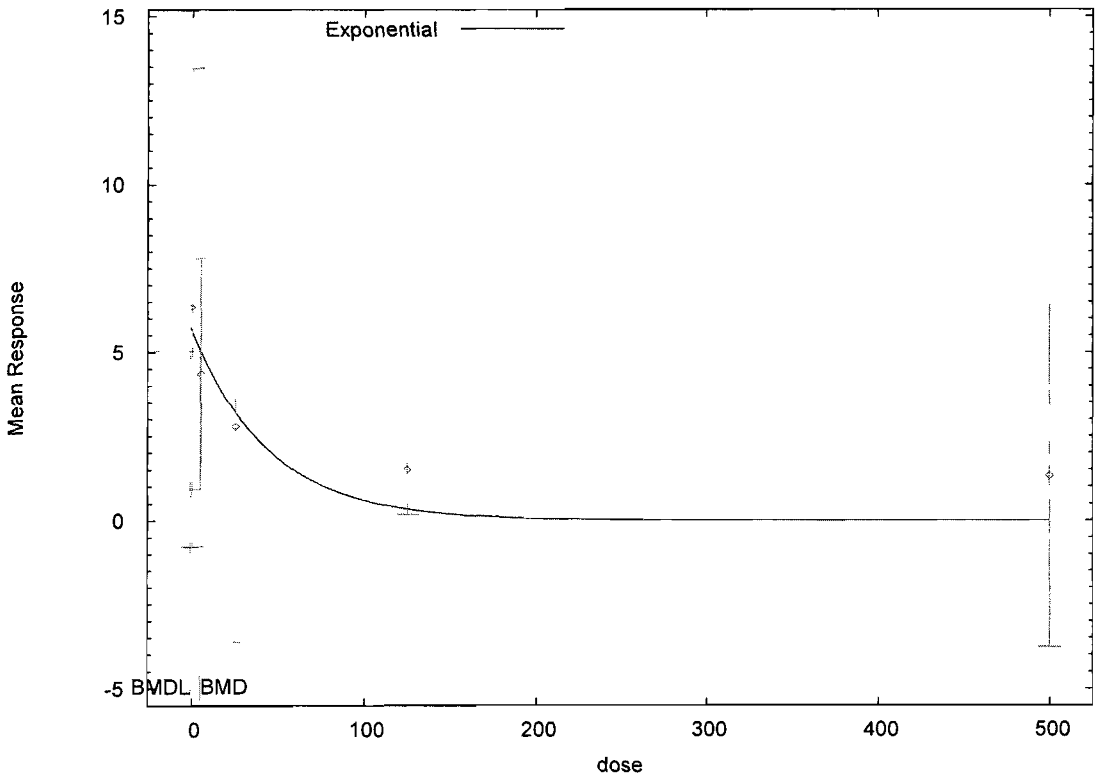
```
               125         1.472       0.5014           0.1084
               500          1.47       0.5014          -0.4781


 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
```



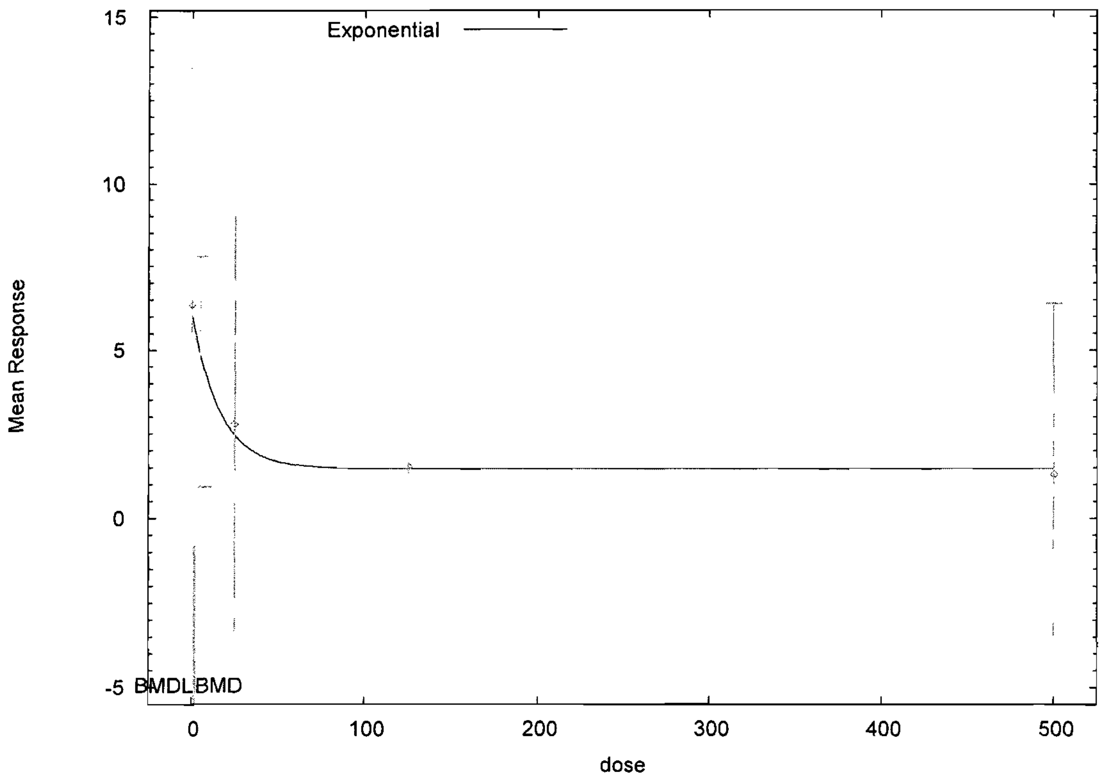
09:33 05/24 2010

Exponential Model 3 with 0.95 Confidence Level

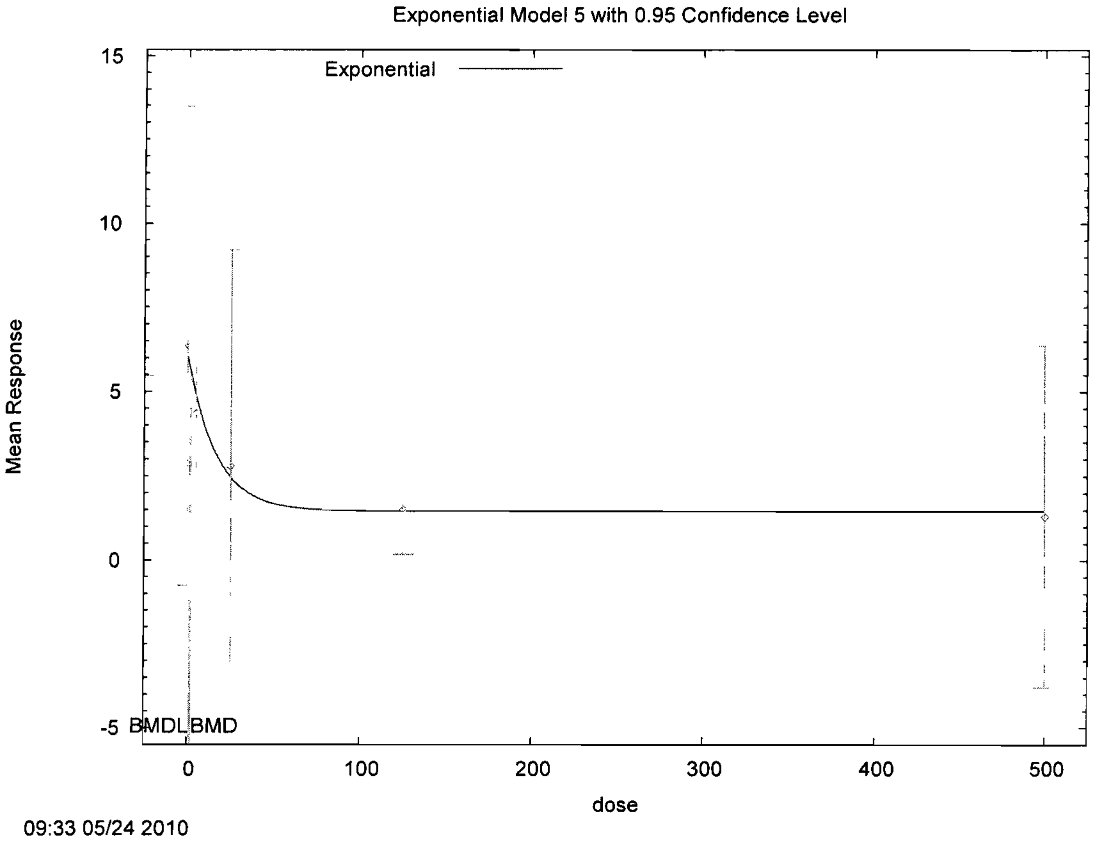


09:33 05/24 2010

Exponential Model 4 with 0.95 Confidence Level



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
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   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}]
```

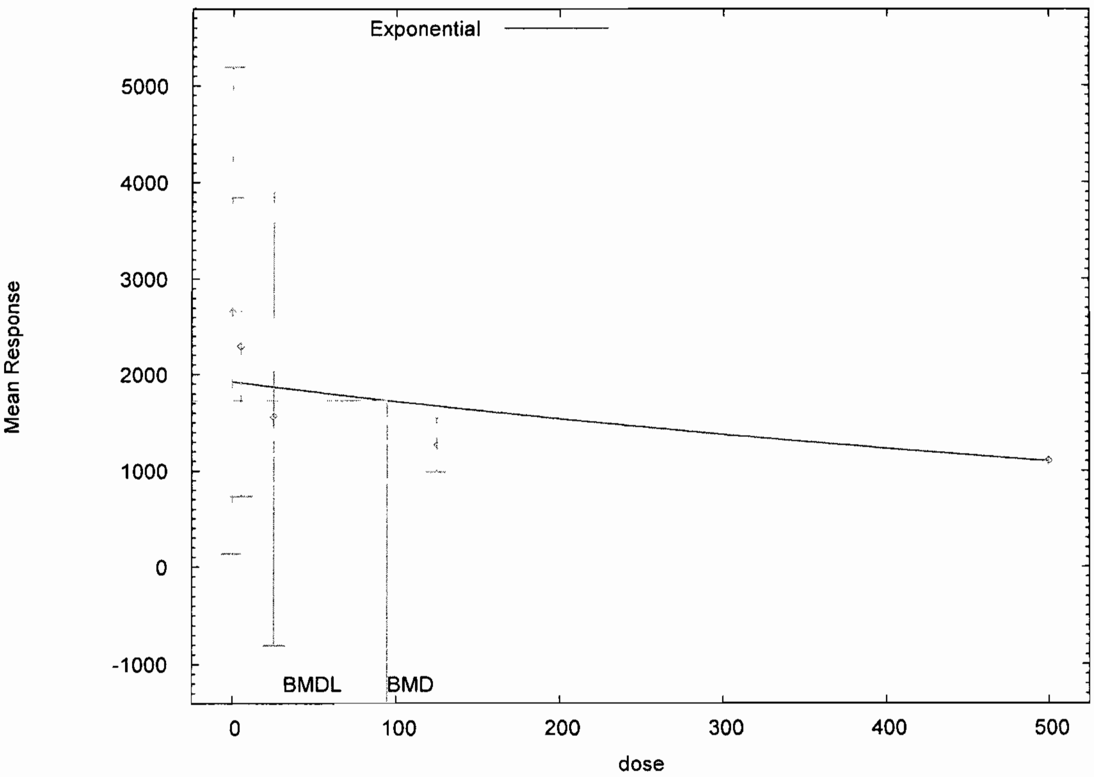
```
     Note: Y[dose] is the median response for exposure = dose;
           sign = +1 for increasing trend in data;
           sign = -1 for decreasing trend.

       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
```

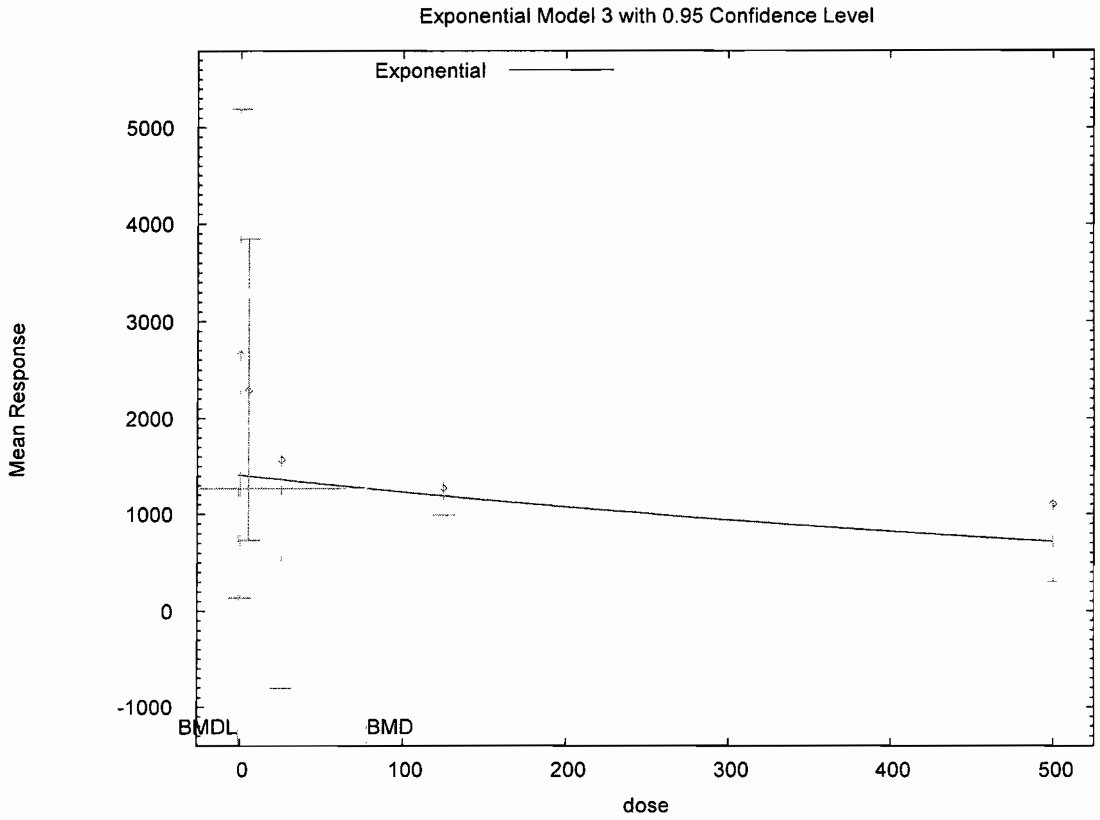
```
Additive constant for all log-likelihoods =     -9.189.  This constant added to the
above values gives the log-likelihood including the term that does not
depend on the model parameters.


                           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
```

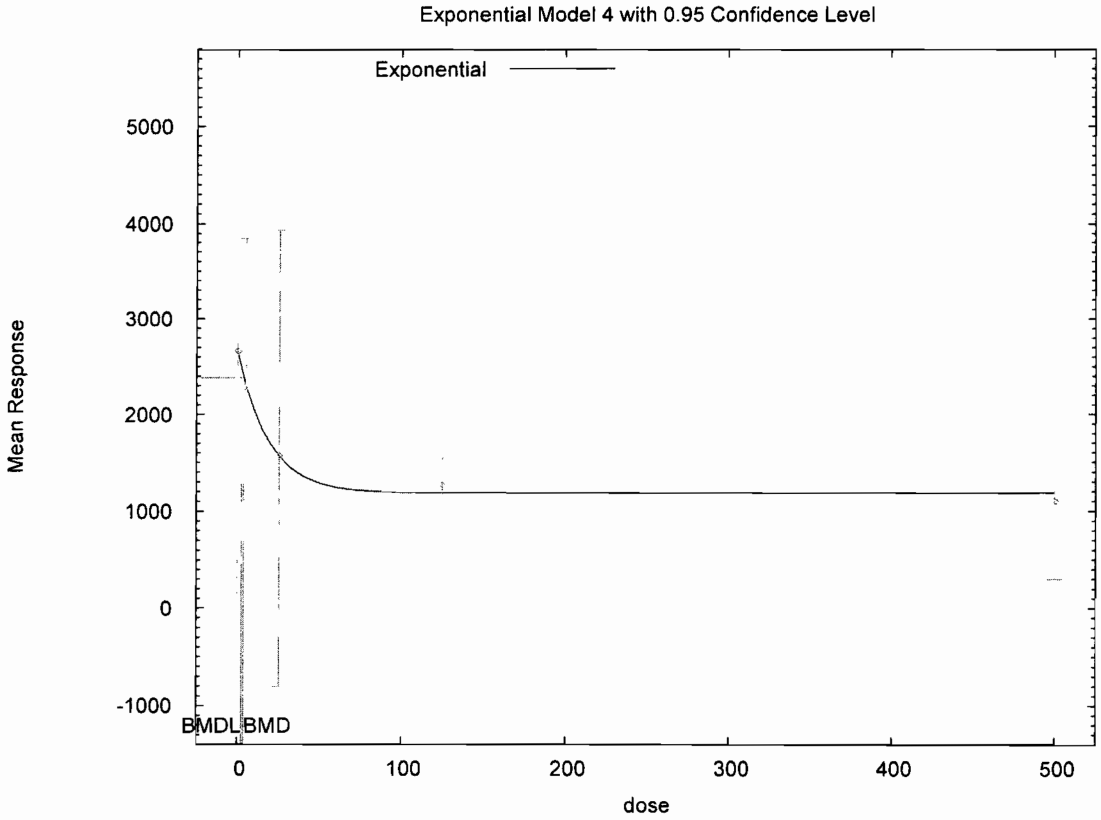
Exponential Model 2 with 0.95 Confidence Level



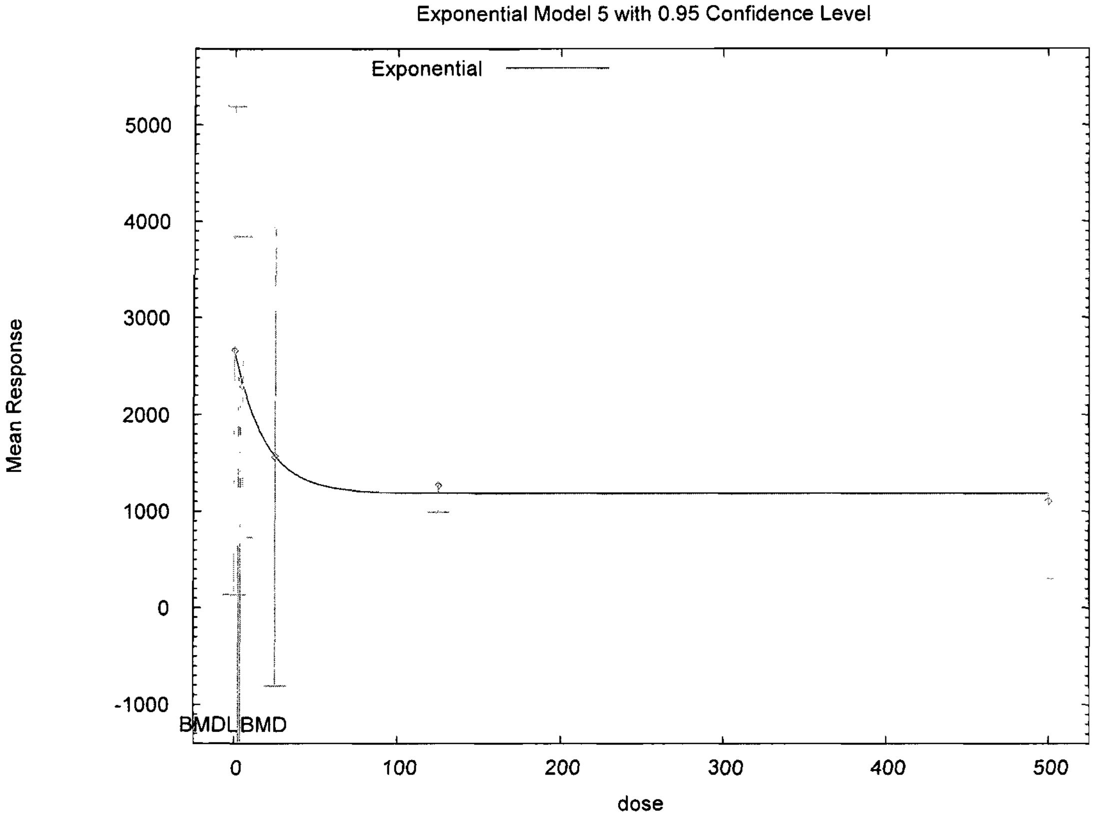
09:42 05/25 2010



09:42 05/25 2010



09:42 05/25 2010



09:42 05/25 2010

Acephate; MRID 44203302
Female RBC ChE

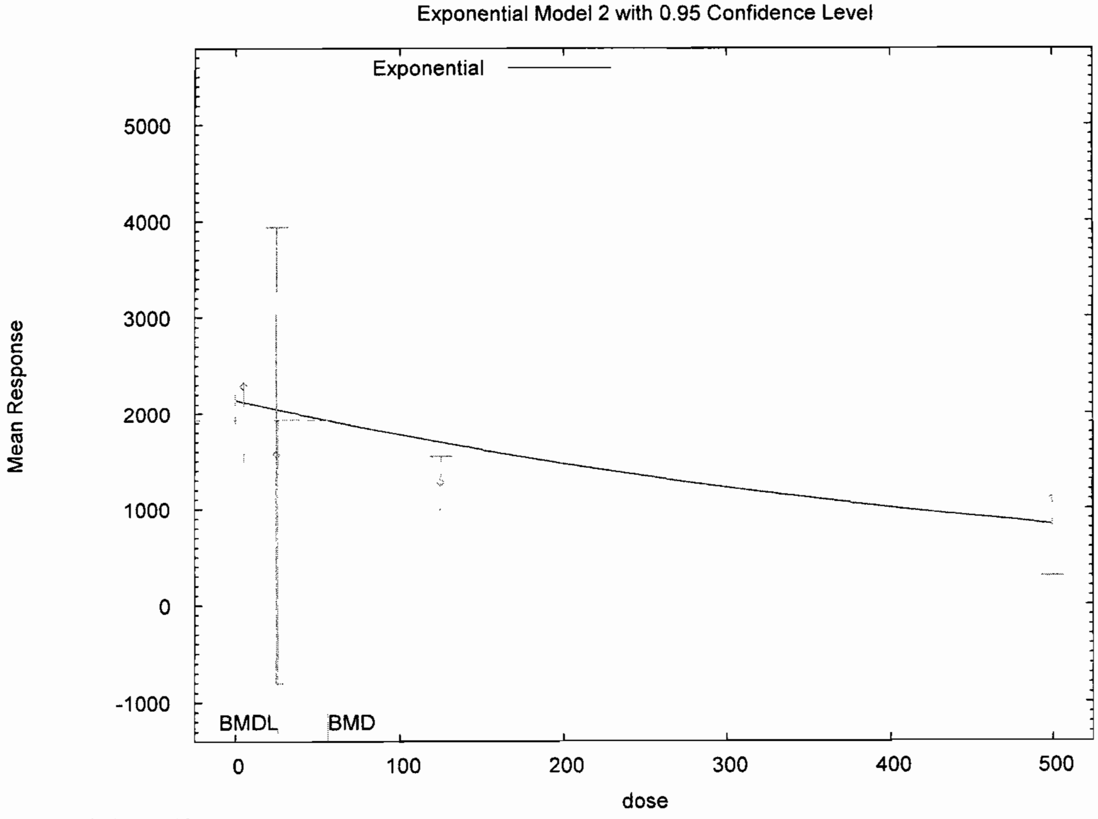
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                            Tue May 25 09:35:54 2010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

 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
```

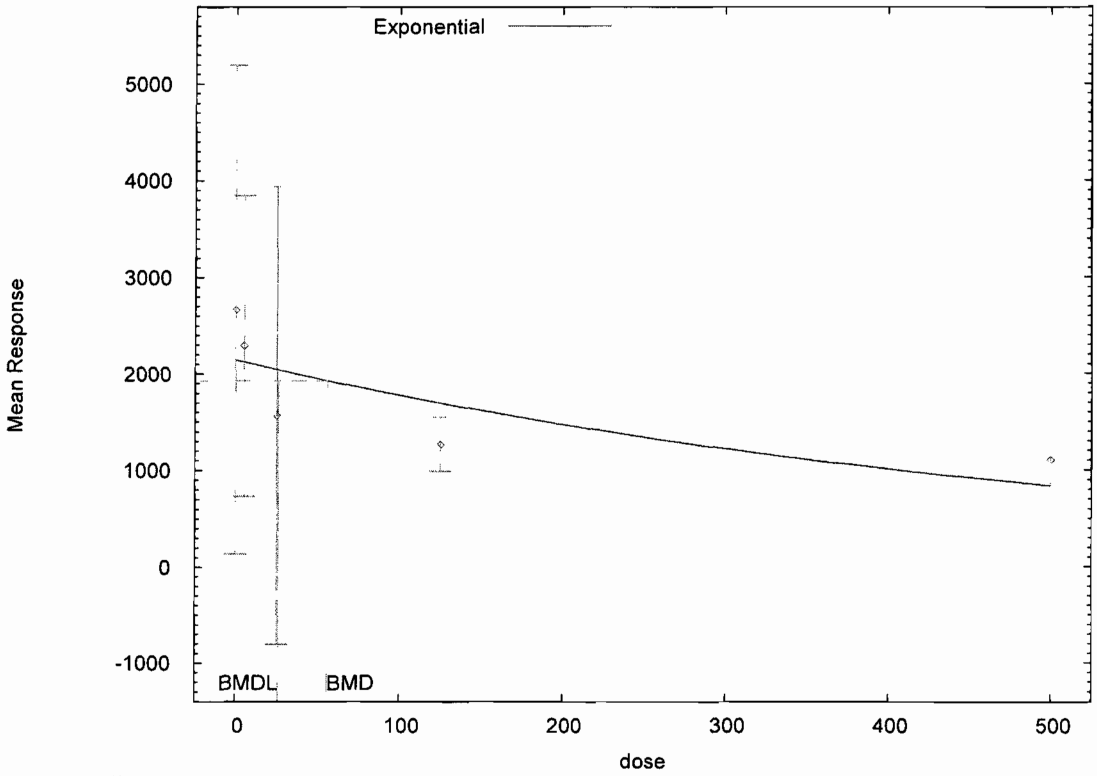
```
Additive constant for all log-likelihoods =      -9.189.  This constant added to the
above values gives the log-likelihood including the term that does not
depend on the model parameters.


                         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
```



