Appendix 1: Chapter 2 GENMOD and PROBIT analysis output for a susceptible strain of House mouse

Deviance values are highlighted

Chlorophacinone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Chloro_hms;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.5 0 5
F 0.6 0 5
F 0.7 0 5
F 0.75 5 15
F 0.8 8 14
F 1 10 15
F 1.2 13 15
M 0.5 0 15
M 0.7 0 12
M 0.8 12 16
M 1 33 44
M 2 32 35
M 3 6 6
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                      The GENMOD Procedure
                       Model Information

        Data Set                           WORK.CHLORO_HMS

        Distribution                              Binomial

        Link Function                               PROBIT

        Response Variable (Events)                    resp

        Response Variable (Trials)                       n


             Number of Observations Read   13

             Number of Observations Used   13

             Number of Events             119

             Number of Trials             202


                 Class Level Information

                 Class    Levels Values

                 SEX           2 F M


                     Response Profile

            Ordered Binary Outcome      Total
              Value                 Frequency

                  1 Event                 119

                  2 Nonevent               83


          Criteria For Assessing Goodness Of Fit

       Criterion                 DF      Value  Value/DF

       Deviance                   9    30.5013    3.3890

       Scaled Deviance            9    30.5013    3.3890

       Pearson Chi-Square         9    24.3595    2.7066

       Scaled Pearson X2          9    24.3595    2.7066

       Log Likelihood                 -93.7748

       Full Log Likelihood            -26.0452

       AIC (smaller is better)         60.0904

       AICC (smaller is better)        65.0904

       BIC (smaller is better)         62.3502

                      Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits     Chi-
                                                          Square

Intercept     1    0.3773     0.1369    0.1090    0.6457    7.59      0.0059

SEX        F  1    0.1820     0.2486   -0.3051    0.6692    0.54      0.4640

SEX        M  0    0.0000     0.0000    0.0000    0.0000       .           .

Ldose*SEX  F  1    8.6537     1.9178    4.8949   12.4125   20.36      <.0001

Ldose*SEX  M  1    5.0490     0.8693    3.3453    6.7527   33.74      <.0001

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

     Data Set                            WORK.CHLORO_HMS

     Distribution                               Binomial

     Link Function                                PROBIT

     Response Variable (Events)                     resp

     Response Variable (Trials)                        n


          Number of Observations Read   13

          Number of Observations Used   13

          Number of Events             119

          Number of Trials             202


                Class Level Information

                Class    Levels Values

                SEX           2  F M


                   Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                 119

               2 Nonevent               83


      Criteria For Assessing Goodness Of Fit

   Criterion                  DF      Value  Value/DF

   Deviance                   10    33.6605    3.3660

   Scaled Deviance            10    33.6605    3.3660

   Pearson Chi-Square         10    31.3570    3.1357

   Scaled Pearson X2          10    31.3570    3.1357

   Log Likelihood                  -95.3544

   Full Log Likelihood             -27.6248

   AIC (smaller is better)          61.2496

   AICC (smaller is better)         63.9162

   BIC (smaller is better)          62.9444


                  Algorithm converged.
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	0.3977	0.1408	0.1217	0.6737	7.97	0.0047
SEX	**F**	1	-0.0249	0.2129	-0.4422	0.3925	0.01	0.9070
SEX	**M**	0	0.0000	0.0000	0.0000	0.0000	.	.
Ldose		1	5.8059	0.8313	4.1767	7.4352	48.78	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

```
                    The GENMOD Procedure
                     Model Information

     Data Set                          WORK.CHLORO_HMS

     Distribution                             Binomial

     Link Function                              PROBIT

     Response Variable (Events)                   resp

     Response Variable (Trials)                      n


          Number of Observations Read   13

          Number of Observations Used   13

          Number of Events             119

          Number of Trials             202


                 Class Level Information

                 Class    Levels Values

                 SEX           2  F M


                    Response Profile

          Ordered  Binary Outcome      Total
            Value                  Frequency

                1  Event                 119

                2  Nonevent               83


                  Parameter Information

                  Parameter  Effect

                  Prm1       Intercept

                  Prm2       Ldose


        Criteria For Assessing Goodness Of Fit

   Criterion                   DF     Value  Value/DF

   Deviance                    11   33.6741    3.0613

   Scaled Deviance             11   33.6741    3.0613

   Pearson Chi-Square          11   31.2663    2.8424

   Scaled Pearson X2           11   31.2663    2.8424

   Log Likelihood                  -95.3612

   Full Log Likelihood             -27.6316

   AIC (smaller is better)          59.2632

   AICC (smaller is better)         60.4632

   BIC (smaller is better)          60.3931
```