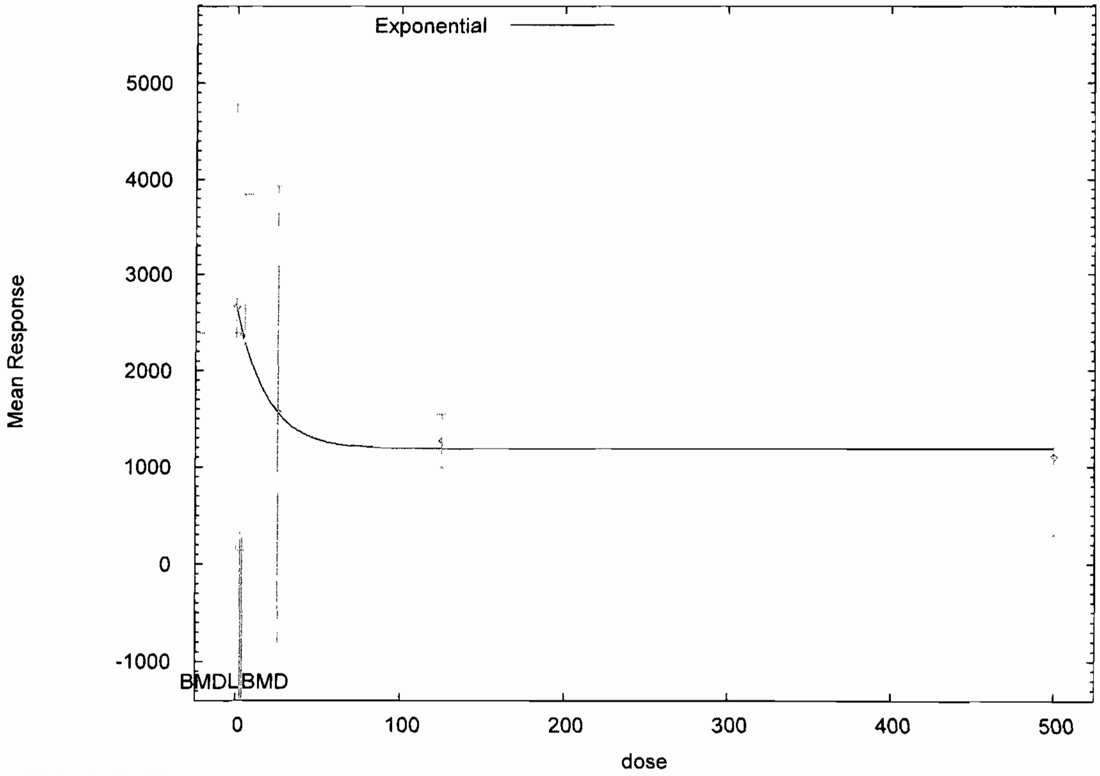
09:35 05/25 2010

Exponential Model 3 with 0.95 Confidence Level

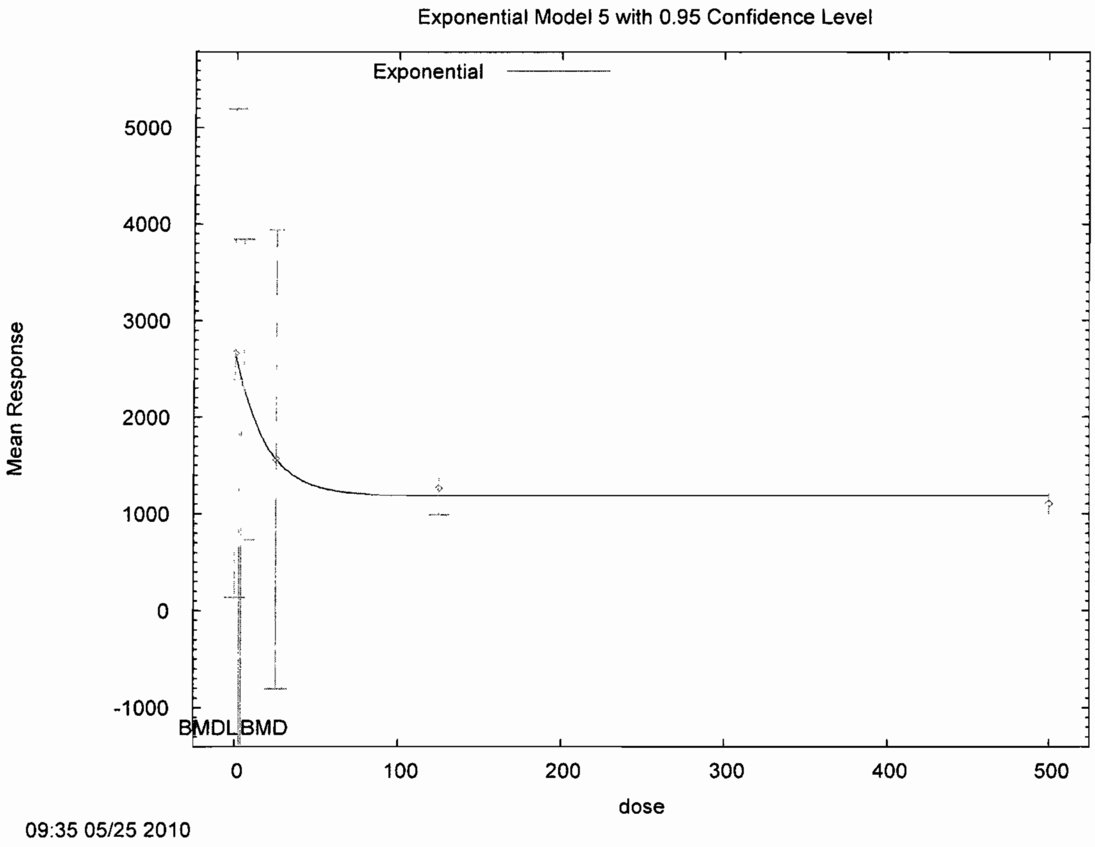


09:35 05/25 2010

Exponential Model 4 with 0.95 Confidence Level



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.
```

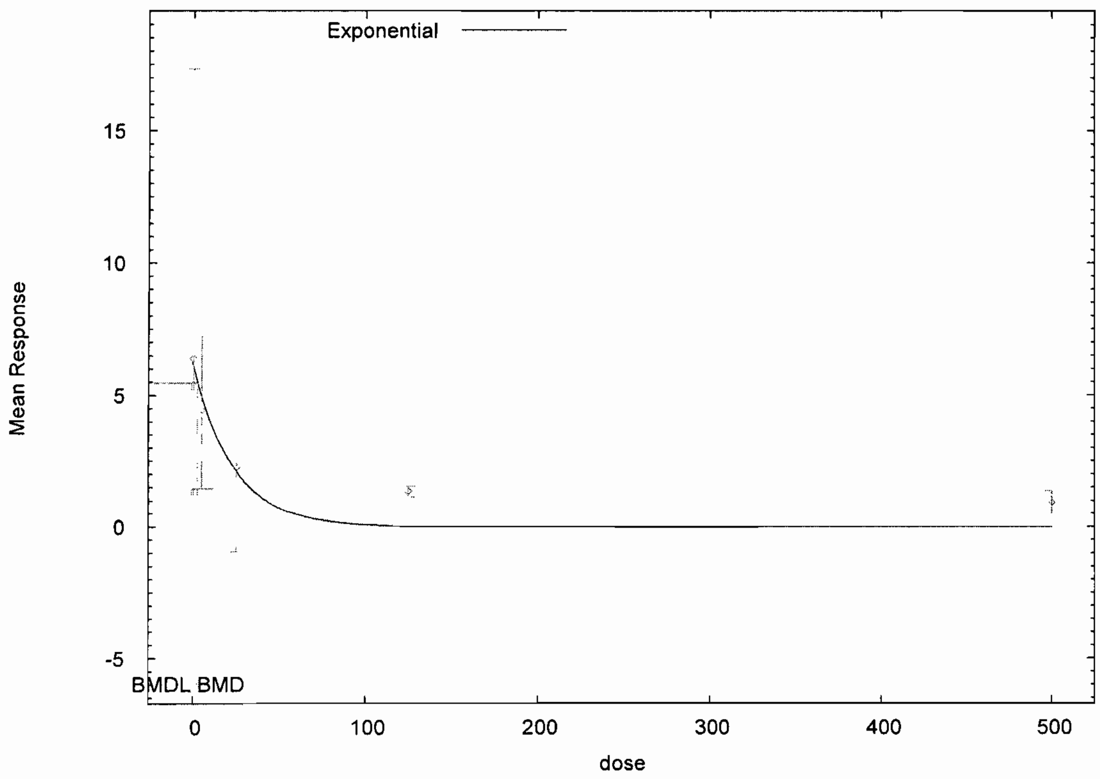
```
   Model 4 is nested within Model 5.


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.
```

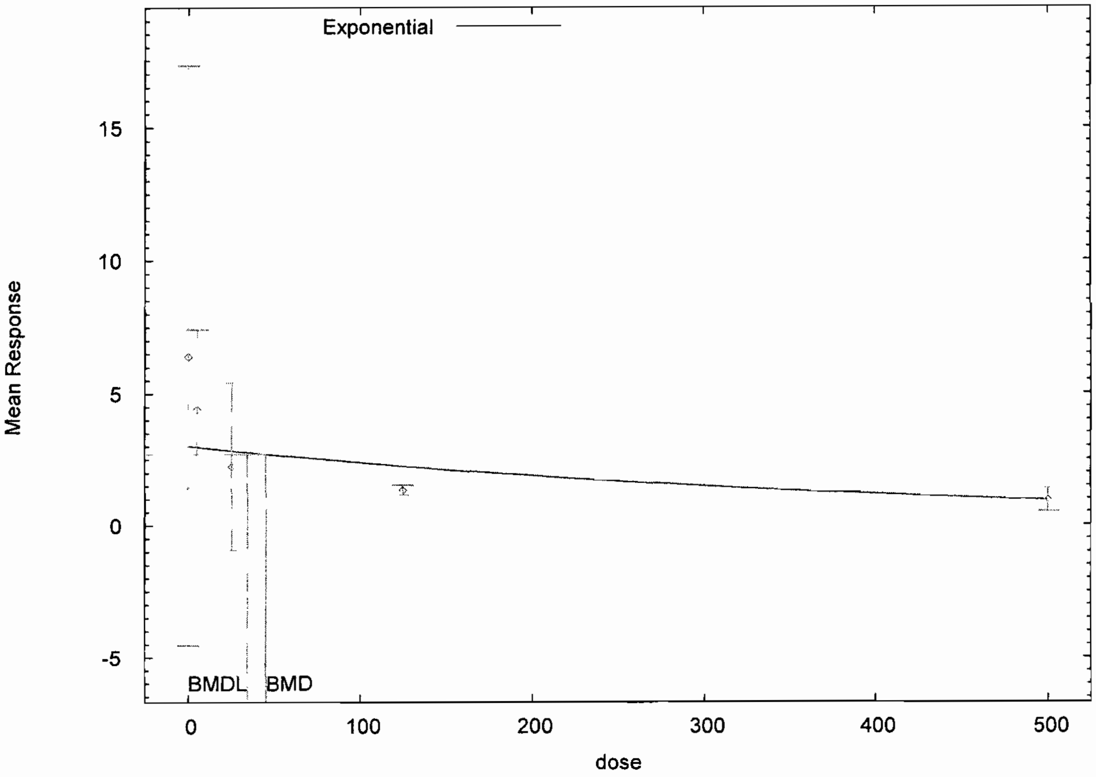
```
     The p-value for Test 7b is less than .05.  Model 5 appears
     to fit the data better than Model 3.

     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 2 with 0.95 Confidence Level



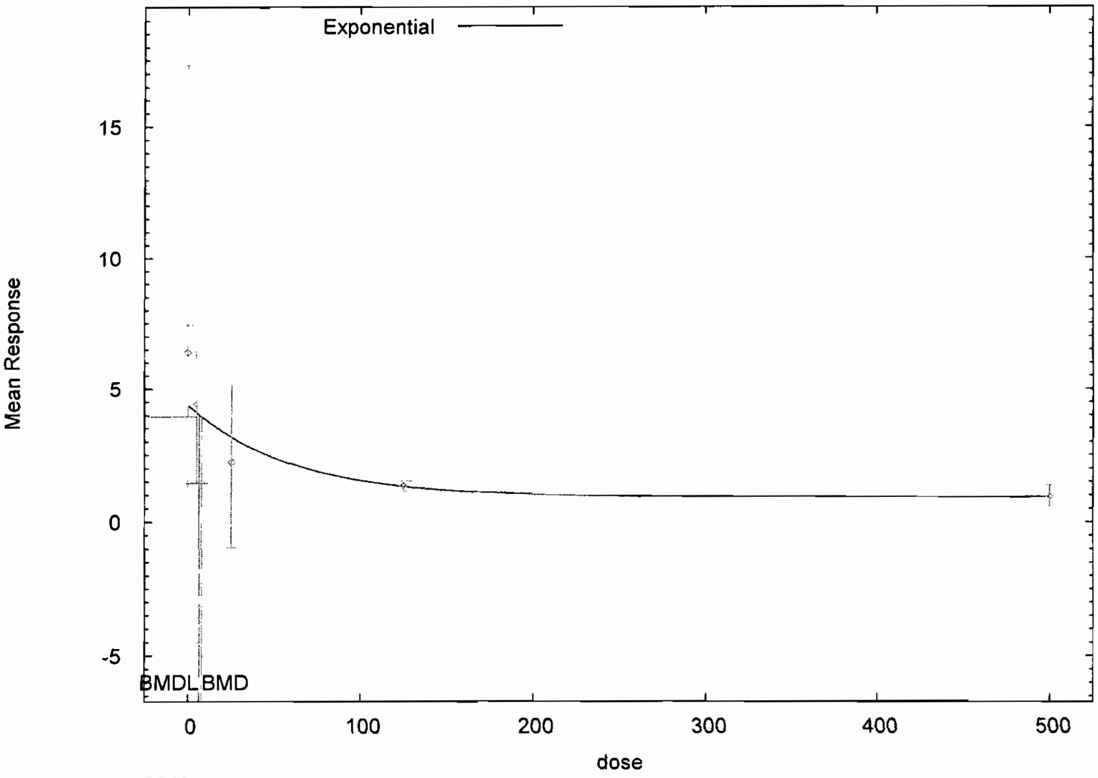
14:46 05/24 2010

Exponential Model 3 with 0.95 Confidence Level

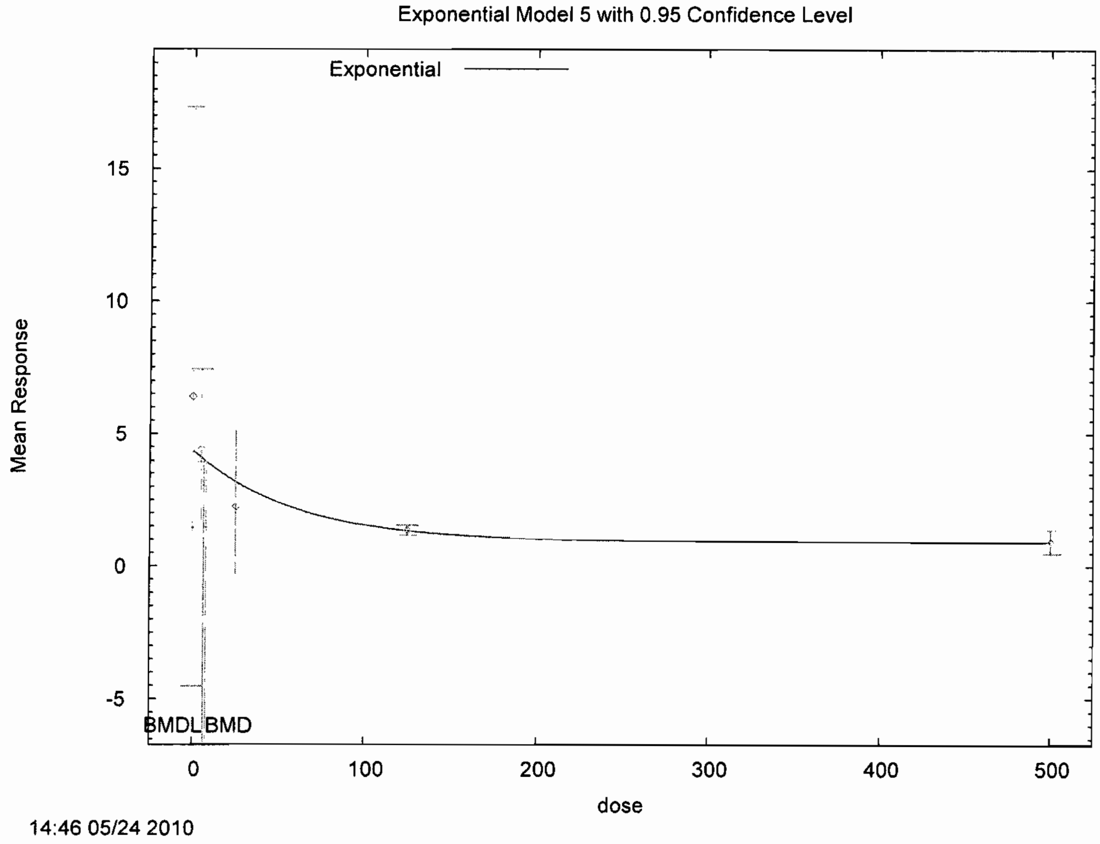


14:46 05/24 2010

Exponential Model 4 with 0.95 Confidence Level



14:46 05/24 2010



Acephate; MRID 44203302
Female Hippocampus ChE

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

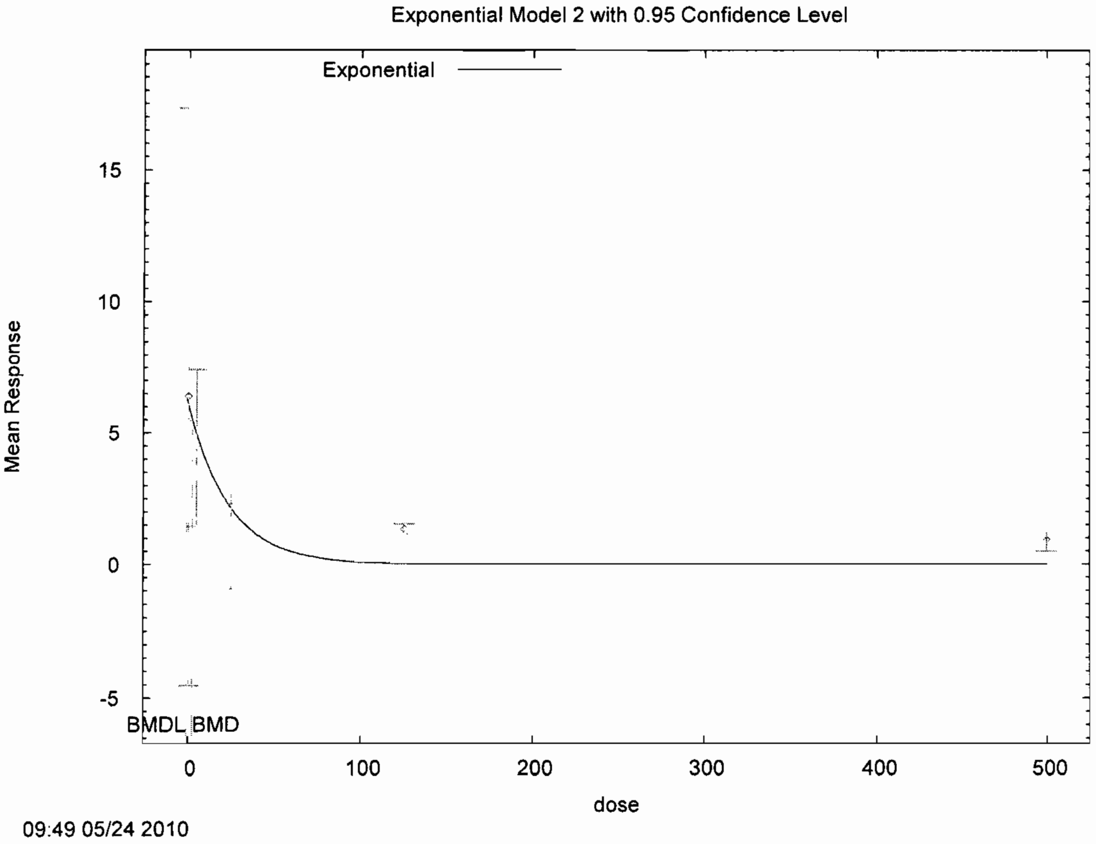
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Mon May 24 09:49:43 2010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

 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         -1.76198         -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
```

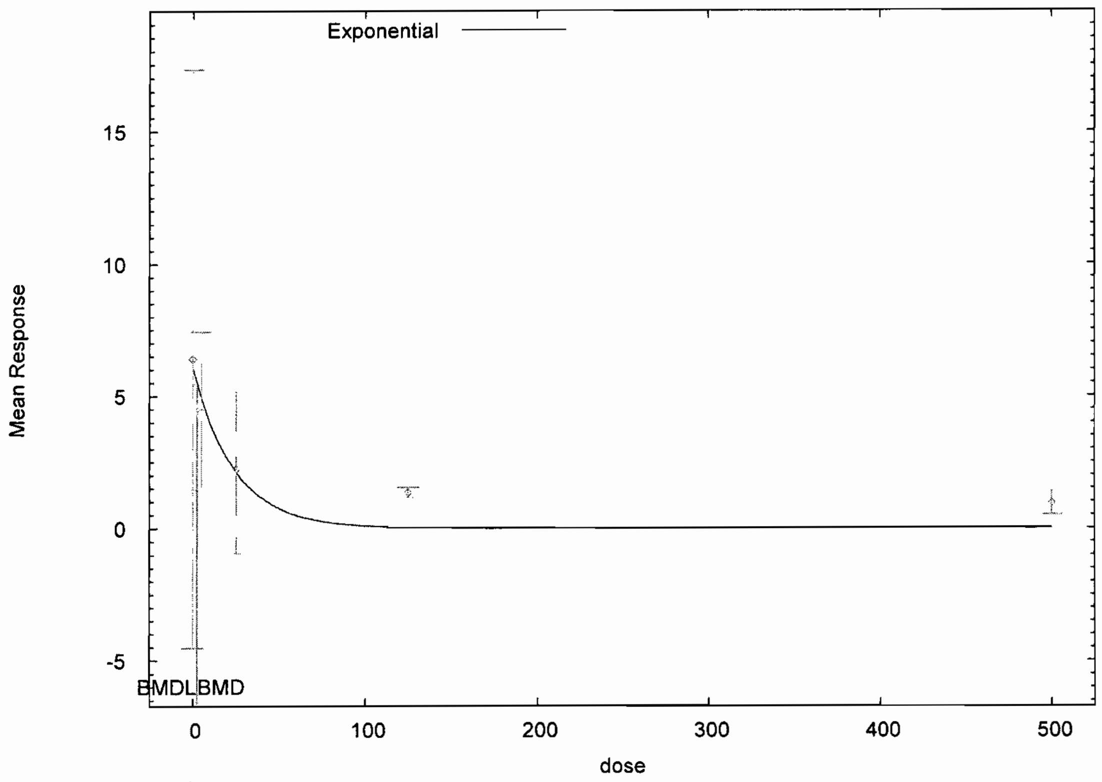
```
 Dose       N         Obs Mean     Obs Std Dev
-----      ---       ----------   -------------
    0       2          6.4        1.216
    5       2         4.44        0.332
   25       2         2.24        0.354
  125       2         1.35        0.021
  500       2         0.93        0.049