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter	DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept	1	0.3875	0.1108	0.1704	0.6047	12.24	0.0005
Ldose	1	5.8206	0.8220	4.2096	7.4316	50.14	<.0001
Scale	0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Observation Statistics

Observation	Raw Residual	Pearson Residual	Deviance Residual	Std Deviance Residual	Std Pearson Residual	Likelihood Residual
1	-0.430907	-0.686691	-0.949332	-0.993842	-0.718887	-0.972874
2	-0.915295	-1.058486	-1.42193	-1.477471	-1.099831	-1.452969
3	-1.517958	-1.476379	-1.902154	-1.953876	-1.516524	-1.933478
4	-0.505651	-0.270869	-0.272755	-0.292592	-0.290569	-0.292328
5	1.9809678	1.069425	1.062374	1.1234346	1.1308909	1.1242254
6	0.2377595	0.1287763	0.129244	0.137663	0.1371648	0.137604
7	0.9715846	0.6294018	0.6601695	0.7286987	0.6947371	0.7227287
8	-1.29272	-1.189384	-1.644291	-1.914941	-1.385157	-1.79101
9	-3.6431	-2.287197	-2.946805	-3.150952	-2.445648	-3.071414
10	5.1211061	2.5860725	2.6000763	2.7730404	2.758105	2.7712396
11	4.3640944	1.3801031	1.4180314	1.7559023	1.7089369	1.7397108
12	-2.433368	-3.259129	-2.304208	-2.932889	-4.148351	-3.449097
13	0.004658	0.0682758	0.0965378	0.0971394	0.0687012	0.0968392

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Chloro_hms;
input SEX$ dose resp n;
cards;
f 0.5 0 5
F 0.6 0 5
F 0.7 0 5
F 0.75 5 15
F 0.8 8 14
F 1 10 15
F 1.2 13 15
M 0.5 0 15
M 0.7 0 12
M 0.8 12 16
M 1 33 44
M 2 32 35
M 3 6 6
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
          PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.01 0.34178   0.11490   0.48797
       0.02 0.38070   0.14372   0.52519
       0.03 0.40766   0.16559   0.55046
       0.04 0.42919   0.18417   0.57040
       0.05 0.44754   0.20077   0.58726
       0.06 0.46377   0.21604   0.60210
       0.07 0.47849   0.23035   0.61549
       0.08 0.49207   0.24394   0.62781
       0.09 0.50475   0.25696   0.63929
       0.10 0.51671   0.26954   0.65012
       0.15 0.56932   0.32807   0.69784
       0.20 0.61493   0.38273   0.73978
       0.25 0.65696   0.43586   0.77950
       0.30 0.69715   0.48858   0.81908
       0.35 0.73658   0.54143   0.86020
       0.40 0.77606   0.59458   0.90456
       0.45 0.81627   0.64789   0.95418
       0.50 0.85787   0.70096   1.01149
       0.55 0.90159   0.75330   1.07947
       0.60 0.94830   0.80461   1.16164
       0.65 0.99913   0.85511   1.26226
       0.70 1.05564   0.90567   1.38702
       0.75 1.12022   0.95792   1.54460
       0.80 1.19678   1.01445   1.75017
       0.85 1.29266   1.07962   2.03385
       0.90 1.42429   1.16244   2.46788
       0.91 1.45804   1.18277   2.58724
       0.92 1.49561   1.20506   2.72393
       0.93 1.53804   1.22981   2.88312
       0.94 1.58686   1.25781   3.07255
       0.95 1.64442   1.29023   3.30457
       0.96 1.71473   1.32904   3.60060
       0.97 1.80530   1.37791   4.00240
       0.98 1.93314   1.44502   4.60886
       0.99 2.15326   1.55624   5.76119
```

Coumatetralyl

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Coum_hms;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 1 0 14
F 2 0 15
F 3 4 15
F 5 6 15
F 6 7 14
F 7 12 15
F 8 10 15
F 9 14 14
M 1 6 20
M 2 6 15
M 2.5 7 15
M 3 11 16
M 5 15 15

;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                    The GENMOD Procedure
                     Model Information

     Data Set                            WORK.COUM_HMS

     Distribution                             Binomial

     Link Function                              PROBIT

     Response Variable (Events)                   resp

     Response Variable (Trials)                      n

          Number of Observations Read   13

          Number of Observations Used   13

          Number of Events              98

          Number of Trials             198

               Class Level Information

               Class    Levels Values

               SEX           2 F M

                  Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                  98

               2 Nonevent              100

       Criteria For Assessing Goodness Of Fit

    Criterion                   DF     Value  Value/DF

    Deviance                     9   16.9882    1.8876

    Scaled Deviance              9   16.9882    1.8876

    Pearson Chi-Square           9   13.3413    1.4824

    Scaled Pearson X2            9   13.3413    1.4824

    Log Likelihood                  -96.6595

    Full Log Likelihood             -22.4189

    AIC (smaller is better)          52.8378

    AICC (smaller is better)         57.8378

    BIC (smaller is better)          55.0976

                    Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter     DF  Estimate   Standard       Wald 95%           Wald  Pr > ChiSq
                                Error  Confidence Limits       Chi-
                                                             Square

Intercept      1   -0.8174     0.2750   -1.3563   -0.2784      8.84      0.0030

SEX         F  1   -2.3870     0.6805   -3.7208   -1.0532     12.30      0.0005

SEX         M  0    0.0000     0.0000    0.0000    0.0000         .           .

Ldose*SEX   F  1    4.4872     0.8124    2.8949    6.0795     30.51      <.0001

Ldose*SEX   M  1    2.8190     0.6948    1.4572    4.1808     16.46      <.0001

Scale          0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                  The GENMOD Procedure
                   Model Information

     Data Set                          WORK.COUM_HMS

     Distribution                           Binomial

     Link Function                            PROBIT

     Response Variable (Events)                 resp

     Response Variable (Trials)                    n


         Number of Observations Read   13

         Number of Observations Used   13

         Number of Events              98

         Number of Trials             198


             Class Level Information

             Class    Levels Values

             SEX           2  F M