                   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
```

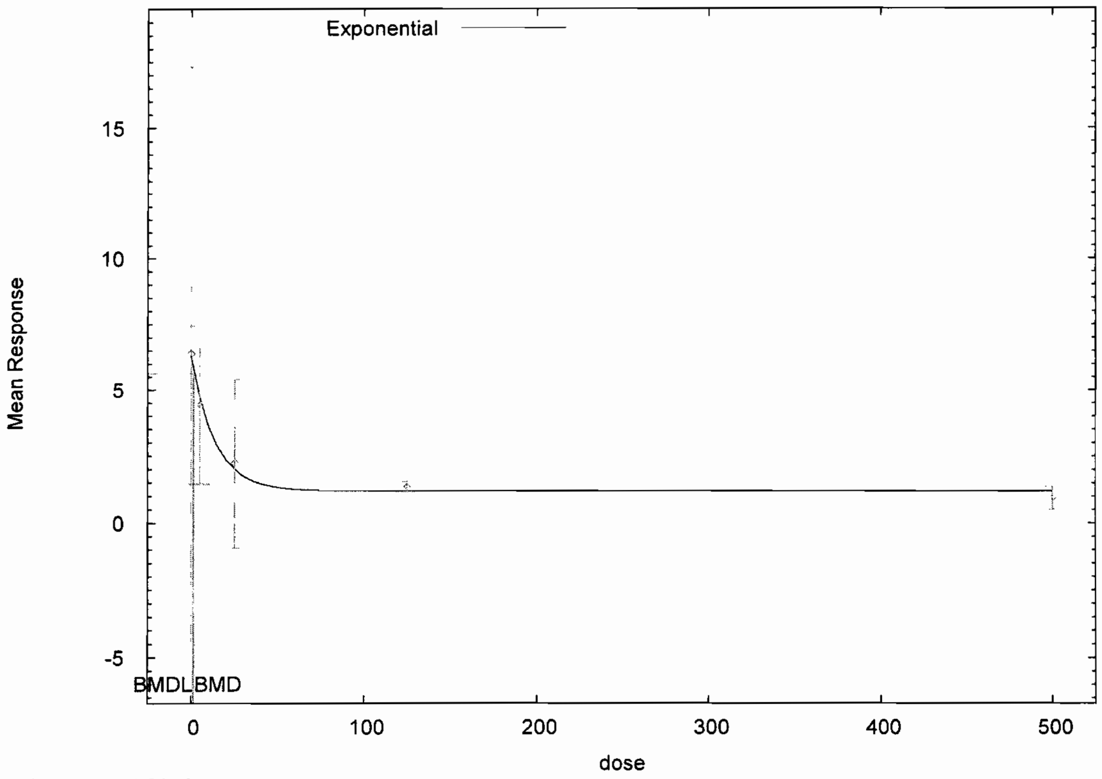


Exponential Model 3 with 0.95 Confidence Level

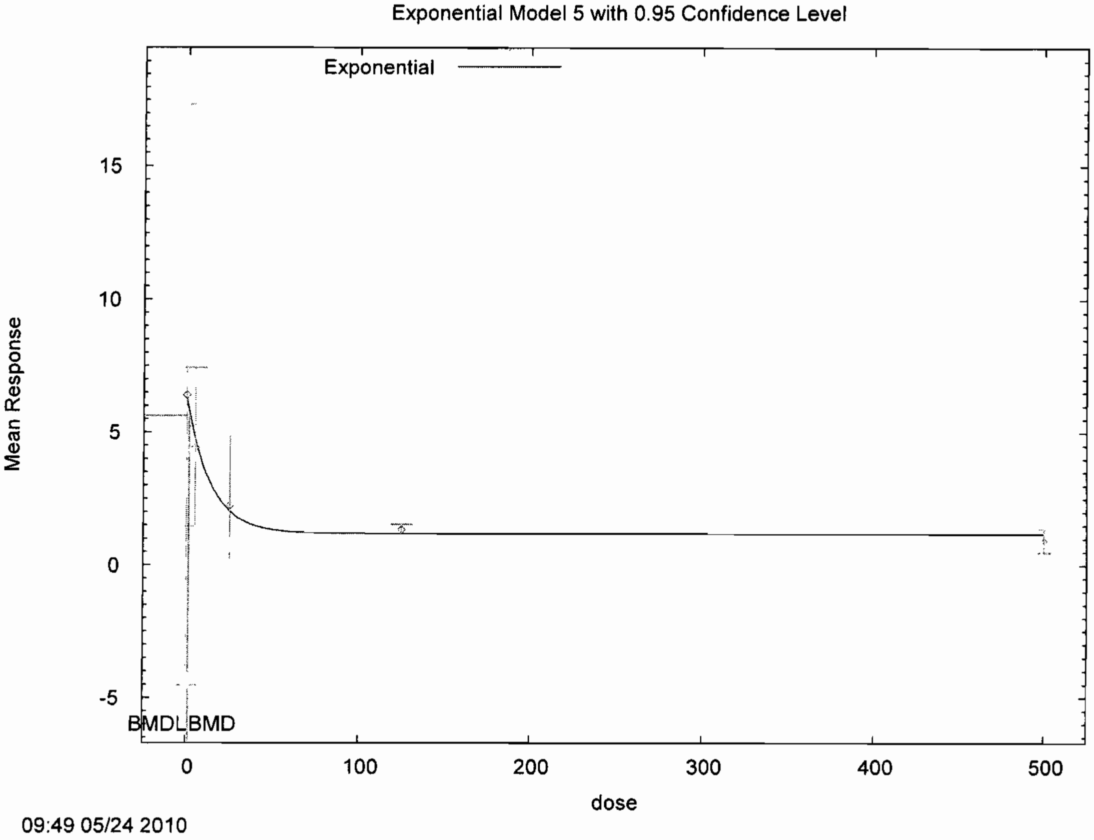


09:49 05/24 2010

Exponential Model 4 with 0.95 Confidence Level



09:49 05/24 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:
                                              Mon May 17 10:42:49 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.
```

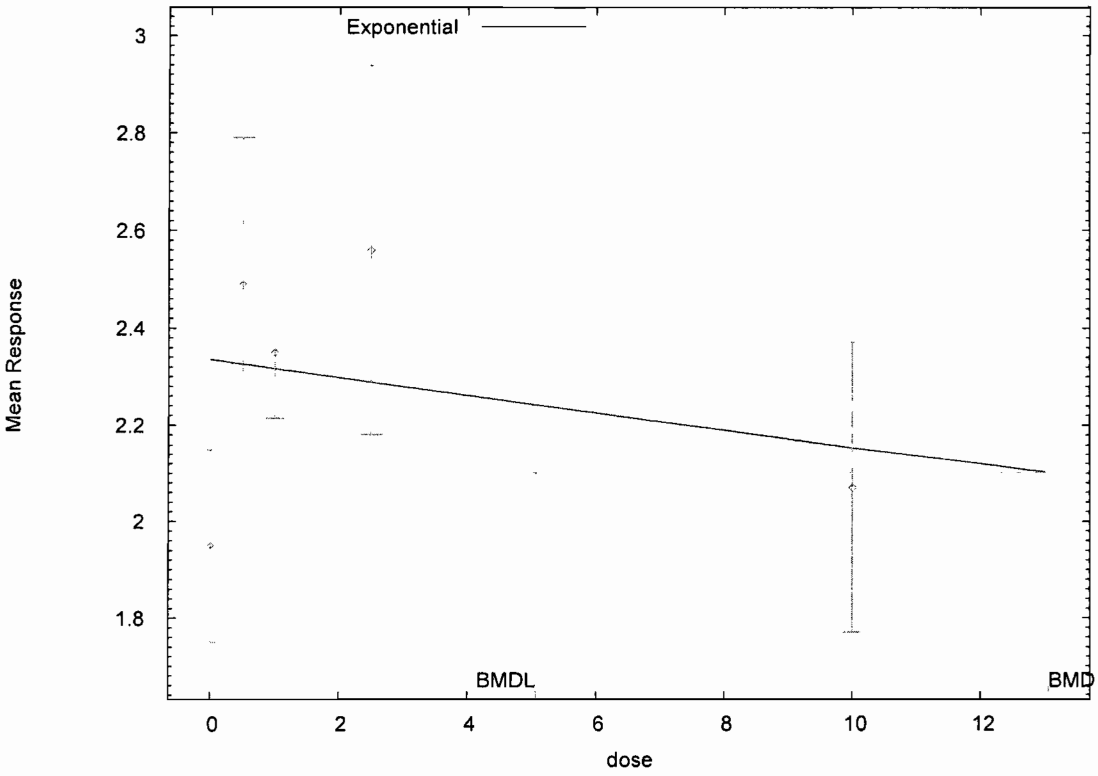
```
      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   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          -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.
```

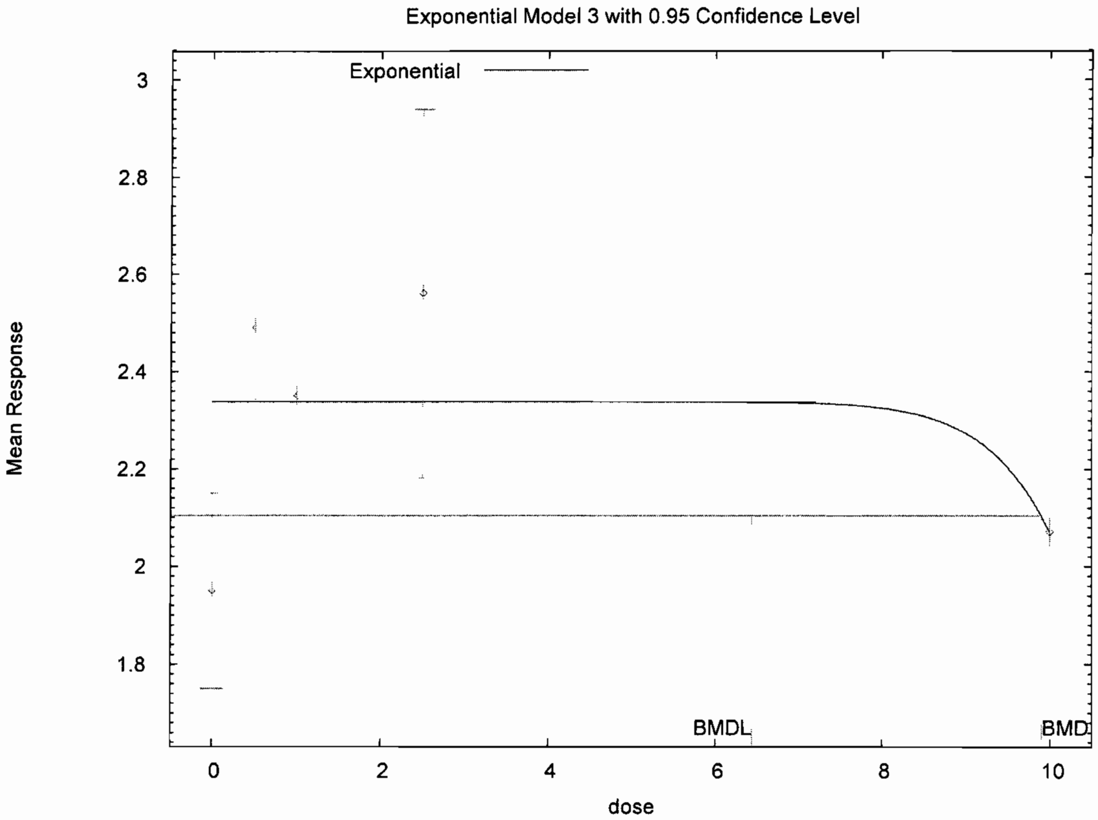
```
                         Explanation of Tests

 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
```

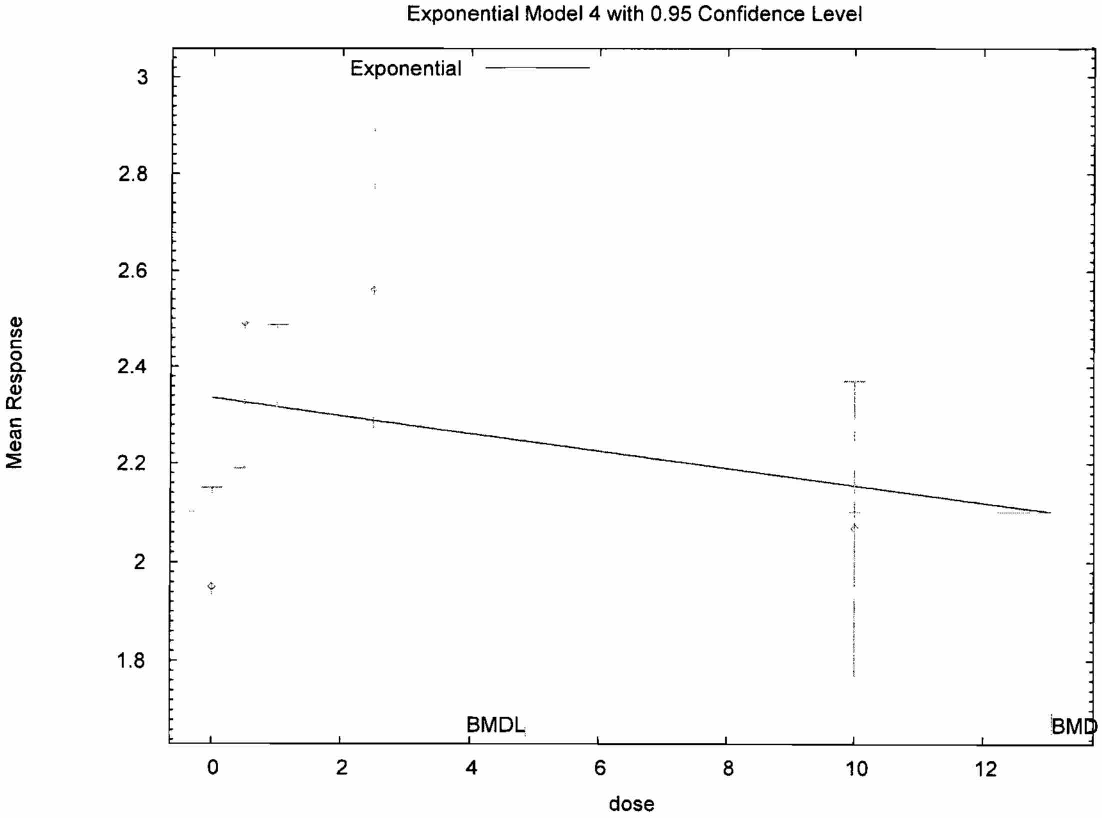
Exponential Model 2 with 0.95 Confidence Level



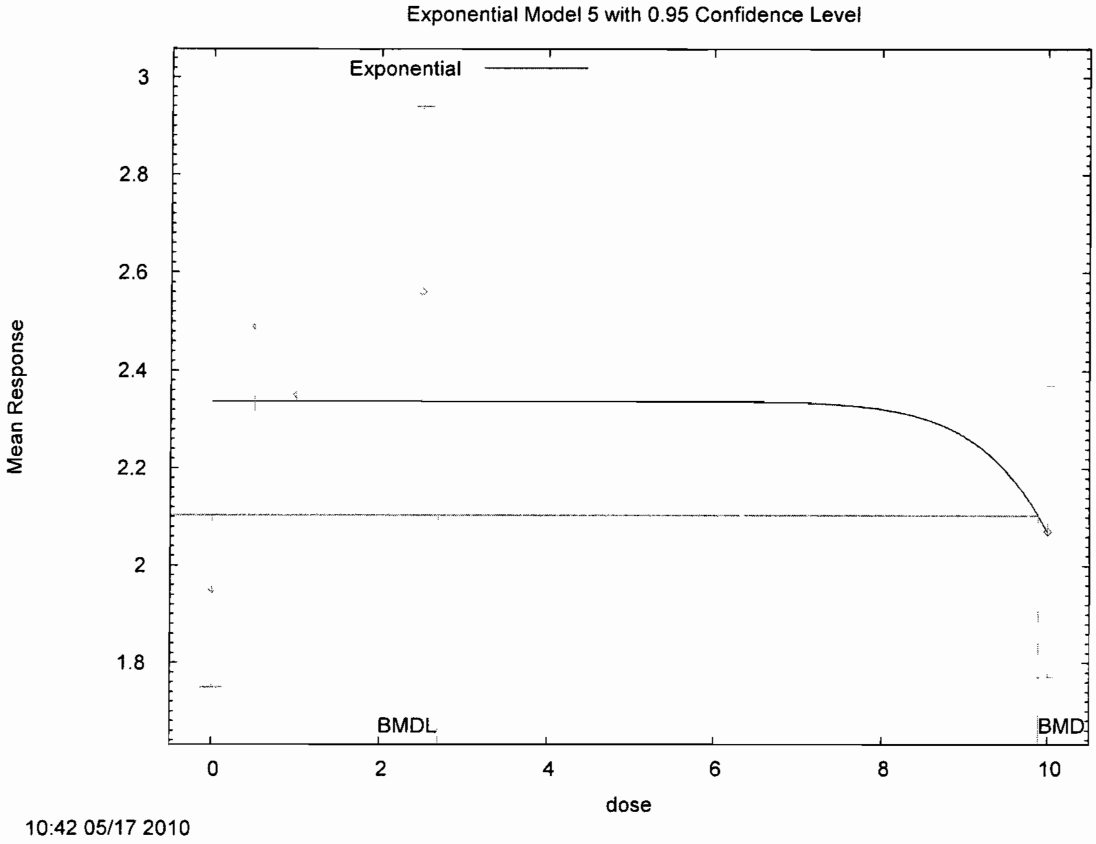
10:42 05/17 2010



10:42 05/17 2010



10:42 05/17 2010



Acephate 4615180
pup female brain che

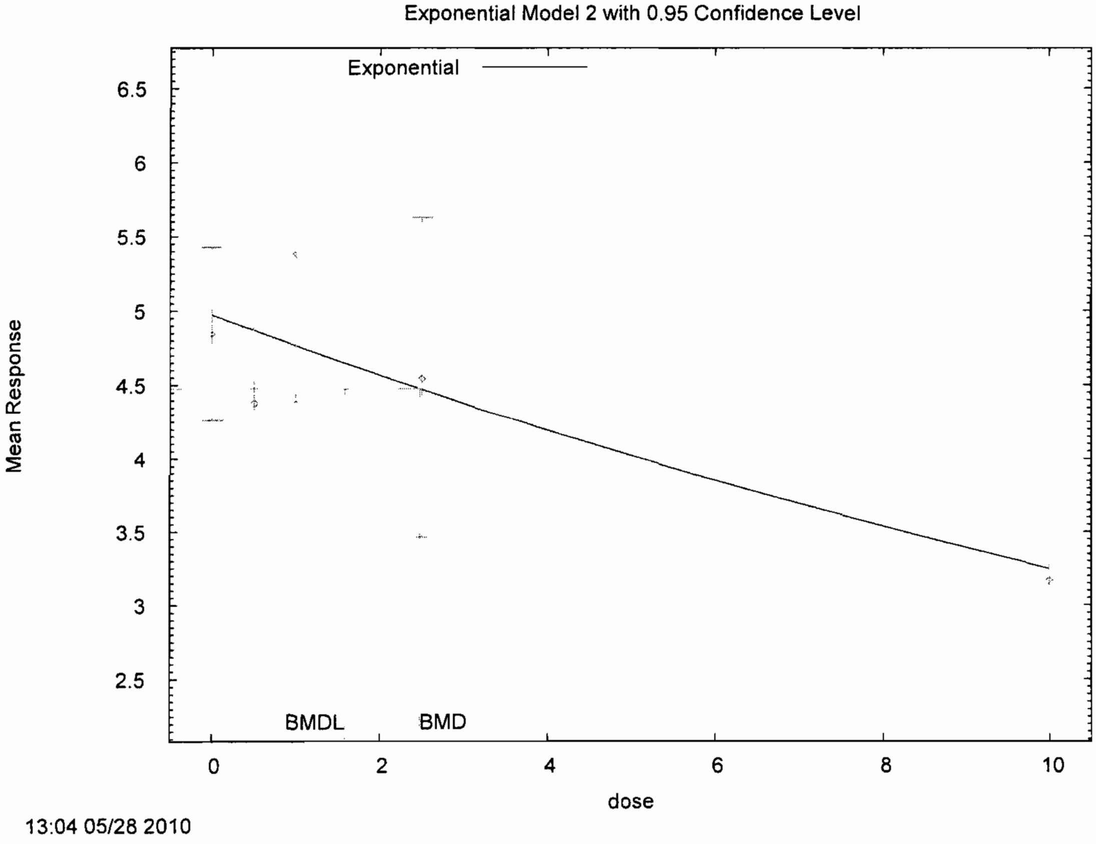
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                            Fri May 28 13:04:09 2010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

 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.
```

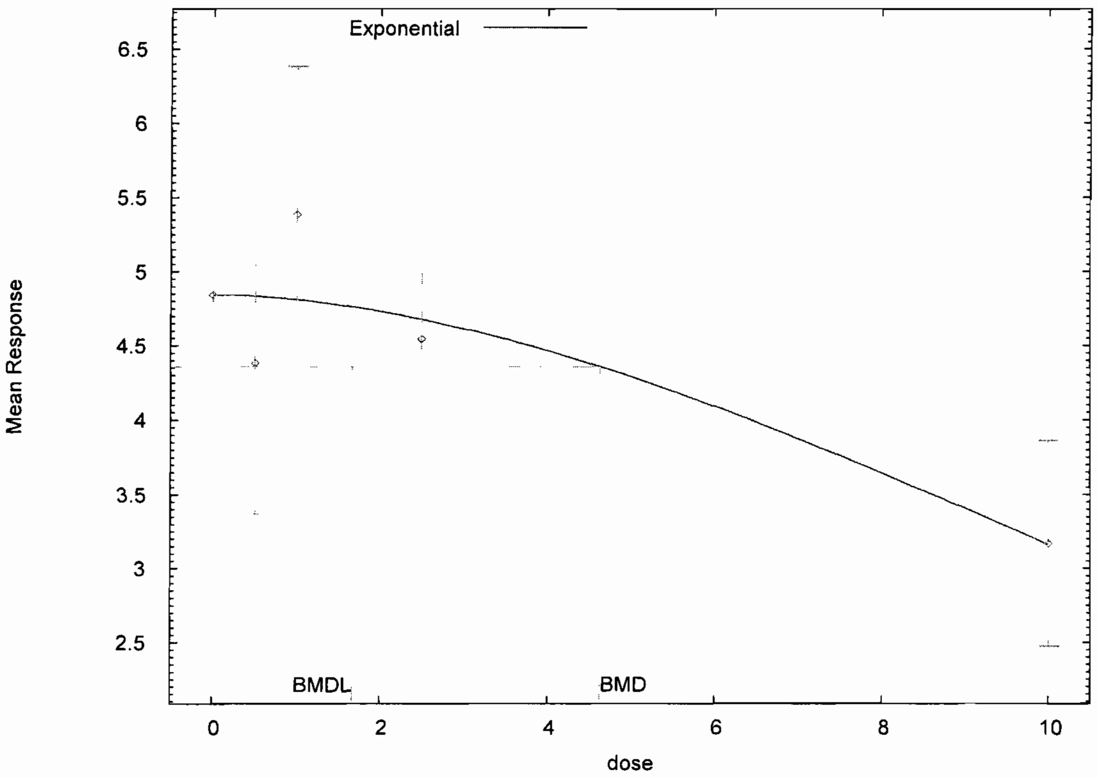
```
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   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         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
```

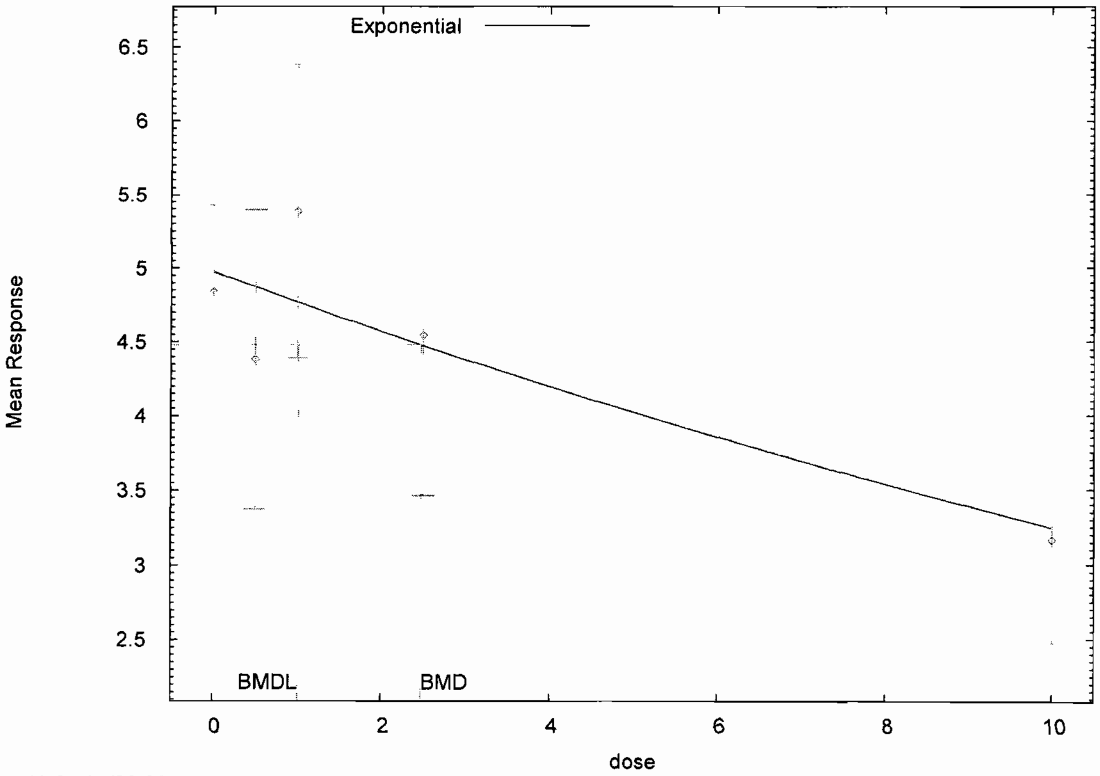
```
above values gives the log-likelihood including the term that does not
depend on the model parameters.


                        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
```

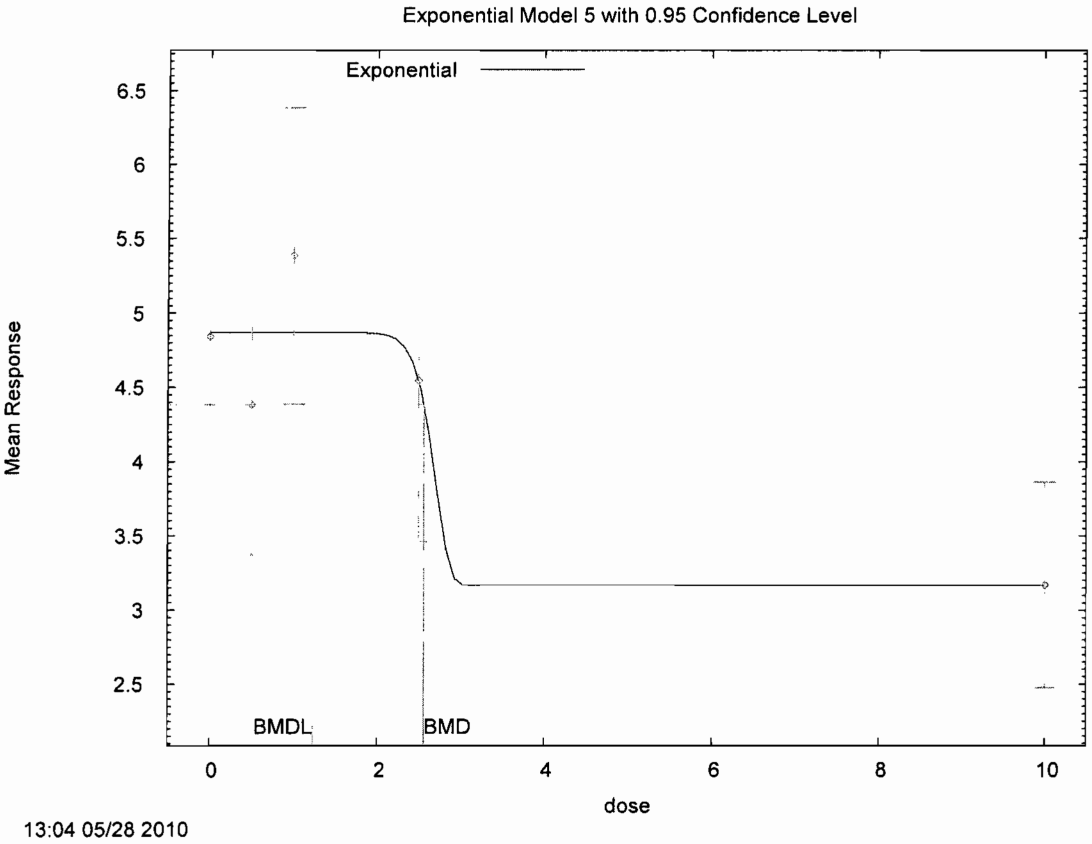



Exponential Model 3 with 0.95 Confidence Level

13:04 05/28 2010


Exponential Model 4 with 0.95 Confidence Level

13:04 05/28 2010



Acephate 46151801
pup 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:
                                             Fri May 28 12:54:49 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.
```

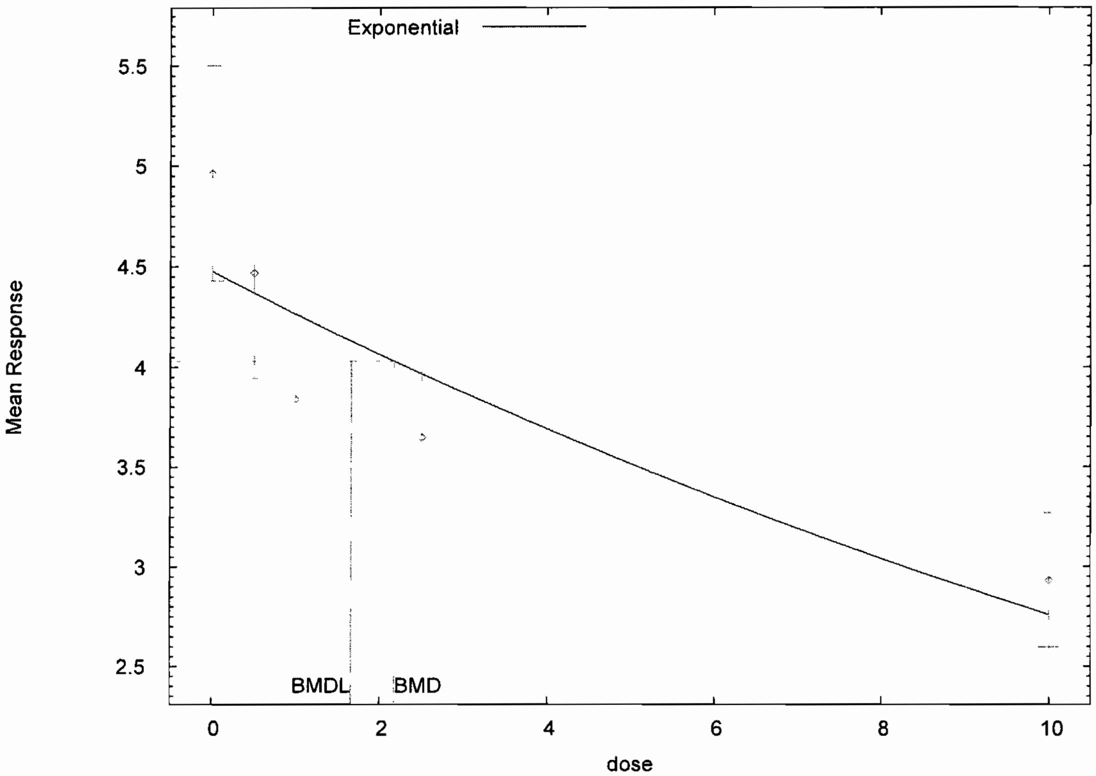
```
   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   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          -1.16404         -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
```

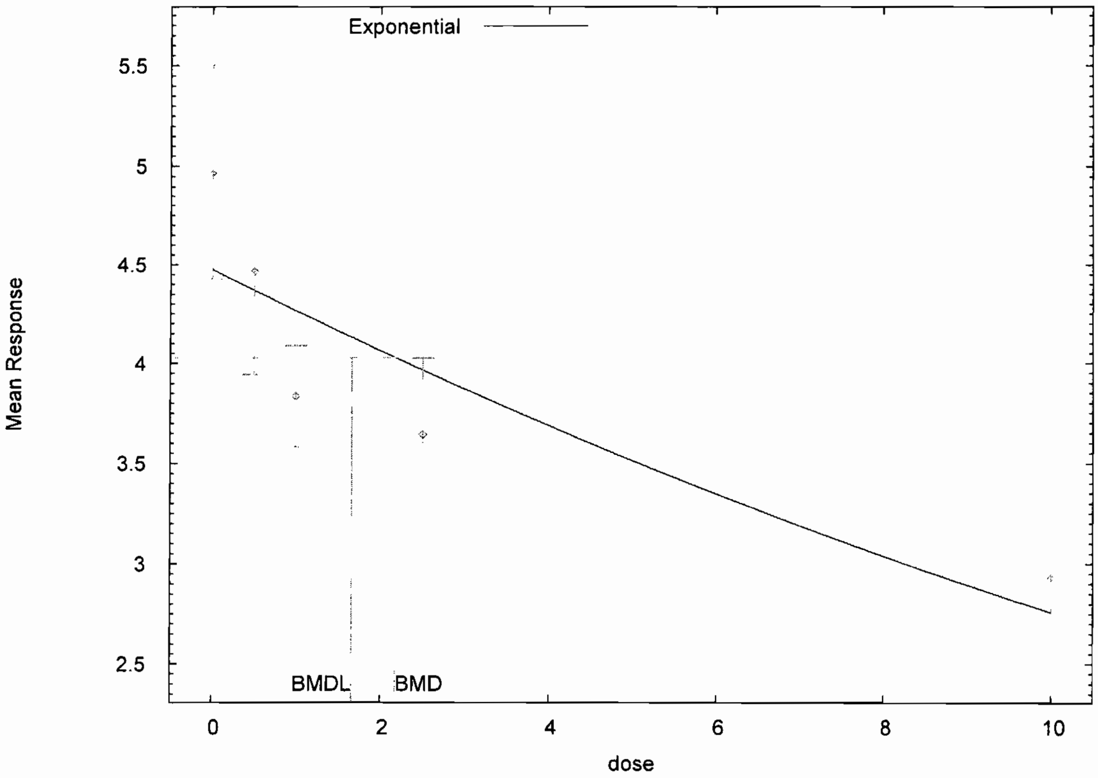
```
    to adequately describe the data.

    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

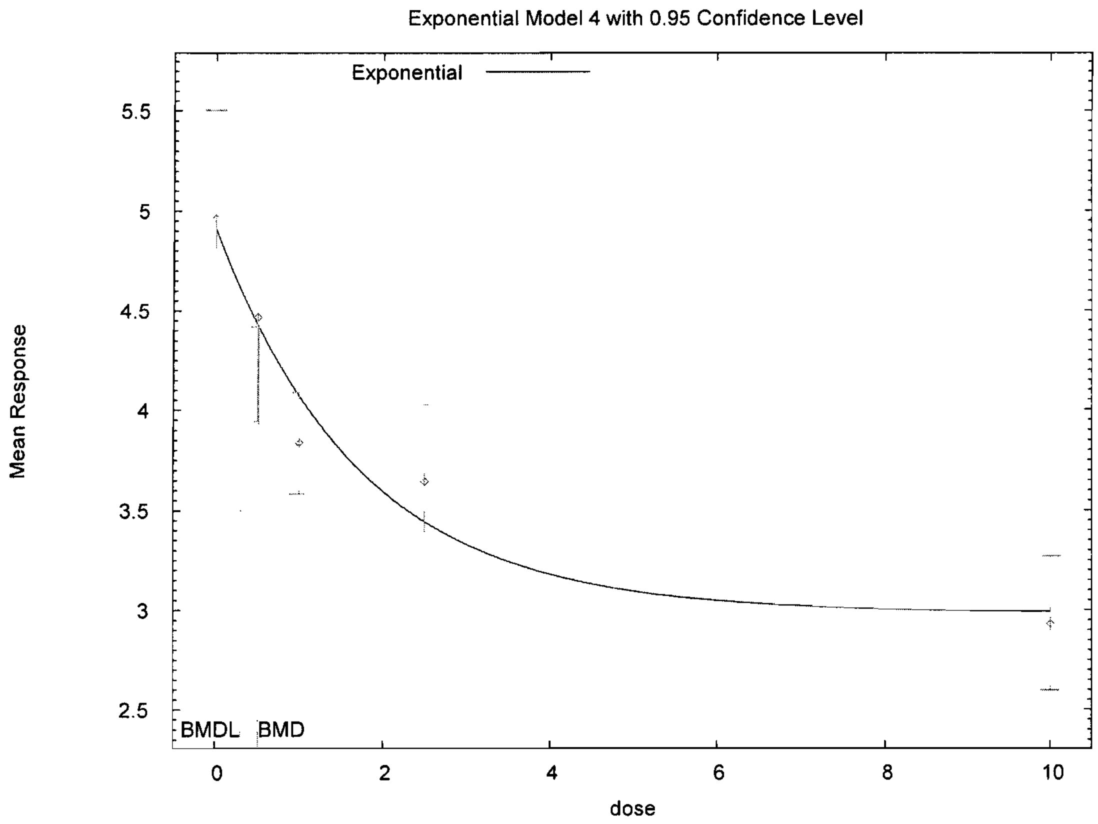


12:54 05/28 2010

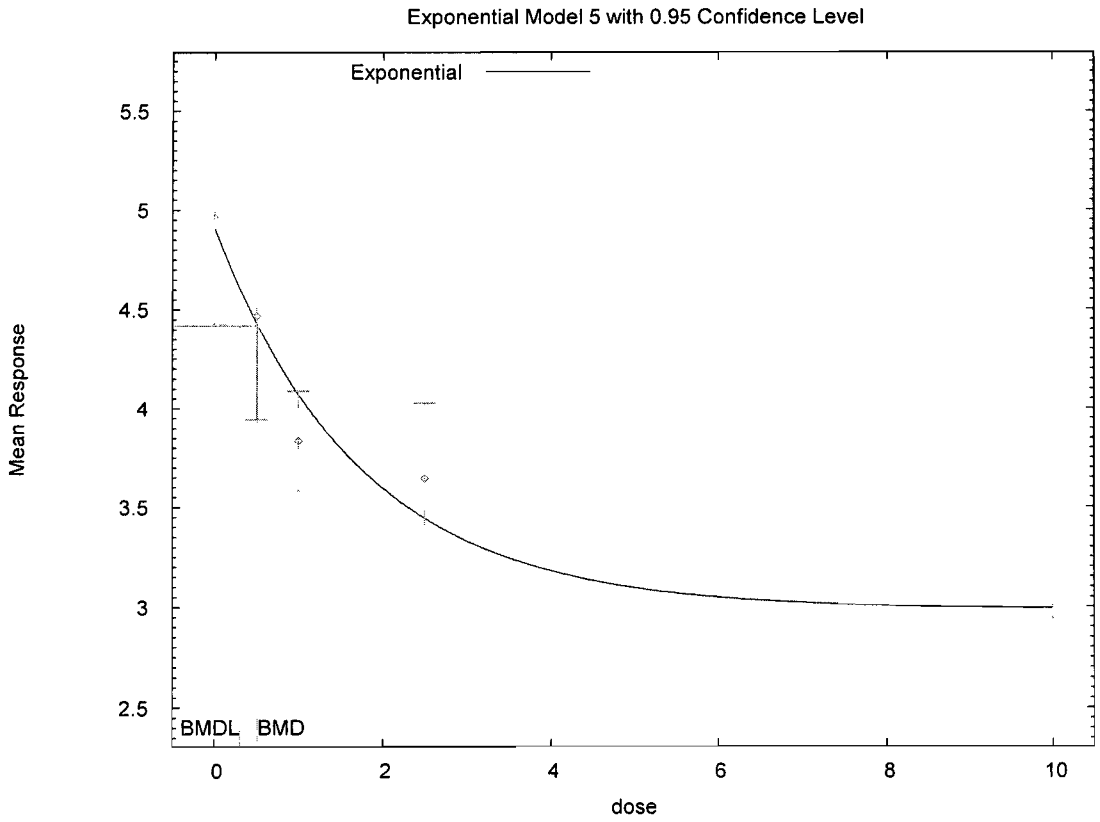
Exponential Model 3 with 0.95 Confidence Level



12:54 05/28 2010



12:54 05/28 2010



12:54 05/28 2010

Acephate
MRID 46151801
Female Brain

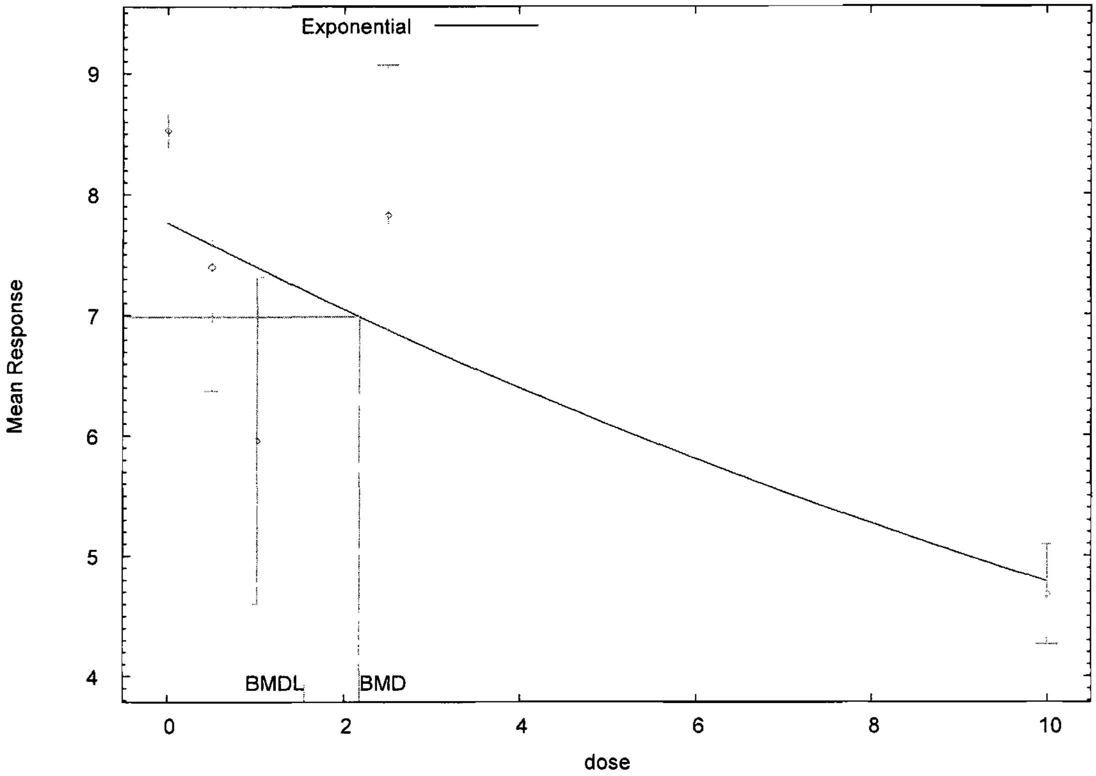
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                              Wed May 05 09:09:48 2010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

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

   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
```

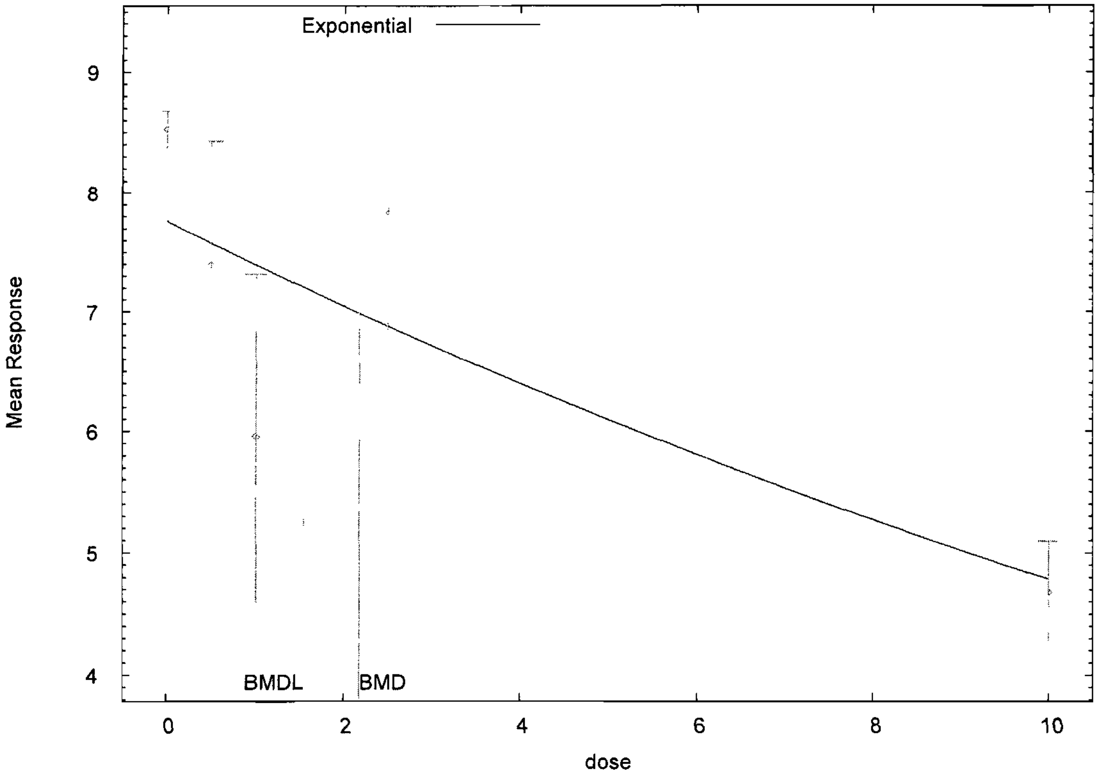
```
   The p-value for Test 1 is less than .05.  There appears to be a
   difference between response and/or variances among the dose
   levels, it seems appropriate to model the data.

   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



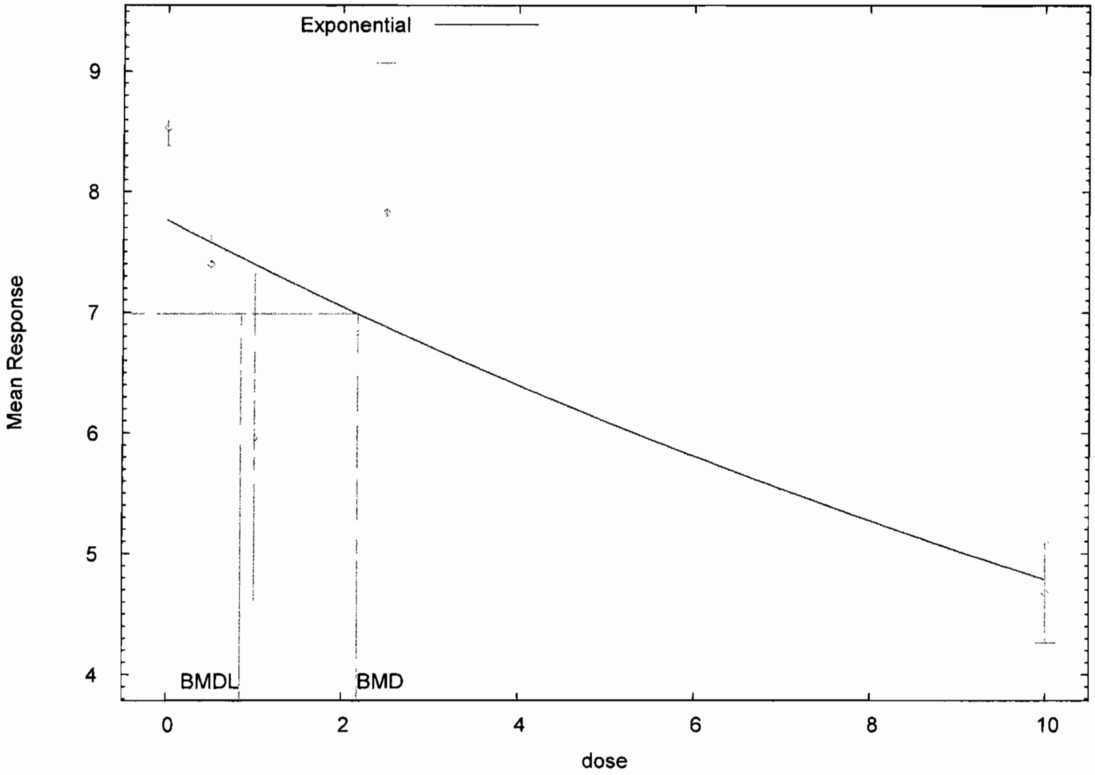
09:09 05/05 2010

Exponential Model 3 with 0.95 Confidence Level



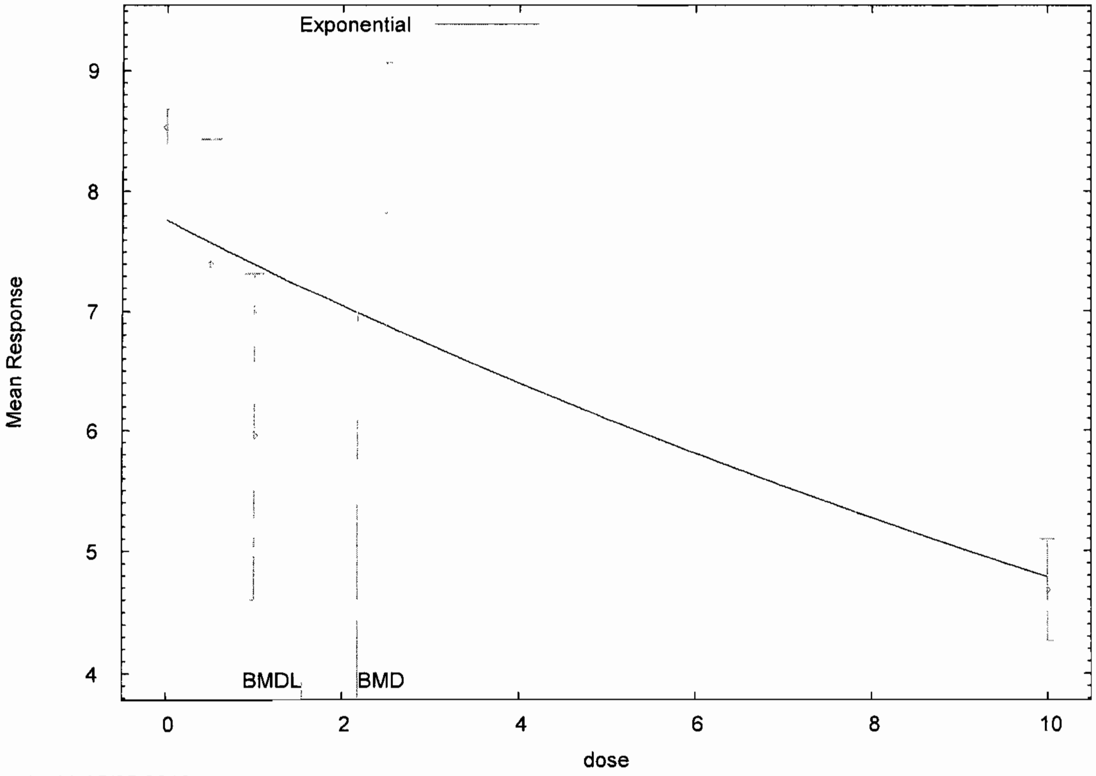
09:09 05/05 2010

Exponential Model 4 with 0.95 Confidence Level



09:09 05/05 2010

Exponential Model 5 with 0.95 Confidence Level



09:09 05/05 2010

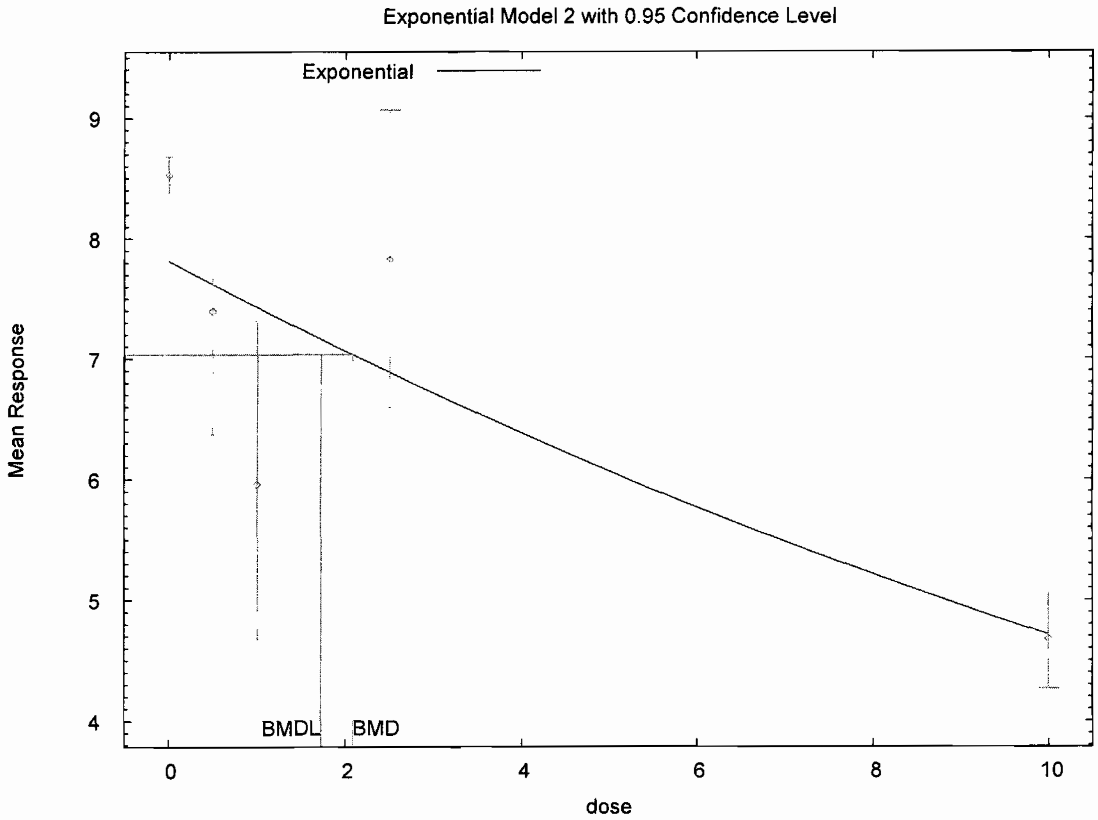
Acephate
MRID 46151801
Female Brain