                Response Profile

        Ordered Binary Outcome      Total
          Value                 Frequency

              1 Event                  98

              2 Nonevent              100


      Criteria For Assessing Goodness Of Fit

  Criterion                  DF     Value  Value/DF

  Deviance                   10   19.5248    1.9525

  Scaled Deviance            10   19.5248    1.9525

  Pearson Chi-Square         10   15.7059    1.5706

  Scaled Pearson X2          10   15.7059    1.5706

  Log Likelihood                 -97.9278

  Full Log Likelihood            -23.6873

  AIC (smaller is better)         53.3745

  AICC (smaller is better)        56.0412

  BIC (smaller is better)         55.0693

                 Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate   Standard     Wald 95%           Wald  Pr > ChiSq
                              Error  Confidence Limits     Chi-
                                                         Square

Intercept     1  -1.0800     0.2266  -1.5242  -0.6359     22.71      <.0001

SEX        F  1  -1.4839     0.2915  -2.0551  -0.9126     25.92      <.0001

SEX        M  0   0.0000     0.0000   0.0000   0.0000         .           .

Ldose         1   3.6193     0.5064   2.6268   4.6119     51.08      <.0001

Scale         0   1.0000     0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                        The GENMOD Procedure
                         Model Information

           Data Set                              WORK.COUM_HMS

           Distribution                               Binomial

           Link Function                                PROBIT

           Response Variable (Events)                     resp

           Response Variable (Trials)                        n


               Number of Observations Read   13

               Number of Observations Used   13

               Number of Events              98

               Number of Trials             198


                   Class Level Information

                   Class    Levels  Values

                   SEX           2  F M


                      Response Profile

              Ordered  Binary Outcome      Total
                Value                  Frequency

                    1  Event                  98

                    2  Nonevent              100


                    Parameter Information

                    Parameter  Effect

                    Prm1       Intercept

                    Prm2       Ldose


             Criteria For Assessing Goodness Of Fit

        Criterion                  DF        Value  Value/DF

        Deviance                   11      52.1907    4.7446

        Scaled Deviance            11      52.1907    4.7446

        Pearson Chi-Square         11      39.9536    3.6321

        Scaled Pearson X2          11      39.9536    3.6321

        Log Likelihood                   -114.2608

        Full Log Likelihood               -40.0202

        AIC (smaller is better)            84.0404

        AICC (smaller is better)           85.2404

        BIC (smaller is better)            85.1703
```

```
                      Algorithm converged.

          Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                           Error  Confidence Limits     Chi-
                                                      Square

Intercept  1  -1.1069     0.1983   -1.4956   -0.7181   31.14      <.0001

Ldose      1   2.1172     0.3317    1.4671    2.7672   40.75      <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.

                         Observation Statistics

Observation       Raw   Pearson  Deviance       Std       Std Likelihood
             Residual  Residual  Residual  Deviance   Pearson   Residual
                                           Residual  Residual

          1   -1.8784 -1.472917 -2.008461 -2.281539  -1.67318  -2.159621

          2 -4.790019 -2.652783 -3.397136  -3.64382 -2.845416  -3.549601

          3 -2.921948 -1.513389 -1.550857 -1.625959 -1.586678  -1.622453

          4 -3.681049 -1.986749 -1.930322 -2.050278 -2.110211  -2.057173

          5 -2.878412 -1.687878 -1.610348 -1.726527 -1.809651  -1.737562

          6 0.7127989 0.4264507 0.4366357 0.4777626 0.4666182  0.4759444

          7 -1.844254 -1.168319 -1.103166 -1.223852 -1.296133  -1.237726

          8 2.5272607 1.7561252 2.3610042 2.6281985 1.9548655  2.5123424

          9  3.316571 2.1758467 1.9243139 2.3361635 2.6415304  2.4385155

         10 1.2099808 0.6701052 0.6573883 0.7051248 0.7187651  0.7069241

         11 1.0638867 0.5617366 0.5570225 0.5880743 0.5930512   0.588588

         12 3.6165888 1.8136894 1.8242795 1.9189791 1.9078393  1.9179096

         13 5.3189509 2.8707634 3.6244169 3.8496481 3.0491606  3.7672928
```