```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                            Thu May 06 08:30:20 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          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
```

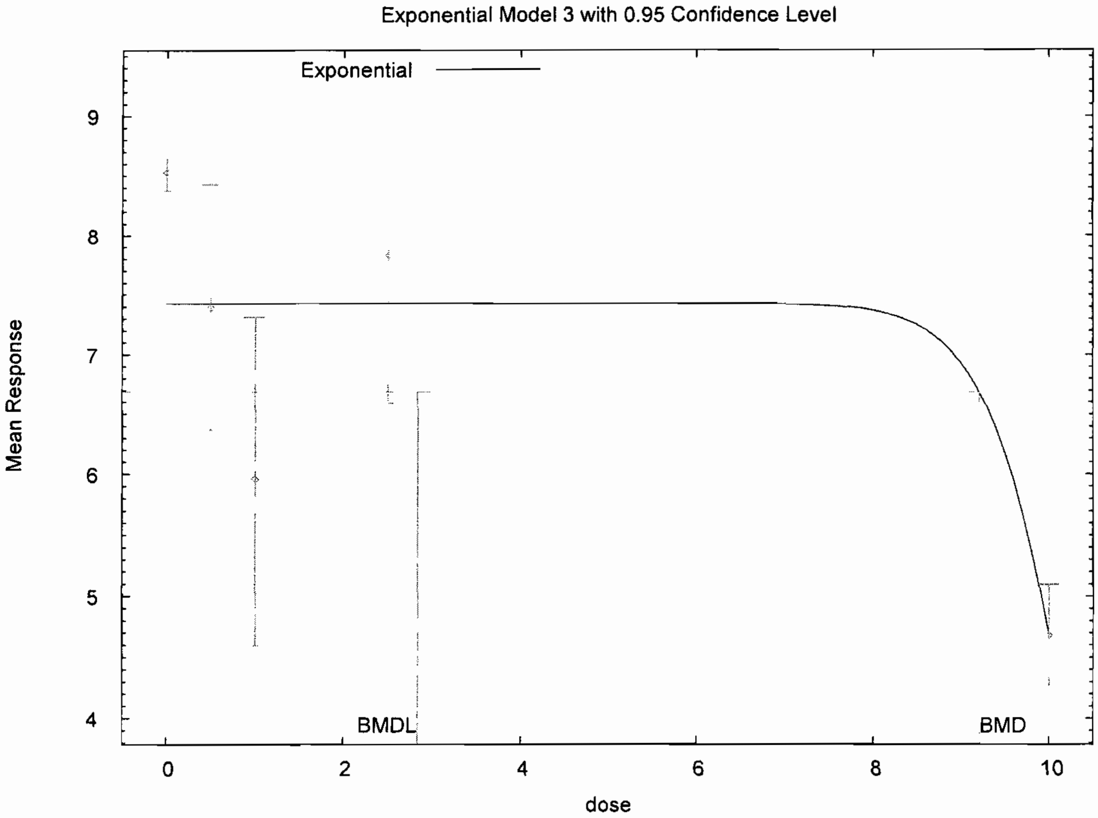
```
                              Parameter Estimates by Model

     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
```

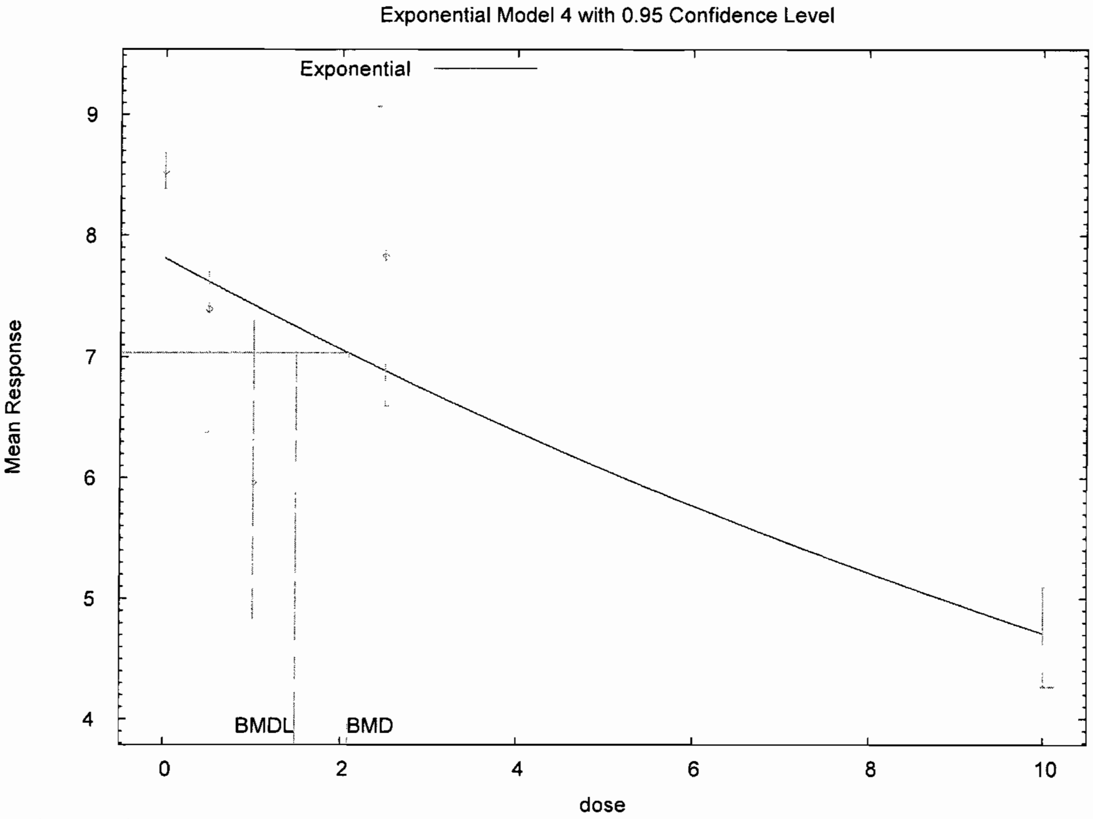
```
   difference between response and/or variances among the dose
   levels, it seems appropriate to model the data.

   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
```



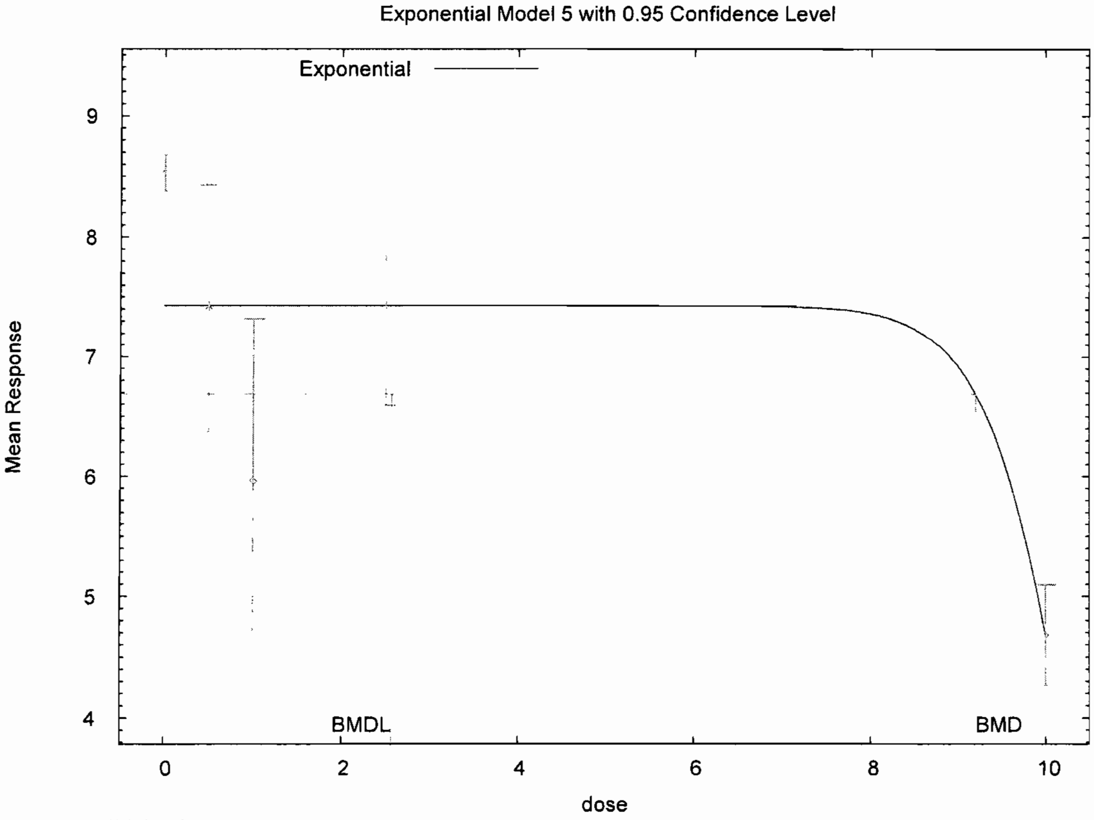
08:30 05/06 2010



08:30 05/06 2010



08:30 05/06 2010



08:30 05/06 2010

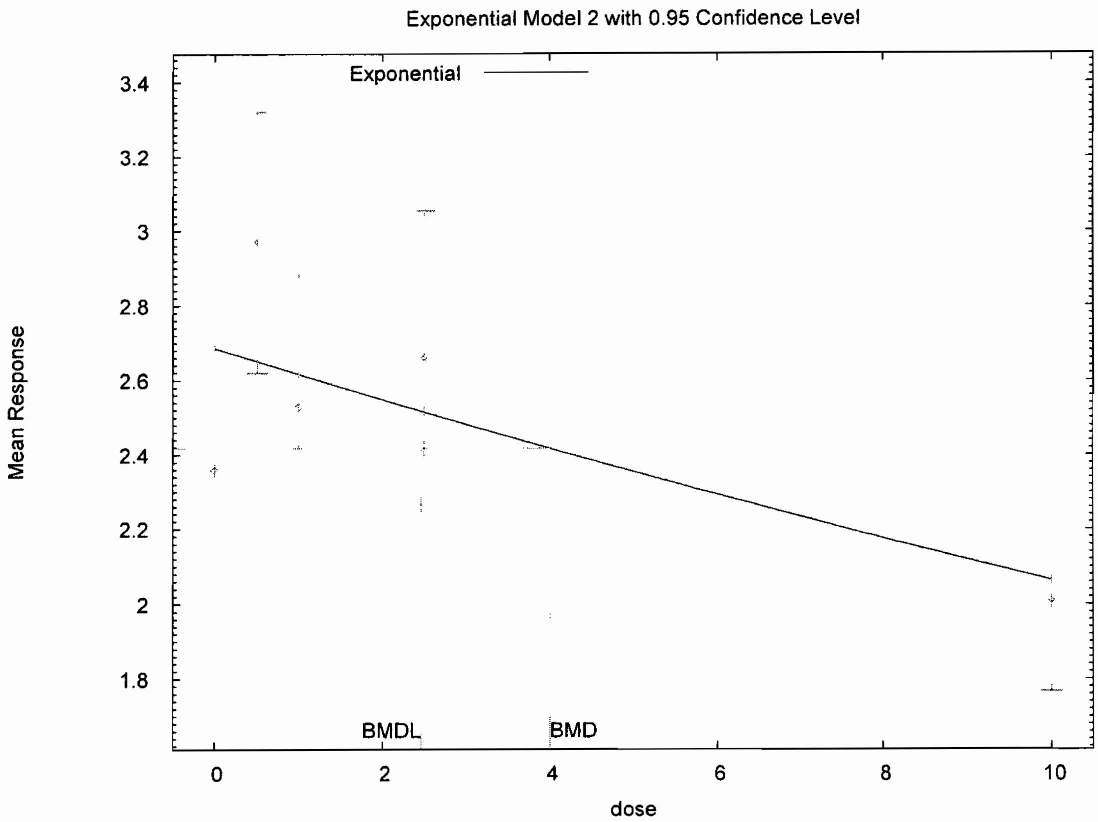
Acephate
MRID 46151801
Female RBC ChE

```
 ====================================================================
        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
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   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
```

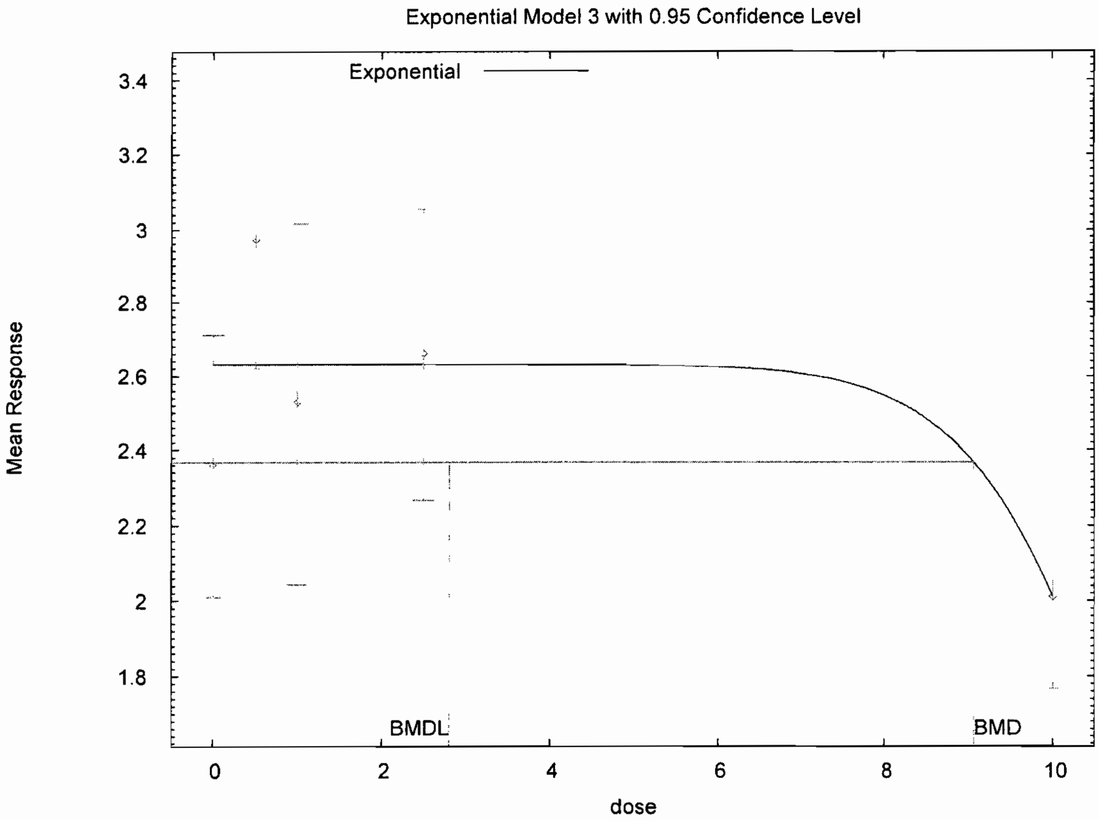
```
      (S) = Specified


                                  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
```

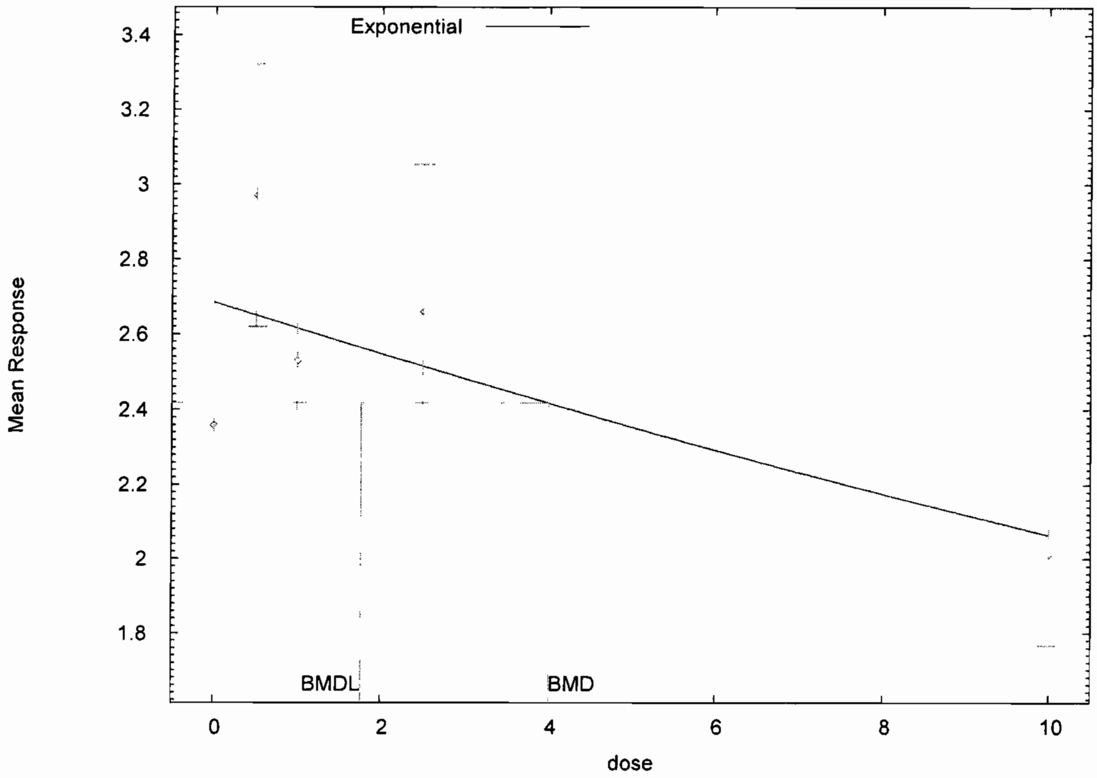


11:19 05/17 2010



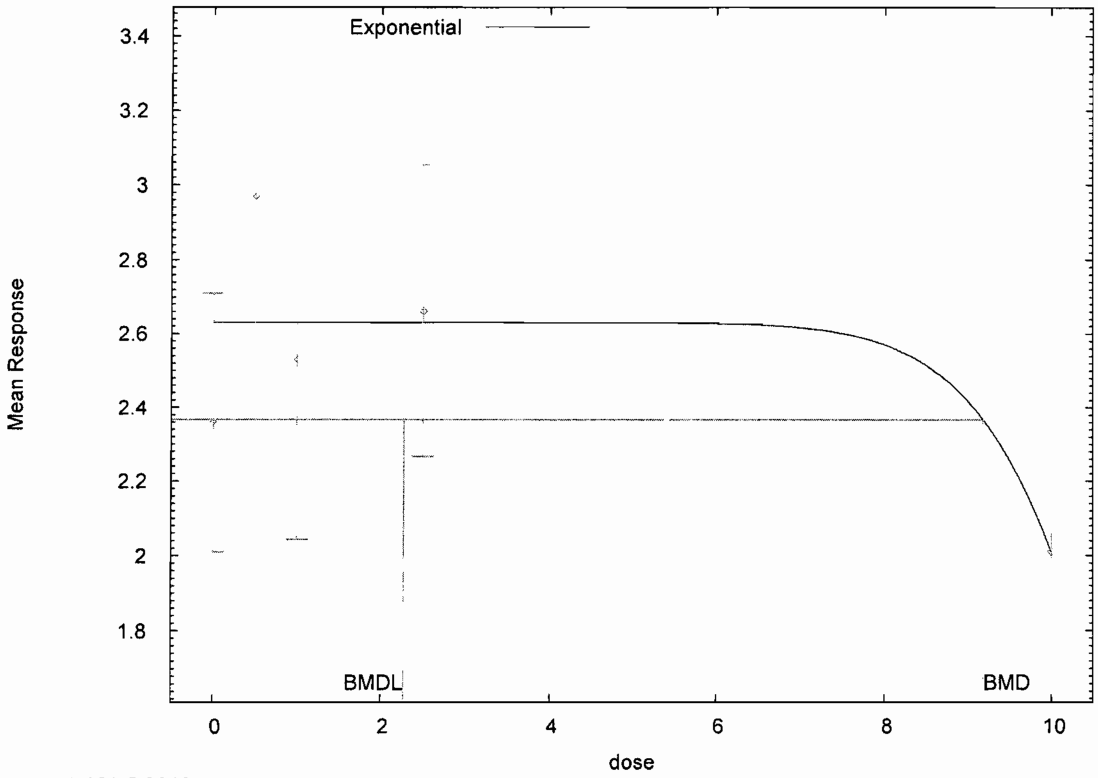
11:19 05/17 2010

Exponential Model 4 with 0.95 Confidence Level



11:19 05/17 2010

Exponential Model 5 with 0.95 Confidence Level



11:19 05/17 2010

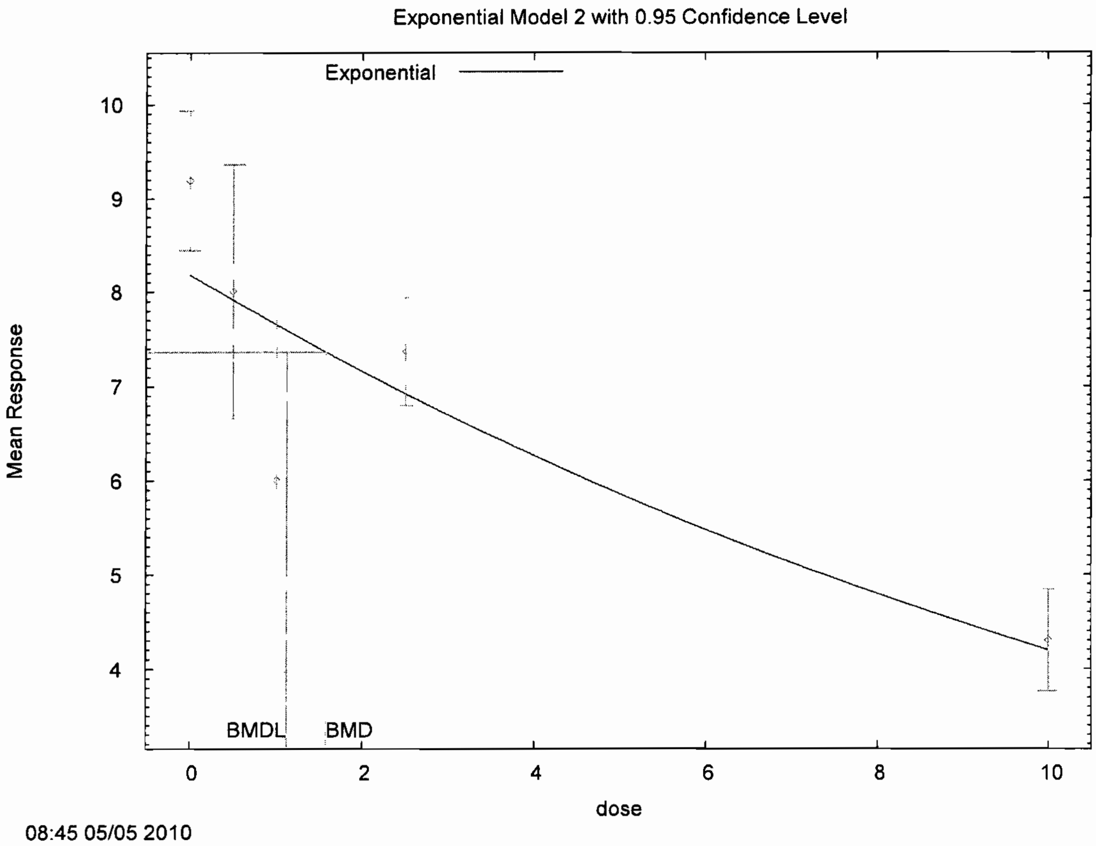
Acephate
MRID 46151801
Male Brain ChE

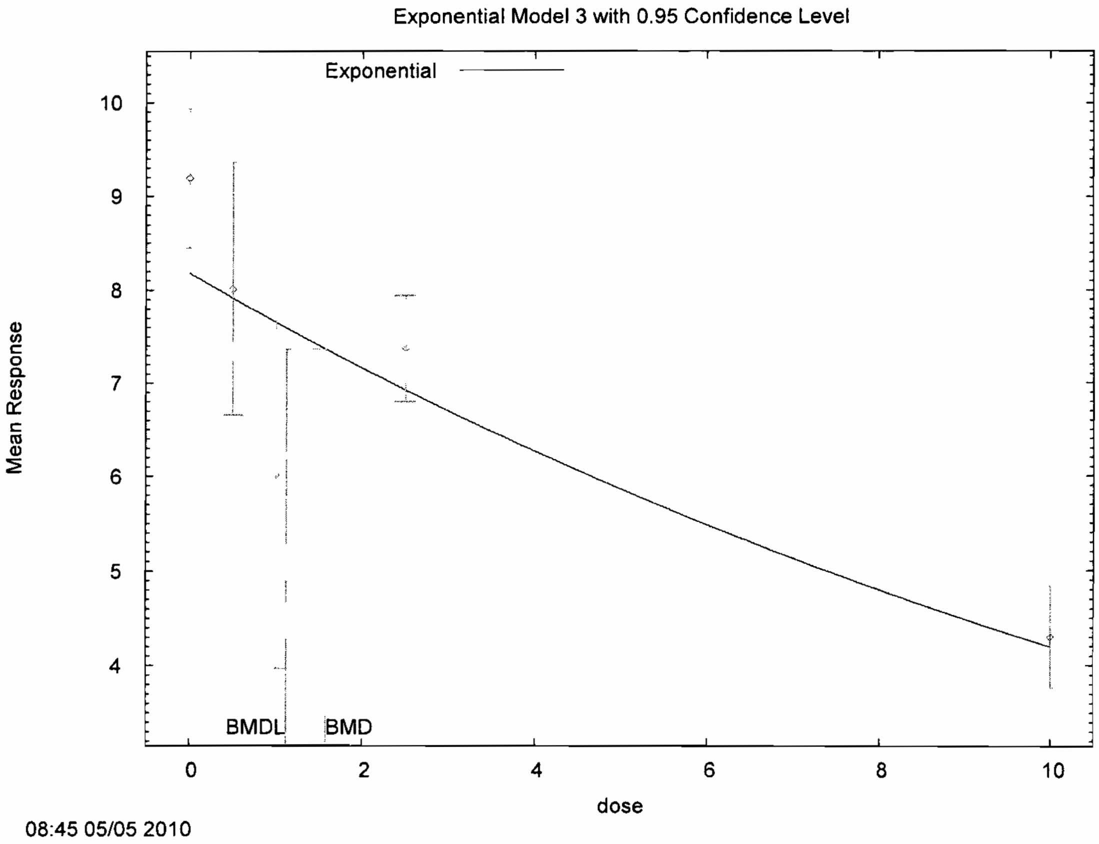
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                             Wed May 05 08:45:16 2010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

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

   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:
```

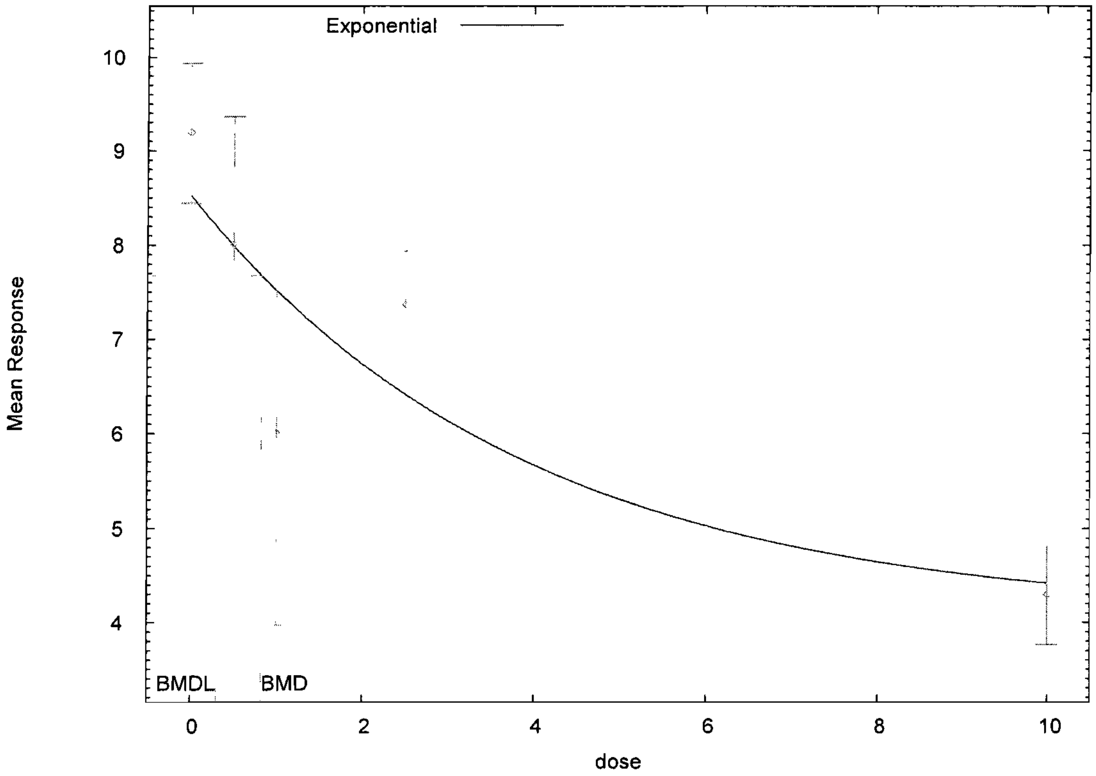
```
  Model A1:        Yij = Mu(i) + e(ij)
            Var{e(ij)} = Sigma^2

  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
10
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:45 05/05 2010

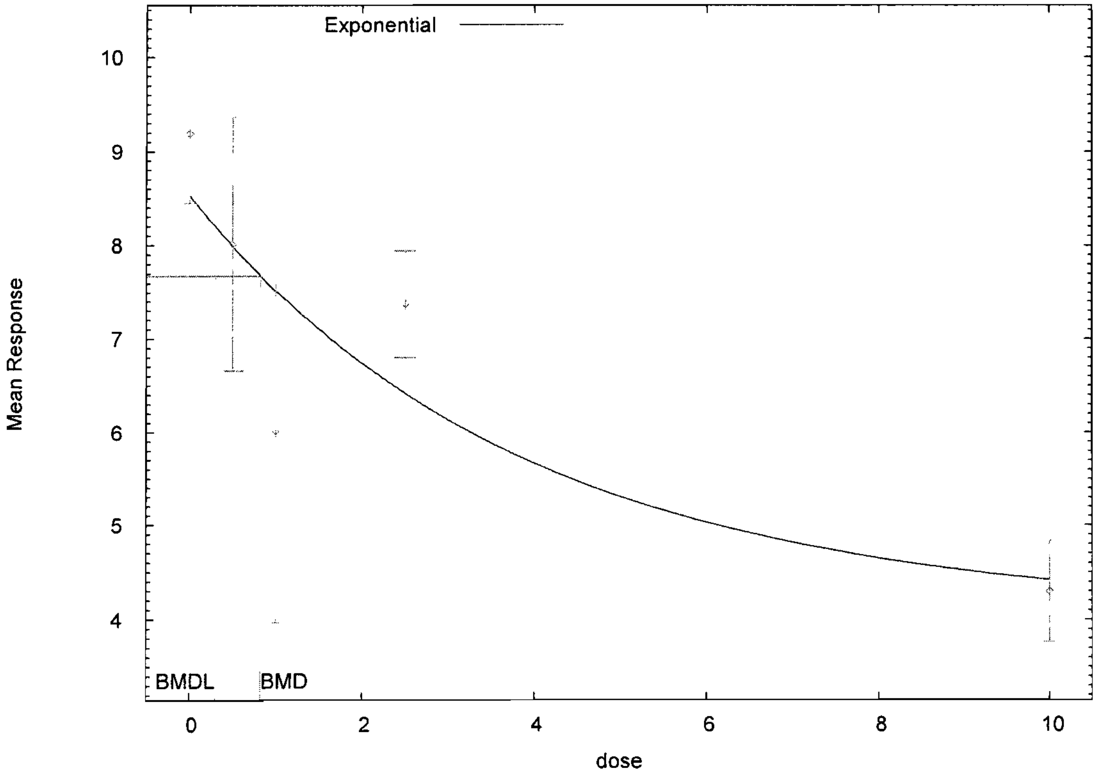

Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
10
9
8
7
6
5
4
BMDL
BMD
0
2
4
6
8
10
dose
08:45 05/05 2010

Exponential Model 4 with 0.95 Confidence Level



08:45 05/05 2010

Exponential Model 5 with 0.95 Confidence Level



08:45 05/05 2010

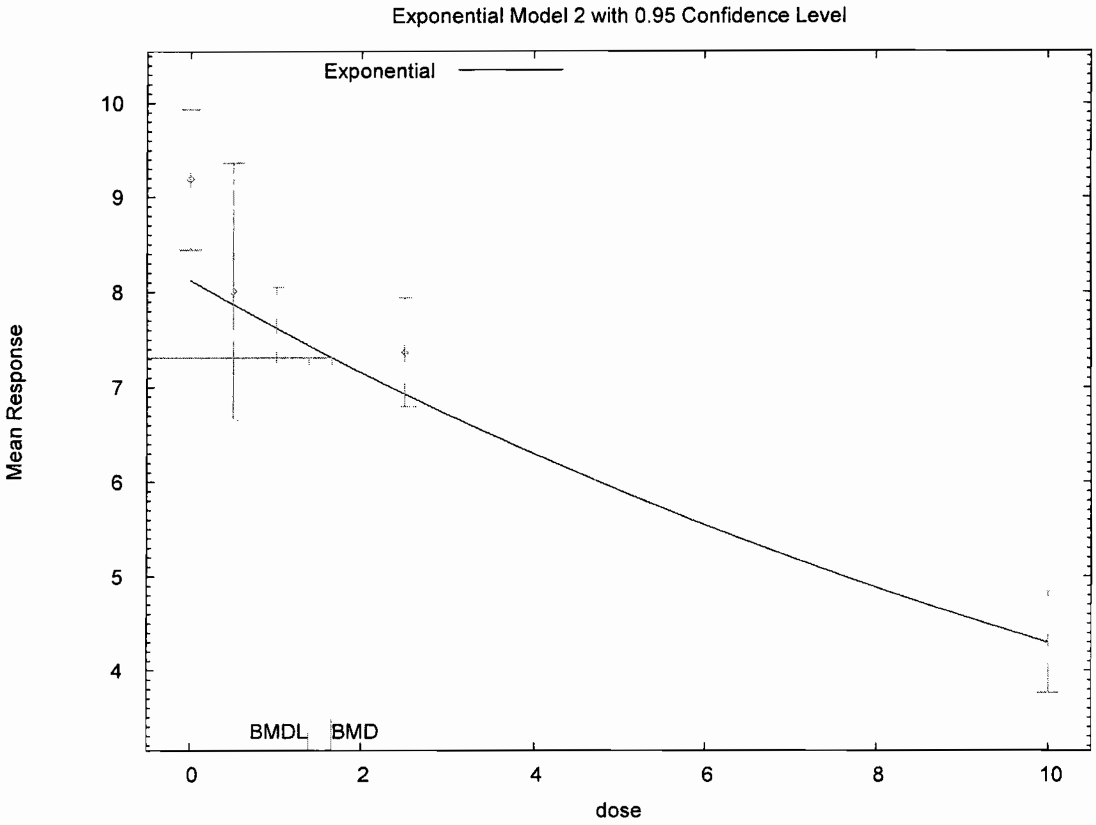
Acephate
MRID 46151801
Male Brain

```
 ====================================================================
        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
 ====================================================================

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

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

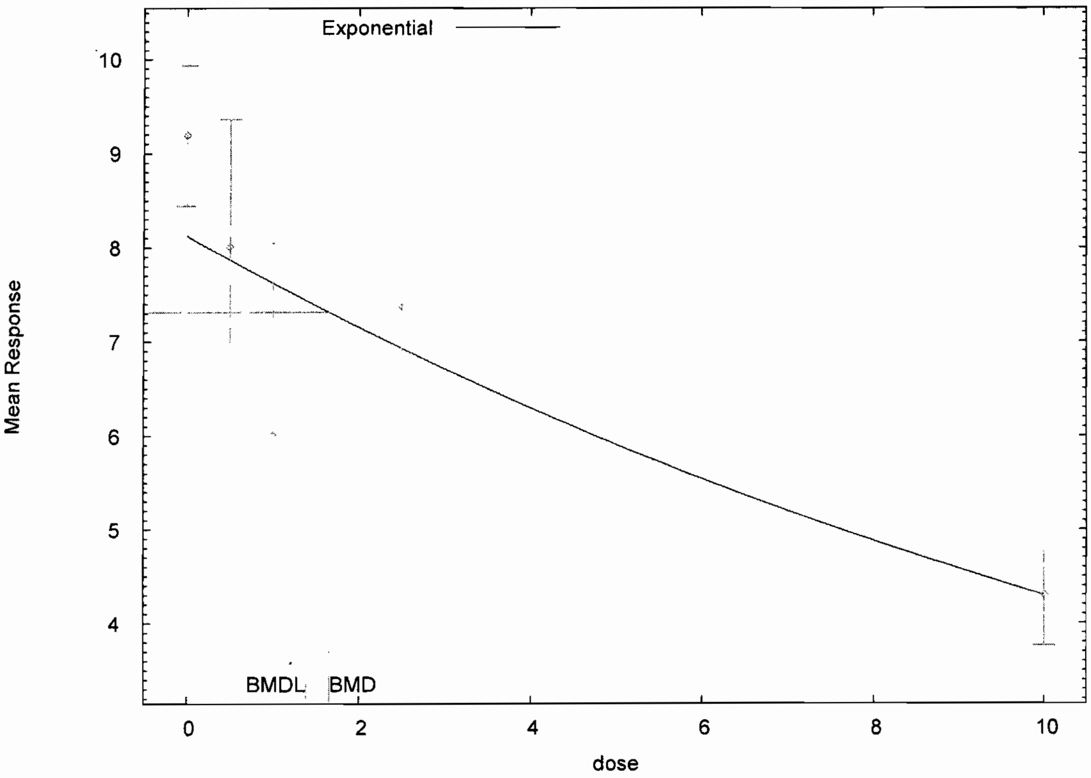
```
                 Var{e(ij)} = Sigma(i)^2

   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       -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
```



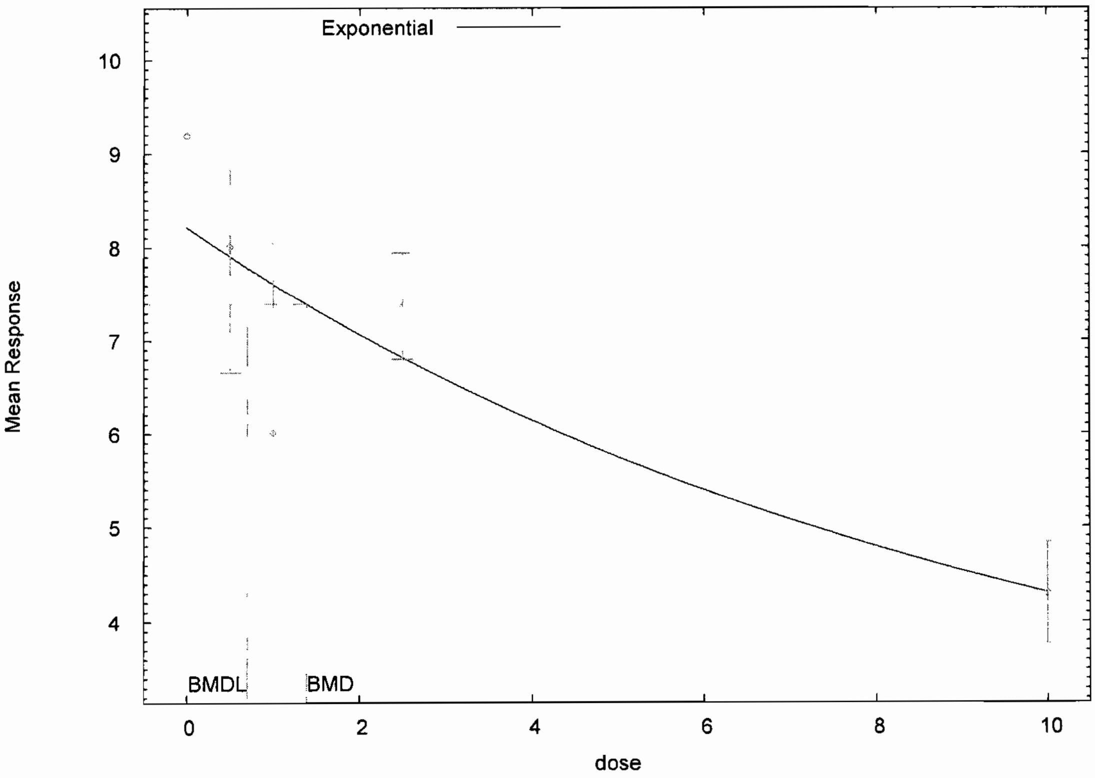
08:56 05/05 2010

Exponential Model 3 with 0.95 Confidence Level

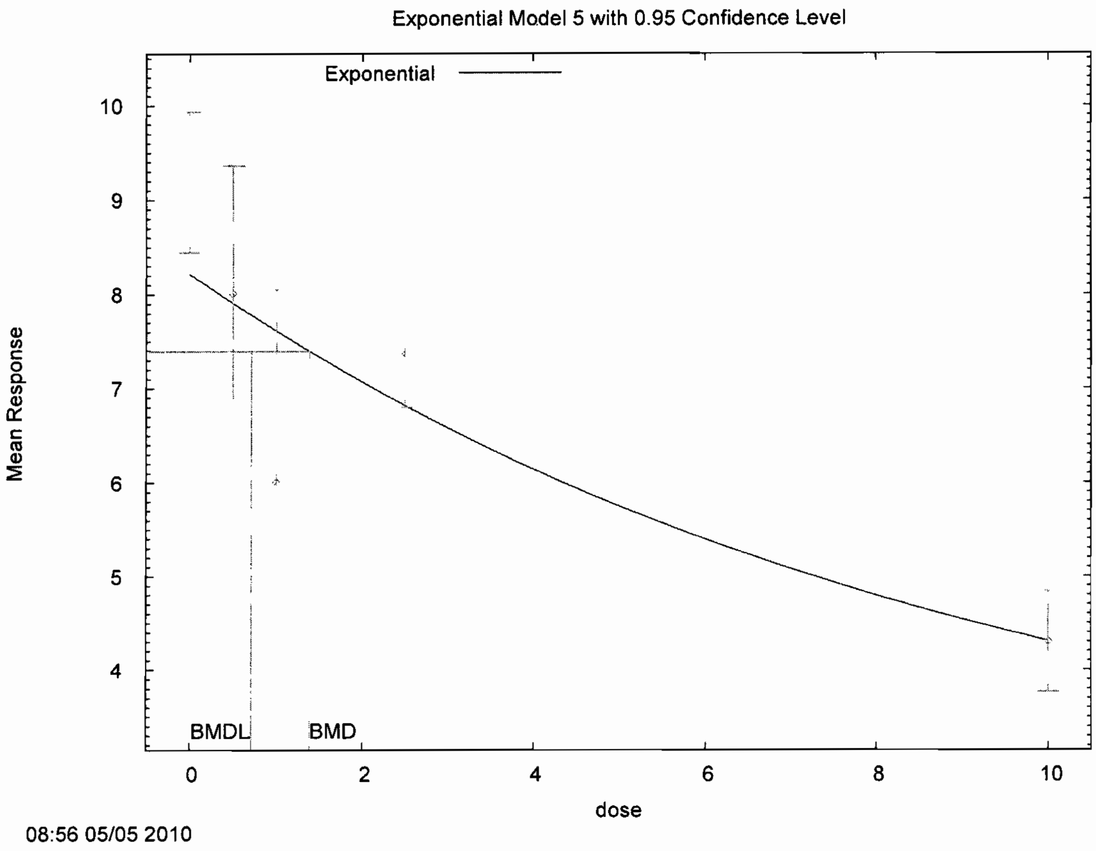


08:56 05/05 2010

Exponential Model 4 with 0.95 Confidence Level



08:56 05/05 2010



Acephate
MRID 46151801
Male RBC ChE

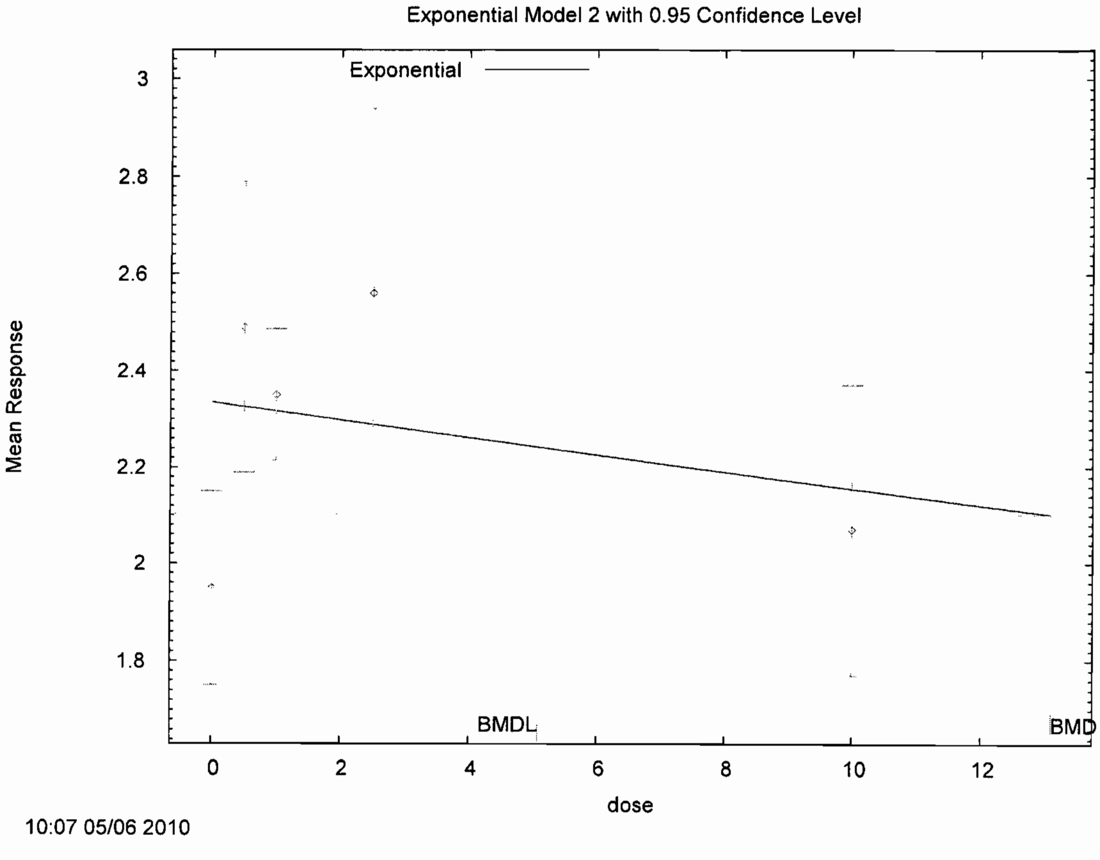
```
====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                            Thu May 06 10:07:27 2010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

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

   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.
```

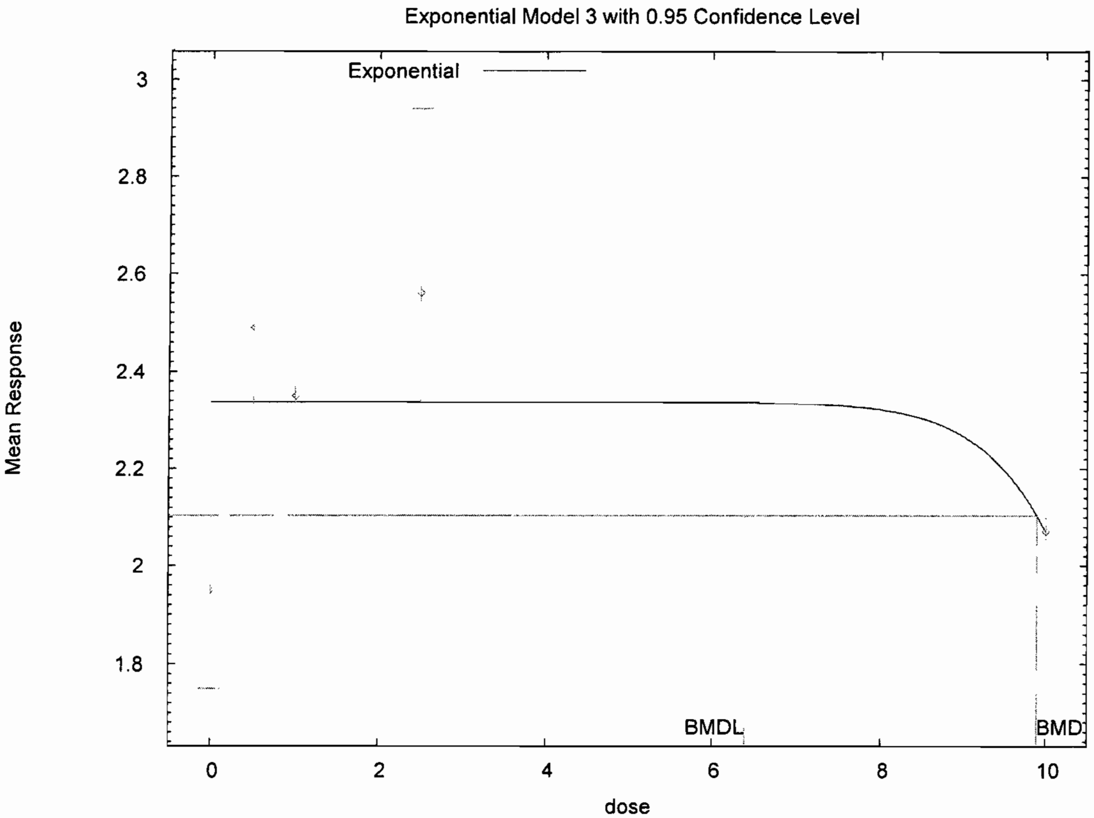
```
   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   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.
```