PROBIT Dose Response data assuming a parallel response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Coum_hms;
input SEX$ dose resp n;
cards;
F 1 0 14
F 2 0 15
F 3 4 15
F 5 6 15
F 6 7 14
F 7 12 15
F 8 10 15
F 9 14 14
M 1 6 20
M 2 6 15
M 2.5 7 15
M 3 11 16
M 5 15 15

;
proc PROBIT log10 inversecl lackfit hprob=0.05;
class sex;
model resp/n=sex dose;
run;
```

PROBIT response data for females

```
                 The PROBIT Procedure
               PROBIT Analysis on dose
  Probability     dose  95% Fiducial Limits
         0.01  1.54900   0.76908   2.20178
         0.02  1.77765   0.94739   2.44606
         0.03  1.93991   1.08096   2.61597
         0.04  2.07167   1.19341   2.75223
         0.05  2.18542   1.29319   2.86885
         0.06  2.28715   1.38446   2.97246
         0.07  2.38023   1.46956   3.06681
         0.08  2.46678   1.55000   3.15420
         0.09  2.54823   1.62679   3.23620
         0.10  2.62558   1.70066   3.31391
         0.15  2.97160   2.04133   3.66067
         0.20  3.27885   2.35555   3.96968
         0.25  3.56765   2.65824   4.26373
         0.30  3.84861   2.95696   4.55571
         0.35  4.12867   3.25624   4.85513
         0.40  4.41325   3.55903   5.17070
         0.45  4.70724   3.86748   5.51155
         0.50  5.01568   4.18342   5.88815
         0.55  5.34433   4.50887   6.31323
         0.60  5.70034   4.84672   6.80286
         0.65  6.09324   5.20166   7.37838
         0.70  6.53665   5.58139   8.07006
         0.75  7.05143   5.99861   8.92455
         0.80  7.67250   6.47503  10.02147
         0.85  8.46581   7.05116  11.51556
         0.90  9.58152   7.81716  13.77250
         0.91  9.87235   8.01024  14.38825
         0.92 10.19831   8.22391  15.09114
         0.93 10.56915   8.46378  15.90681
         0.94 10.99930   8.73808  16.87365
         0.95 11.51128   9.05958  18.05266
         0.96 12.14333   9.44972  19.54916
         0.97 12.96810   9.94883  21.56781
```

```
         PROBIT Analysis on dose
Probability     dose 95% Fiducial Limits
       0.98 14.15187  10.64791  24.59013
       0.99 16.24081  11.83996  30.26405
```

PROBIT data response data for males

```
                      The PROBIT Procedure
                   PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.01   0.29155   0.04389    0.57521
       0.02   0.36427   0.06727    0.67084
       0.03   0.41954   0.08817    0.73997
       0.04   0.46658   0.10803    0.79688
       0.05   0.50871   0.12741    0.84661
       0.06   0.54755   0.14658    0.89155
       0.07   0.58404   0.16573    0.93309
       0.08   0.61877   0.18496    0.97209
       0.09   0.65214   0.20434    1.00912
       0.10   0.68446   0.22394    1.04460
       0.15   0.83618   0.32661    1.20755
       0.20   0.98040   0.43950    1.35915
       0.25   1.12381   0.56506    1.50940
       0.30   1.27038   0.70524    1.66518
       0.35   1.42322   0.86156    1.83326
       0.40   1.58521   1.03481    2.02202
       0.45   1.75947   1.22454    2.24306
       0.50   1.94966   1.42857    2.51306
       0.55   2.16041   1.64340    2.85532
       0.60   2.39790   1.86605    3.30099
       0.65   2.67083   2.09674    3.89186
       0.70   2.99215   2.34062    4.68903
       0.75   3.38241   2.60832    5.79368
       0.80   3.87716   2.91787    7.39471
       0.85   4.54591   3.30193    9.89711
       0.90   5.55358   3.83275   14.37511
       0.91   5.82874   3.97037   15.74278
       0.92   6.14313   4.12446   17.38067
       0.93   6.50844   4.29970   19.38401
       0.94   6.94216   4.50297   21.90167
       0.95   7.47222   4.74509   25.18240
       0.96   8.14690   5.04442   29.68063
```

```
         PROBIT Analysis on dose

Probability      dose 95% Fiducial Limits

       0.97   9.06037   5.43601   36.34232

       0.98  10.43517   6.00037   47.59671

       0.99  13.03769   7.00370   72.89622
```

Diphacinone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Diphac_hms;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.5 0 15
F 0.8 2 15
F 1 10 14
F 2 15 15
M 0.5 1 15
M 0.8 2 15
M 1 12 15
M 2 15 15
M 3 8 8
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                 The GENMOD Procedure
                  Model Information

     Data Set                          WORK.DIPHAC_HMS

     Distribution                             Binomial

     Link Function                              PROBIT

     Response Variable (Events)                   resp

     Response Variable (Trials)                      n


           Number of Observations Read    9

           Number of Observations Used    9

           Number of Events              65

           Number of Trials             127


               Class Level Information

               Class    Levels Values

               SEX           2 F M


                  Response Profile

          Ordered Binary Outcome      Total
            Value                 Frequency

                1 Event                  65

                2 Nonevent               62


       Criteria For Assessing Goodness Of Fit

    Criterion                  DF     Value  Value/DF

    Deviance                    5    6.1933    1.2387

    Scaled Deviance             5    6.1933    1.2387

    Pearson Chi-Square          5    6.2510    1.2502

    Scaled Pearson X2           5    6.2510    1.2502

    Log Likelihood                 -34.4327

    Full Log Likelihood             -9.3876

    AIC (smaller is better)         26.7753

    AICC (smaller is better)        36.7753

    BIC (smaller is better)         27.5642

                 Algorithm converged.
```

```
           Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate  Standard       Wald 95%          Wald Pr > ChiSq
                             Error  Confidence Limits      Chi-
                                                         Square

Intercept      1   0.4156    0.2775  -0.1282   0.9594      2.24      0.1342

SEX         F  1   0.1504    0.4507  -0.7329   1.0337      0.11      0.7386

SEX         M  0   0.0000    0.0000   0.0000   0.0000         .           .

Ldose*SEX  F  1  17.3028    5.5765   6.3730  28.2326      9.63      0.0019

Ldose*SEX  M  1   8.2839    2.2069   3.9584  12.6094     14.09      0.0002

Scale          0   1.0000    0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

 Data Set                         WORK.DIPHAC_HMS

 Distribution                            Binomial

 Link Function                             PROBIT

 Response Variable (Events)                  resp

 Response Variable (Trials)                     n


      Number of Observations Read    9

      Number of Observations Used    9

      Number of Events              65

      Number of Trials             127


          Class Level Information

          Class    Levels  Values

          SEX           2  F M


              Response Profile

     Ordered  Binary Outcome      Total
       Value                  Frequency

           1  Event                  65

           2  Nonevent               62


      Criteria For Assessing Goodness Of Fit

 Criterion                 DF      Value  Value/DF

 Deviance                   6     8.6217    1.4370

 Scaled Deviance            6     8.6217    1.4370

 Pearson Chi-Square         6    13.5265    2.2544

 Scaled Pearson X2          6    13.5265    2.2544

 Log Likelihood                 -35.6469

 Full Log Likelihood            -10.6018

 AIC (smaller is better)         27.2037

 AICC (smaller is better)        32.0037

 BIC (smaller is better)         27.7953

                 Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF  Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits     Chi-
                                                          Square
Intercept     1    0.5434     0.2805  -0.0063    1.0931     3.75      0.0527
SEX        F  1   -0.2980     0.3440  -0.9723    0.3763     0.75      0.3864
SEX        M  0    0.0000     0.0000   0.0000    0.0000        .           .
Ldose         1   10.0701     2.2107   5.7373   14.4030    20.75      <.0001
Scale         0    1.0000     0.0000   1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                               WORK.DIPHAC_HMS

 Distribution                                  Binomial

 Link Function                                   PROBIT

 Response Variable (Events)                        resp

 Response Variable (Trials)                           n


      Number of Observations Read     9

      Number of Observations Used     9

      Number of Events               65

      Number of Trials              127


          Class Level Information

          Class    Levels  Values

          SEX           2  F M


            Response Profile

     Ordered  Binary Outcome      Total
       Value                  Frequency

           1  Event                  65

           2  Nonevent               62


     Criteria For Assessing Goodness Of Fit

 Criterion                  DF      Value  Value/DF

 Deviance                    7     9.3796    1.3399

 Scaled Deviance             7     9.3796    1.3399

 Pearson Chi-Square          7    16.9244    2.4178

 Scaled Pearson X2           7    16.9244    2.4178

 Log Likelihood                  -36.0258

 Full Log Likelihood             -10.9808

 AIC (smaller is better)          25.9616

 AICC (smaller is better)         27.9616

 BIC (smaller is better)          26.3560

                  Algorithm converged.
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter	DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept	1	0.3893	0.2126	-0.0274	0.8060	3.35	0.0671
Ldose	1	9.8739	2.1487	5.6625	14.0854	21.12	<.0001
Scale	0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Diphac_hms;
input SEX$ dose resp n;
cards;
f 0.5 0 15
F 0.8 2 15
F 1 10 14
F 2 15 15
M 0.5 1 15
M 0.8 2 15
M 1 12 15
M 2 15 15
M 3 8 8
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                The PROBIT Procedure
              PROBIT Analysis on dose

  Probability     dose  95% Fiducial Limits

         0.01  0.53084   0.07117    0.67918
         0.02  0.56569   0.09746    0.70624
         0.03  0.58897   0.11890    0.72440
         0.04  0.60711   0.13802    0.73868
         0.05  0.62228   0.15577    0.75074
         0.06  0.63549   0.17262    0.76138
         0.07  0.64731   0.18884    0.77104
         0.08  0.65807   0.20460    0.77997
         0.09  0.66801   0.22002    0.78836
         0.10  0.67730   0.23519    0.79634
         0.15  0.71714   0.30901    0.83279
         0.20  0.75047   0.38179    0.86769
         0.25  0.78030   0.45460    0.90501
         0.30  0.80810   0.52687    0.94859
         0.35  0.83473   0.59659    1.00325
         0.40  0.86082   0.66070    1.07493
         0.45  0.88684   0.71643    1.16976
         0.50  0.91321   0.76297    1.29274
         0.55  0.94037   0.80162    1.44809
         0.60  0.96879   0.83460    1.64124
         0.65  0.99907   0.86400    1.88120
         0.70  1.03201   0.89157    2.18322
         0.75  1.06877   0.91878    2.57360
         0.80  1.11124   0.94714    3.10048
         0.85  1.16289   0.97871    3.86248
         0.90  1.23130   1.01730    5.10592
         0.91  1.24842   1.02653    5.46365
         0.92  1.26728   1.03654    5.88135
         0.93  1.28836   1.04754    6.37833
         0.94  1.31230   1.05983    6.98406
         0.95  1.34016   1.07387    7.74652
         0.96  1.37365   1.09042    8.75079
         0.97  1.41597   1.11088   10.16771
         0.98  1.47424   1.13833   12.41634
```

```
        PROBIT Analysis on dose
Probability    dose 95% Fiducial Limits
       0.99 1.57100   1.18234   17.02118
```