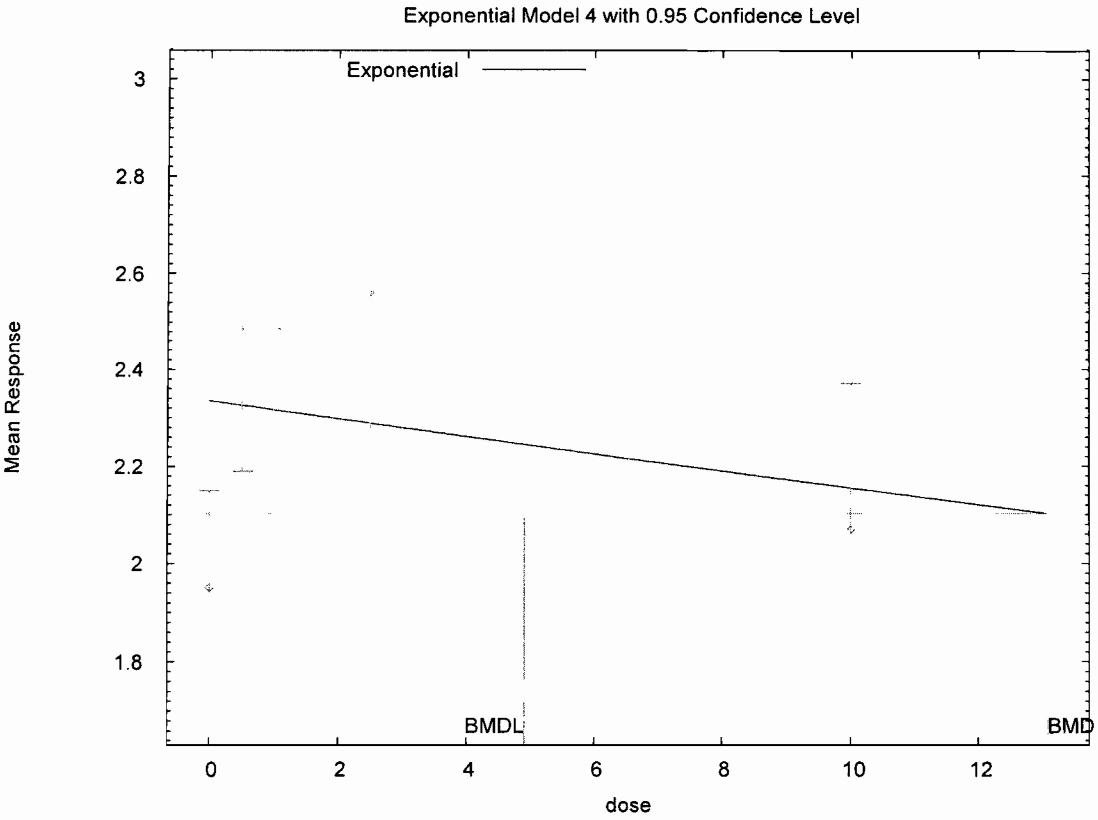
```
                            Explanation of Tests

 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
```

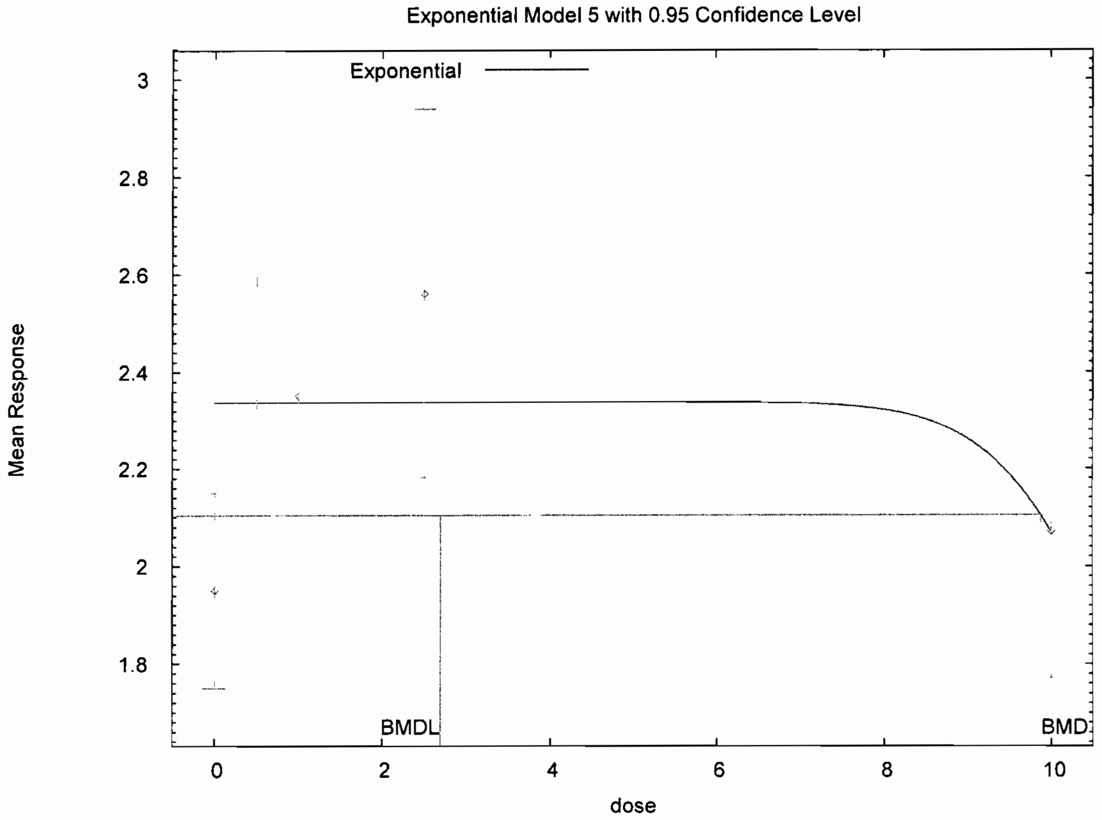




10:07 05/06 2010



10:07 05/06 2010



10:07 05/06 2010

Methamidophos; MRID 43025001
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:
                                             Mon May 17 12:38:57 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.
```

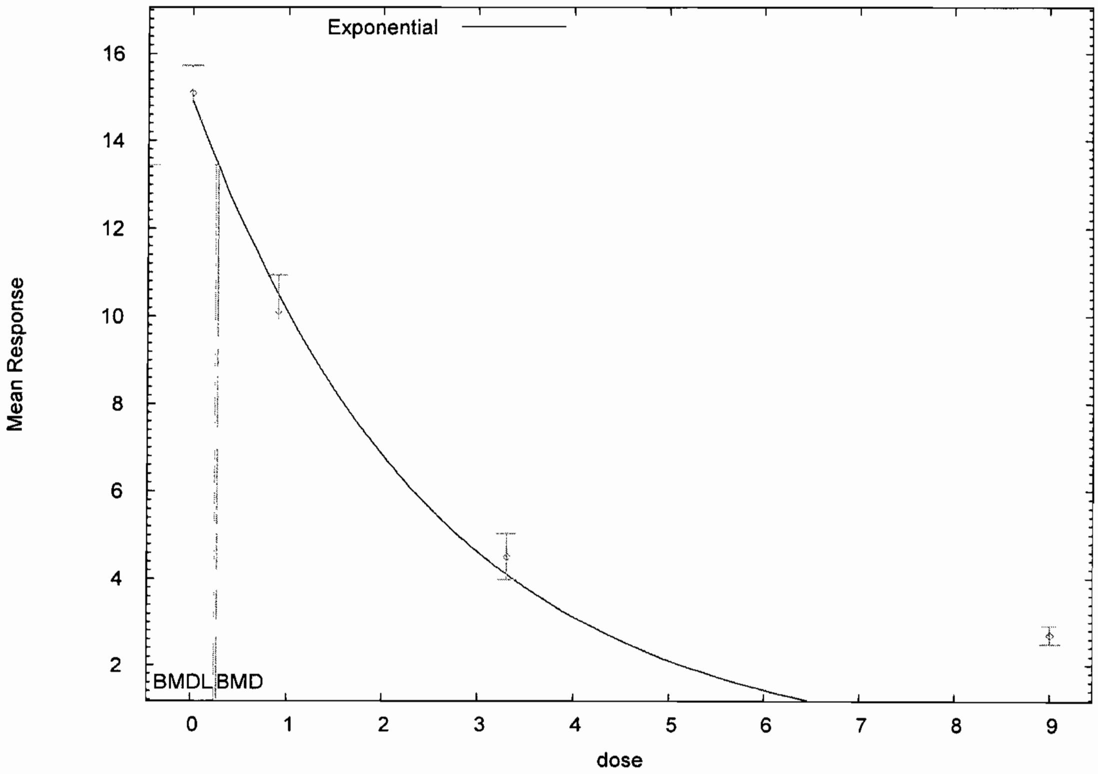
```
   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   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         -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:
```

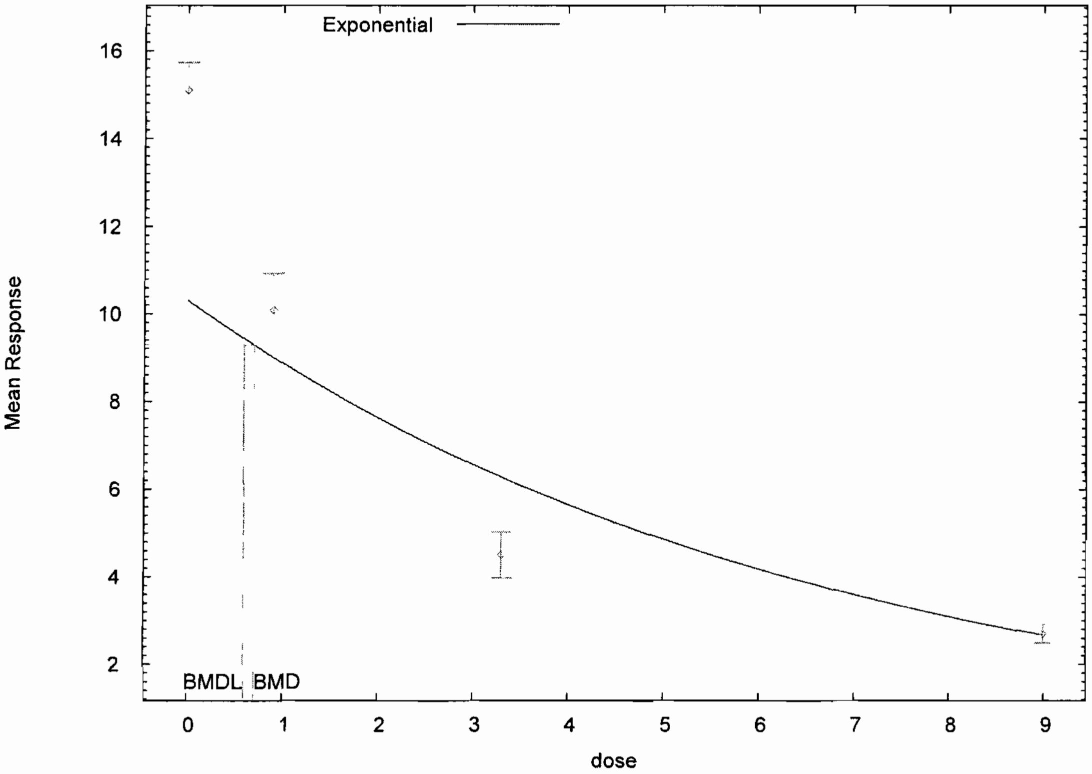
```
Specified Effect = 0.100000

       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 2 with 0.95 Confidence Level



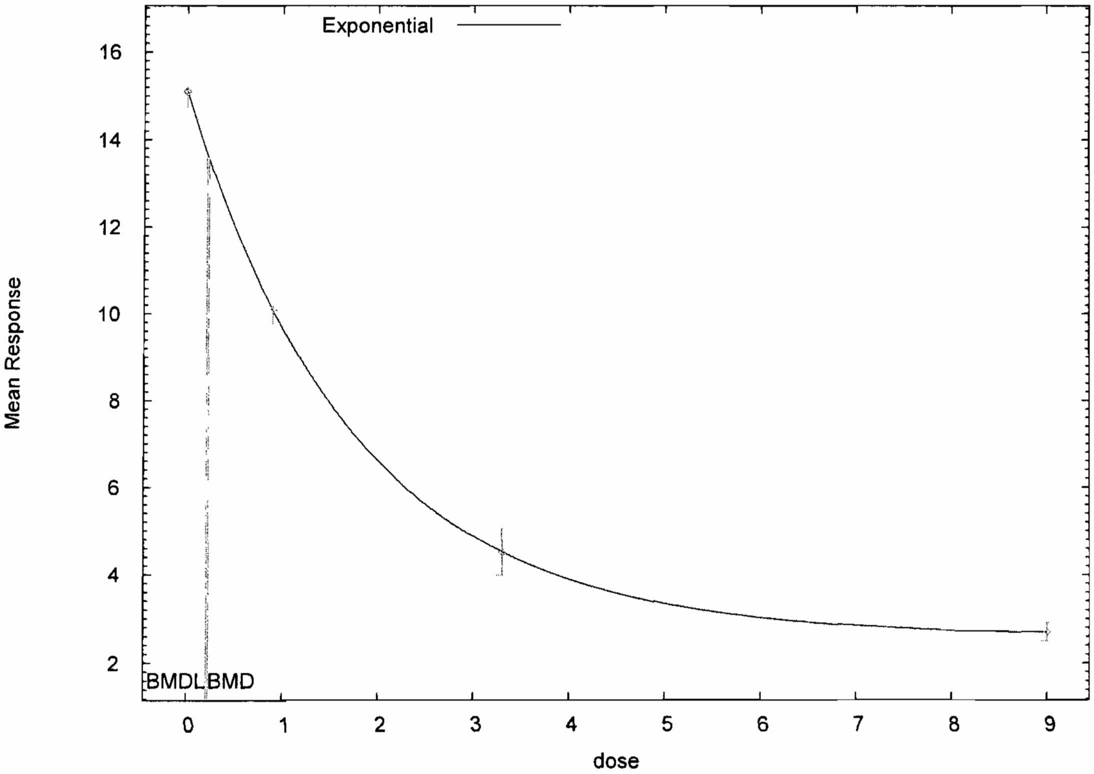
12:38 05/17 2010

Exponential Model 3 with 0.95 Confidence Level

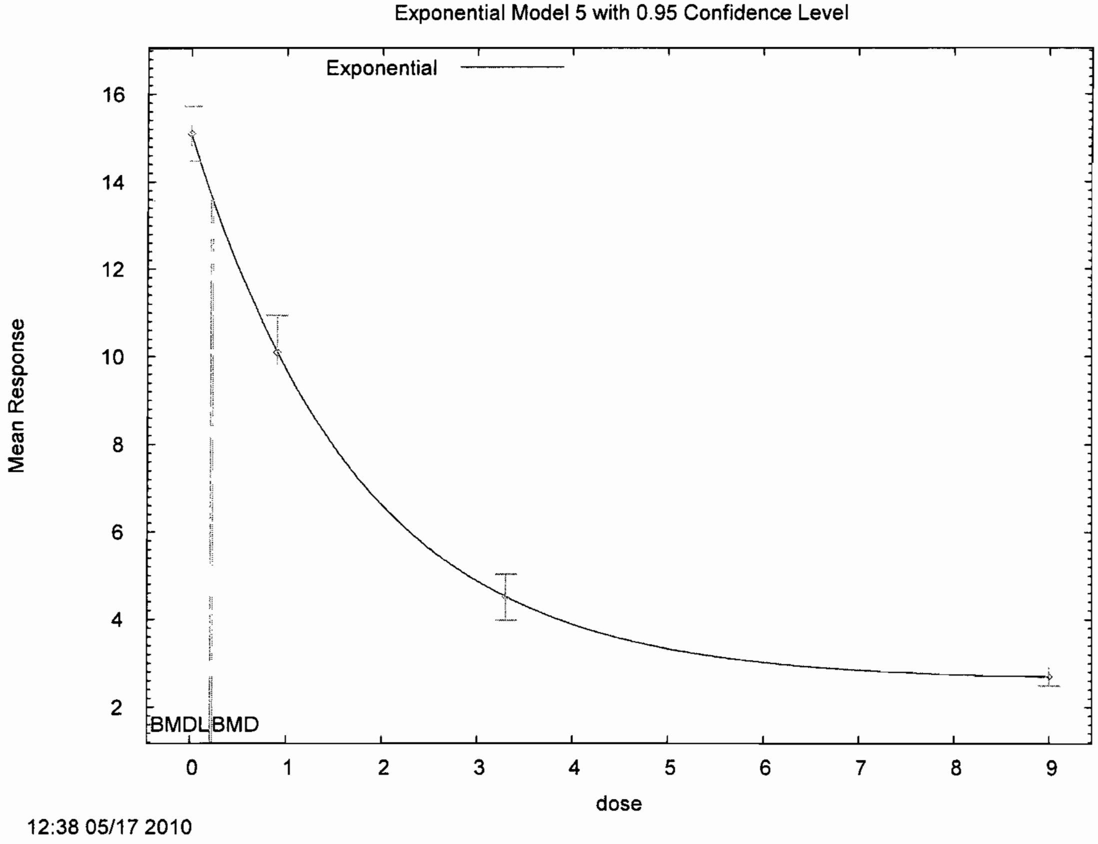


12:38 05/17 2010

Exponential Model 4 with 0.95 Confidence Level



12:38 05/17 2010



Methamidophos; MRID 46594003
Adult 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:
                                              Mon May 10 11:45:51 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;
```

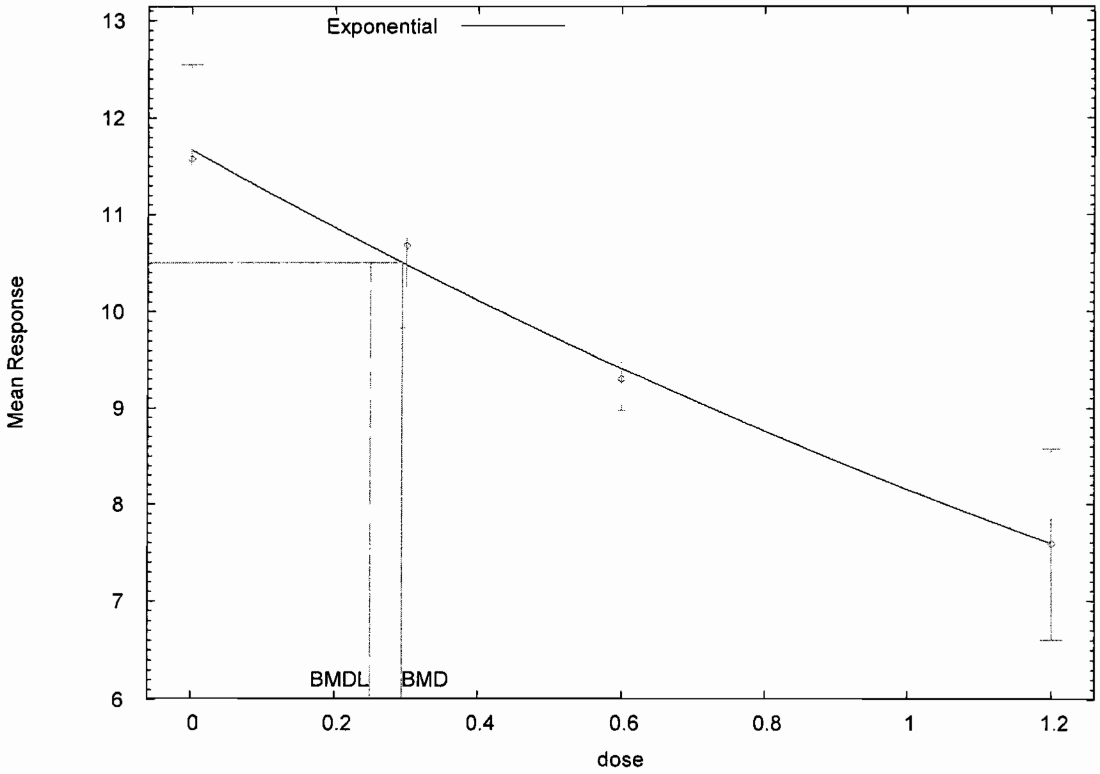
```
         sign = +1 for increasing trend in data;
         sign = -1 for decreasing trend.

     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]))
   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.
```

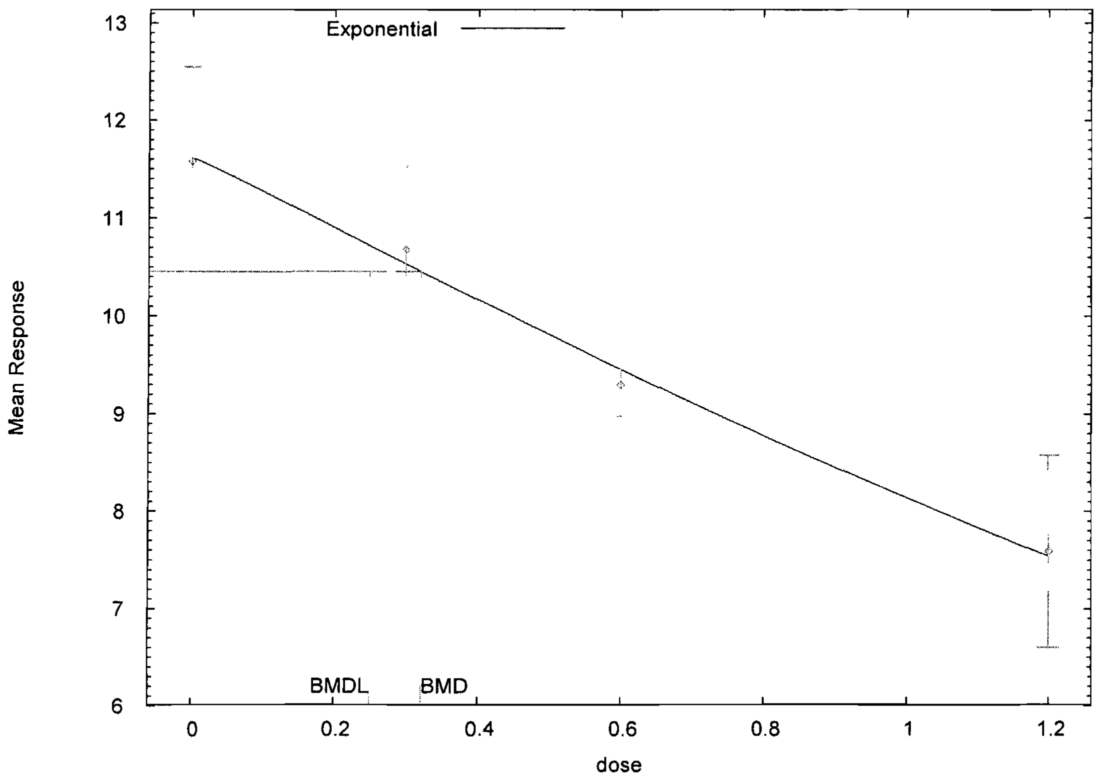
```
     The p-value for Test 7b is greater than .05.  Model 5 does
     not seem to fit the data better than Model 3.