Warfarin sodium

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data WarfSod_hms;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.5 1 14
F 1 2 15
F 2 11 15
F 2.5 9 15
F 3 15 15
M 0.5 1 15
M 1 2 15
M 2 10 15
M 2.5 15 15
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                    The GENMOD Procedure
                     Model Information

  Data Set                            WORK.WARFSOD_HMS

  Distribution                                Binomial

  Link Function                                 PROBIT

  Response Variable (Events)                      resp

  Response Variable (Trials)                         n


        Number of Observations Read     9

        Number of Observations Used     9

        Number of Events               66

        Number of Trials              134


                Class Level Information

                Class    Levels Values

                SEX           2 F M


                    Response Profile

       Ordered  Binary Outcome      Total
         Value                  Frequency

             1  Event                  66

             2  Nonevent               68


       Criteria For Assessing Goodness Of Fit

 Criterion                   DF     Value  Value/DF

 Deviance                     5   15.8495    3.1699

 Scaled Deviance              5   15.8495    3.1699

 Pearson Chi-Square           5   13.6699    2.7340

 Scaled Pearson X2            5   13.6699    2.7340

 Log Likelihood                  -55.3230

 Full Log Likelihood             -16.9235

 AIC (smaller is better)          41.8470

 AICC (smaller is better)         51.8470

 BIC (smaller is better)          42.6359

                    Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate  Standard      Wald 95%          Wald Pr > ChiSq
                             Error Confidence Limits      Chi-
                                                        Square

Intercept     1  -0.7049    0.2630  -1.2204  -0.1894      7.18     0.0074

SEX         F 1  -0.0574    0.3664  -0.7755   0.6607      0.02     0.8755

SEX         M 0   0.0000    0.0000   0.0000   0.0000         .          .