     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 2 with 0.95 Confidence Level



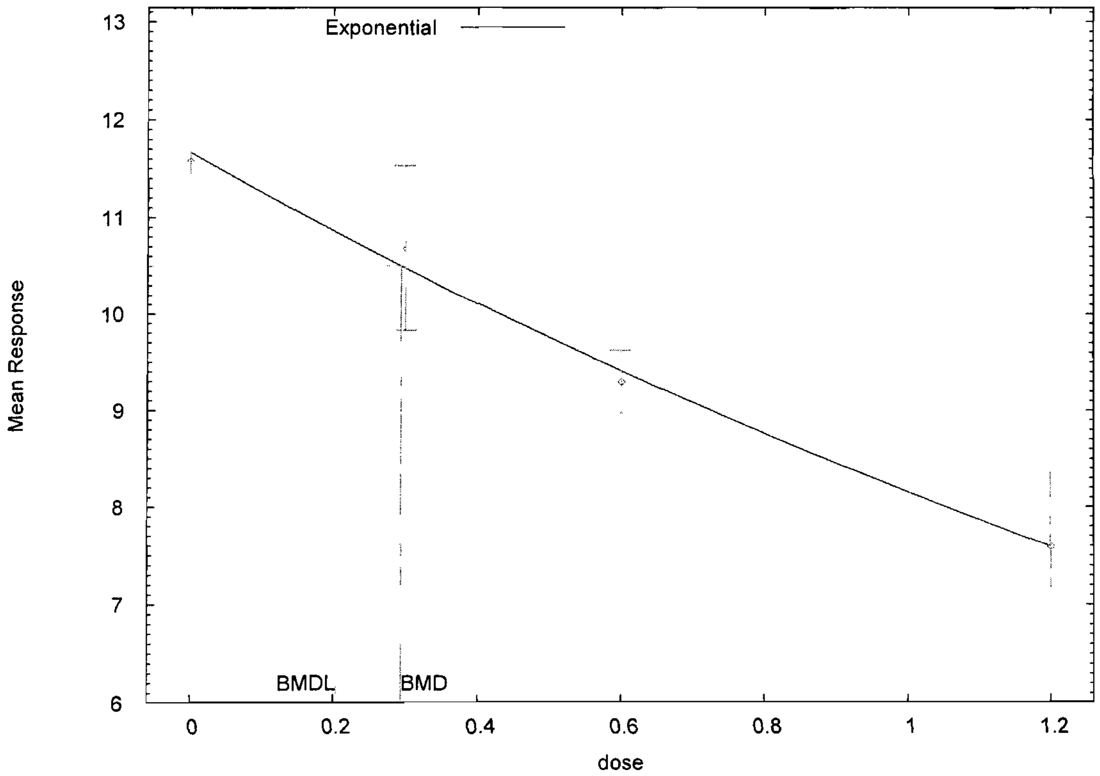
11:45 05/10 2010

Exponential Model 3 with 0.95 Confidence Level

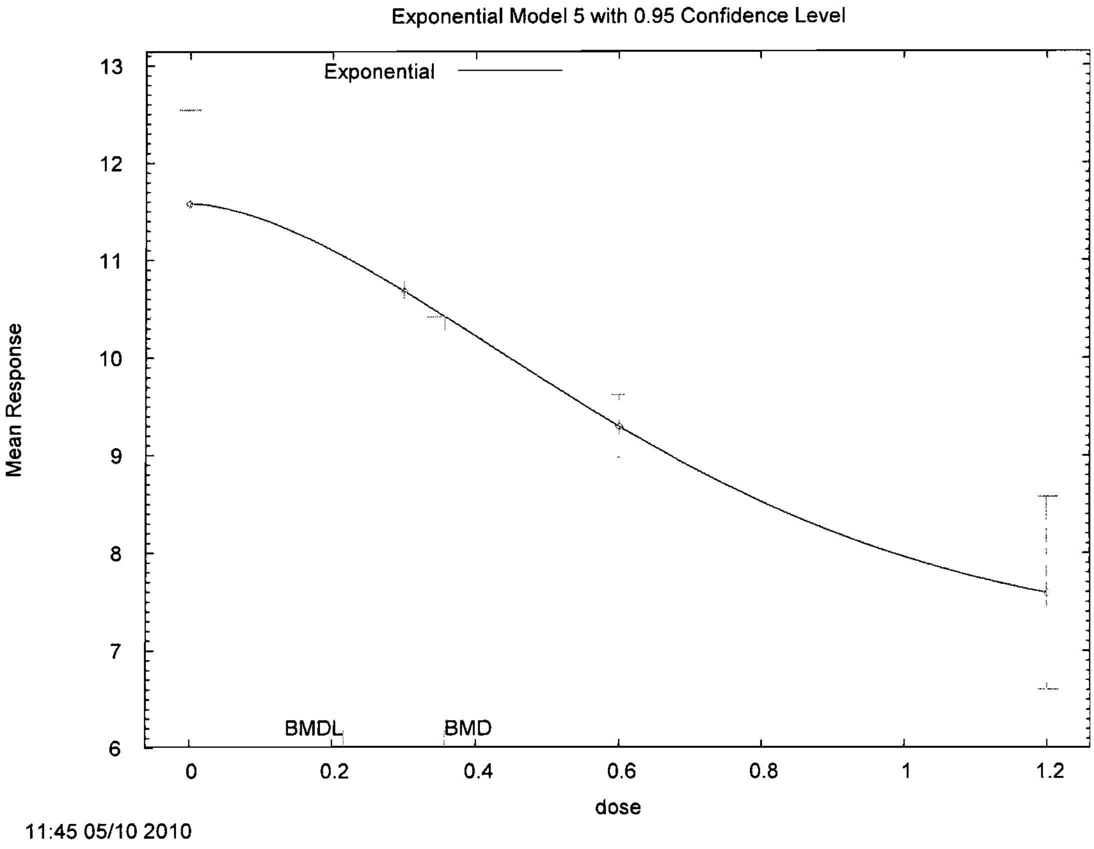


11:45 05/10 2010

Exponential Model 4 with 0.95 Confidence Level



11:45 05/10 2010



Methamidophos; MRID 46594003
Pup Male Brain ChE

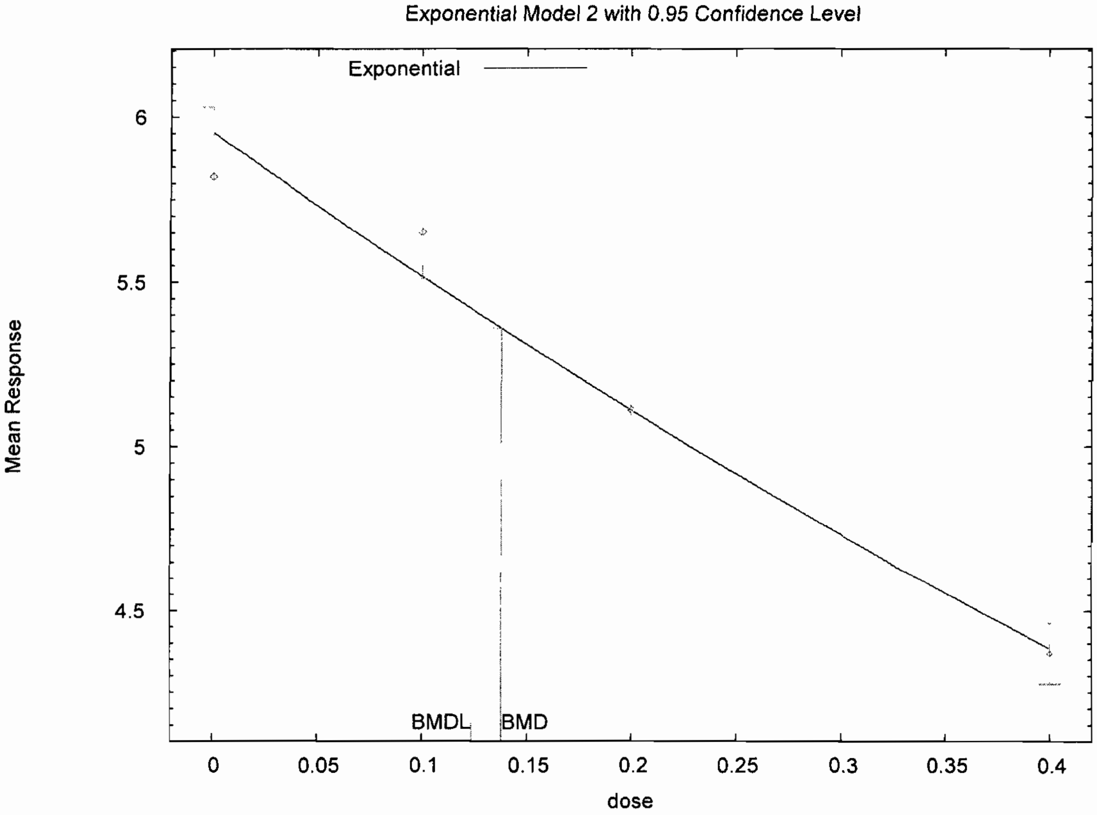
```
 ====================================================================
        Exponential Model. (Version: 1.61;  Date: 7/24/2009)
        Input Data File: C:\Usepa\BMDS21\Data\exp_test_Setting.(d)
        Gnuplot Plotting File:
                                                     Tue May 11 12:34:02 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          -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)
```

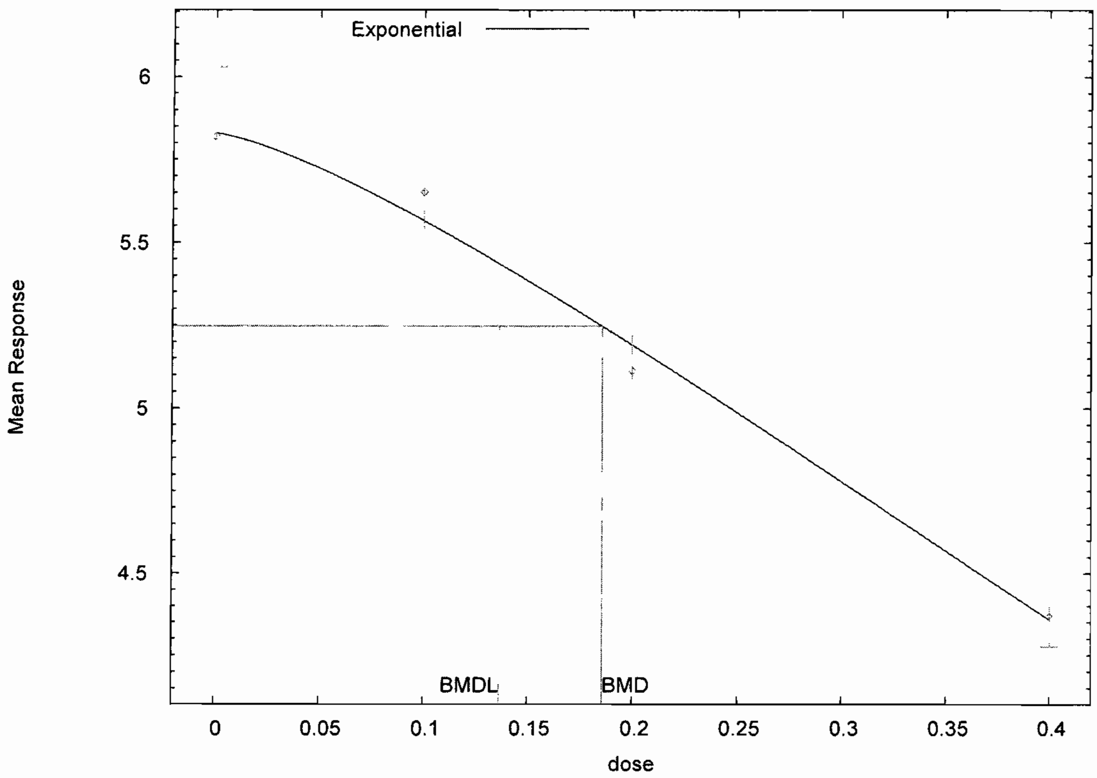
```
Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

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
```



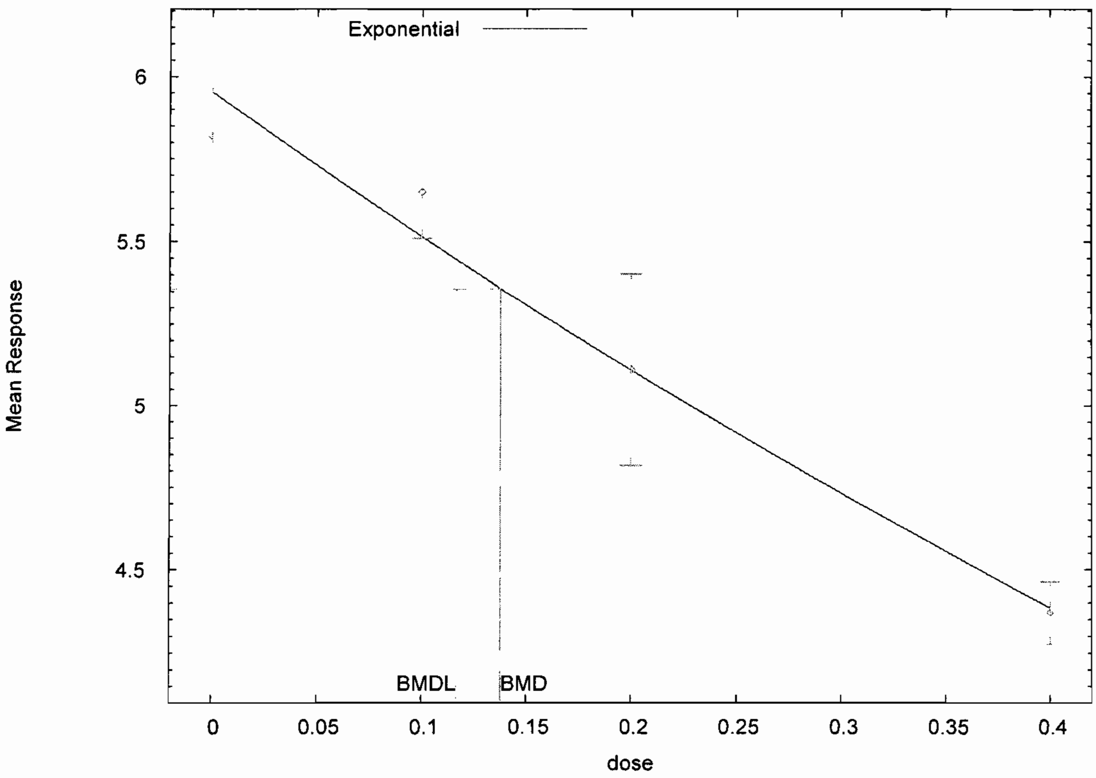
12:34 05/11 2010

Exponential Model 3 with 0.95 Confidence Level

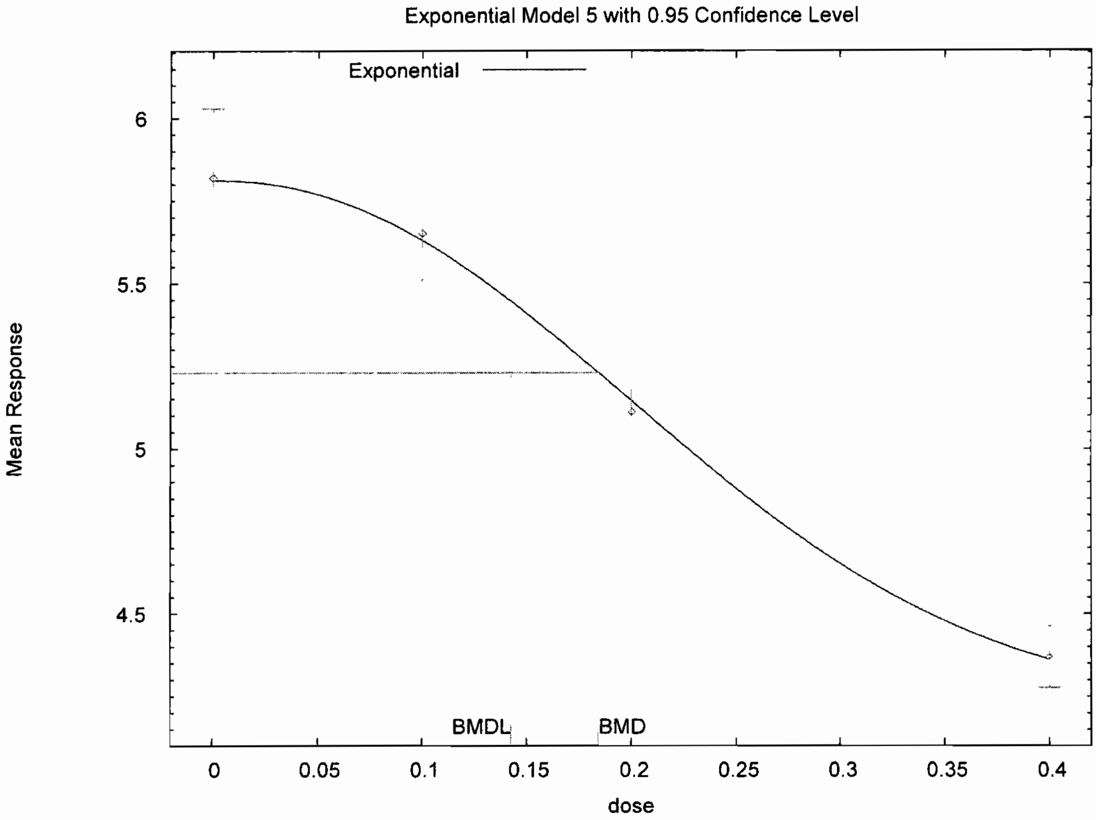


12:34 05/11 2010

Exponential Model 4 with 0.95 Confidence Level



12:34 05/11 2010



12:34 05/11 2010

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}]
```

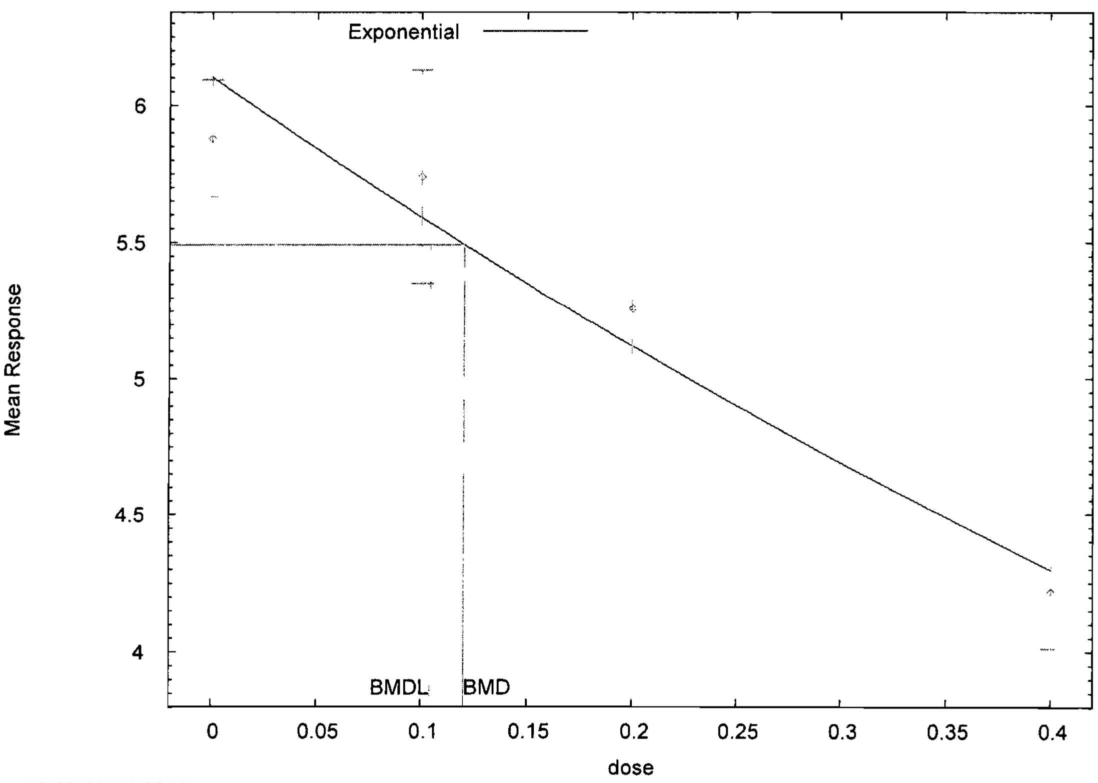
```
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    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
```

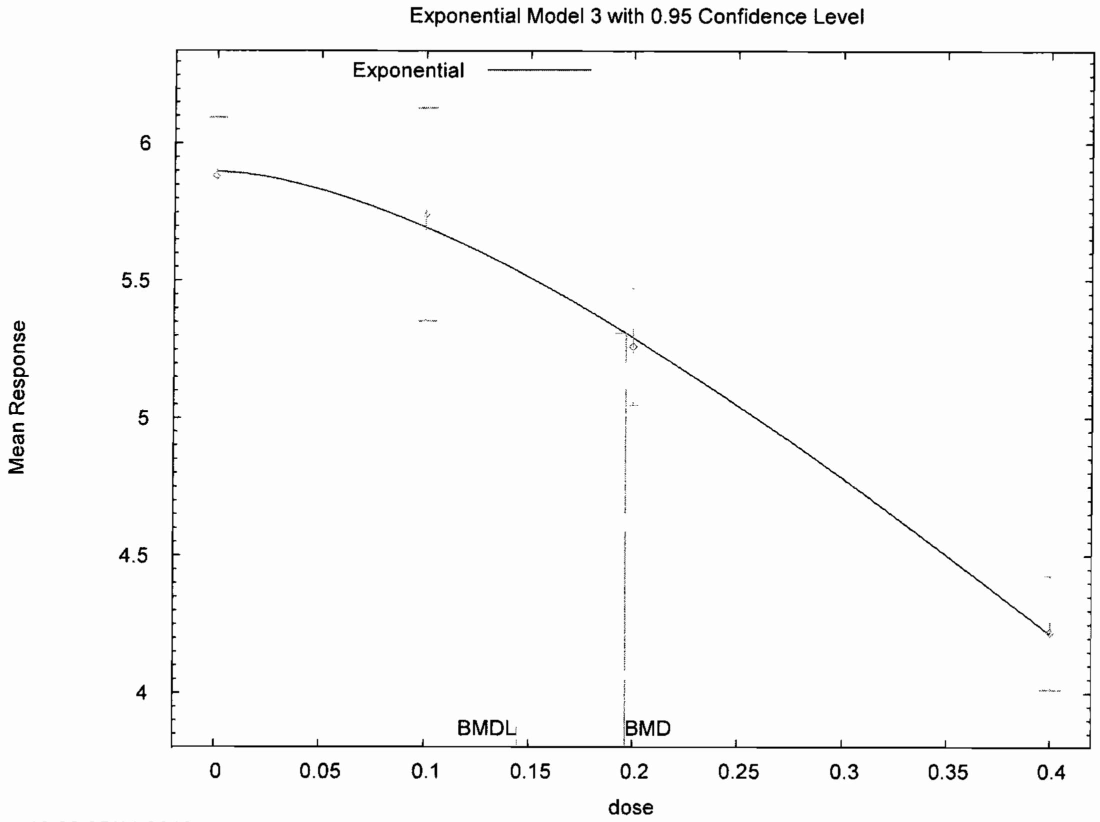
```
depend on the model parameters.


                          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 2 with 0.95 Confidence Level

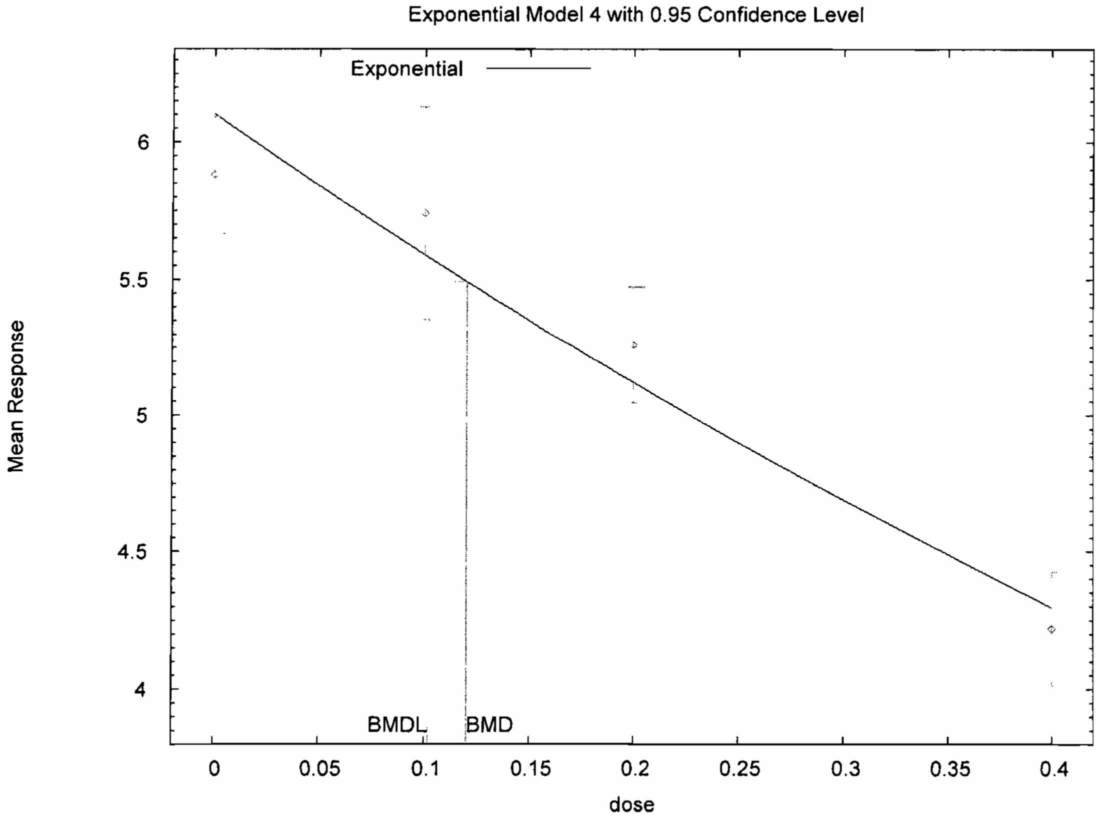


13:02 05/11 2010



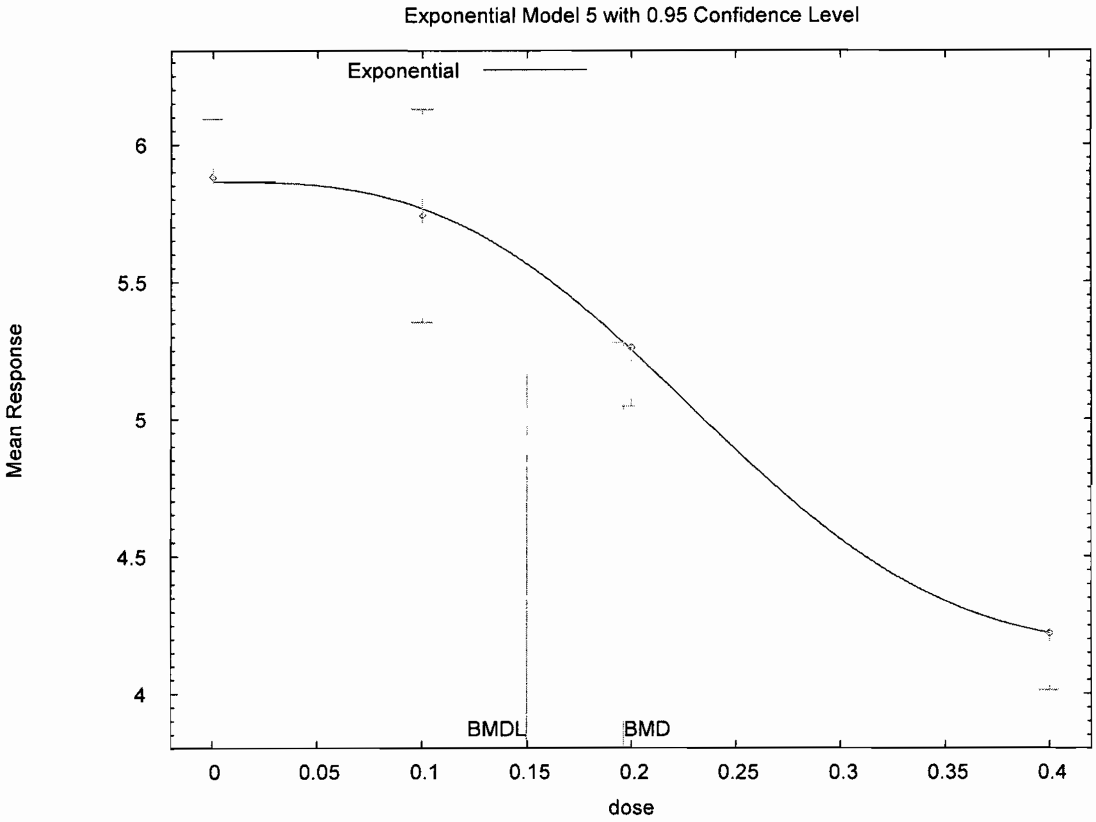
Exponential Model 3 with 0.95 Confidence Level

13:02 05/11 2010



Exponential Model 4 with 0.95 Confidence Level

13:02 05/11 2010



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