Ldose*SEX F 1   3.8959    0.7693   2.3880   5.4038     25.64     <.0001

Ldose*SEX M 1   4.7480    0.9606   2.8653   6.6306     24.43     <.0001

Scale         0   1.0000    0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

     Data Set                           WORK.WARFSOD_HMS

     Distribution                               Binomial

     Link Function                                PROBIT

     Response Variable (Events)                     resp

     Response Variable (Trials)                        n


           Number of Observations Read    9

           Number of Observations Used    9

           Number of Events              66

           Number of Trials             134


                 Class Level Information

                 Class    Levels Values

                 SEX           2 F M


                     Response Profile

          Ordered  Binary Outcome      Total
            Value                  Frequency

                1  Event                  66

                2  Nonevent               68


       Criteria For Assessing Goodness Of Fit

   Criterion                  DF     Value  Value/DF

   Deviance                    6   16.3355    2.7226

   Scaled Deviance             6   16.3355    2.7226

   Pearson Chi-Square          6   14.1950    2.3658

   Scaled Pearson X2           6   14.1950    2.3658

   Log Likelihood                 -55.5660

   Full Log Likelihood            -17.1665

   AIC (smaller is better)         40.3330

   AICC (smaller is better)        45.1330

   BIC (smaller is better)         40.9247

                   Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate   Standard     Wald 95%          Wald  Pr > ChiSq
                              Error Confidence Limits     Chi-
                                                        Square

Intercept     1  -0.6250     0.2244  -1.0650  -0.1851     7.76      0.0054

SEX         F 1  -0.2244     0.2765  -0.7663   0.3176     0.66      0.4171

SEX         M 0   0.0000     0.0000   0.0000   0.0000        .           .

Ldose         1   4.2540     0.6018   3.0746   5.4334    49.97      <.0001

Scale         0   1.0000     0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                  The GENMOD Procedure
                   Model Information

  Data Set                          WORK.WARFSOD_HMS

  Distribution                              Binomial

  Link Function                               PROBIT

  Response Variable (Events)                    resp

  Response Variable (Trials)                       n


        Number of Observations Read    9

        Number of Observations Used    9

        Number of Events              66

        Number of Trials             134


              Class Level Information

              Class    Levels  Values

              SEX           2  F M


                 Response Profile

        Ordered  Binary Outcome      Total
          Value                  Frequency

              1  Event                  66

              2  Nonevent               68


               Parameter Information

               Parameter  Effect

               Prm1       Intercept

               Prm2       Ldose


     Criteria For Assessing Goodness Of Fit

 Criterion                  DF      Value  Value/DF

 Deviance                    7    17.0003    2.4286

 Scaled Deviance             7    17.0003    2.4286

 Pearson Chi-Square          7    14.5500    2.0786

 Scaled Pearson X2           7    14.5500    2.0786

 Log Likelihood                  -55.8984

 Full Log Likelihood             -17.4989

 AIC (smaller is better)          38.9979

 AICC (smaller is better)         40.9979

 BIC (smaller is better)          39.3923
```

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter	DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept	1	-0.7341	0.1813	-1.0895	-0.3787	16.39	<.0001
Ldose	1	4.1741	0.5890	3.0197	5.3285	50.23	<.0001
Scale	0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Observation Statistics

Observation	Raw Residual	Pearson Residual	Deviance Residual	Std Deviance Residual	Std Pearson Residual	Likelihood Residual
1	0.6743453	1.1956785	0.9638259	1.089495	1.3515778	1.1515537
2	-1.471692	-0.900968	-0.957997	-1.124873	-1.057909	-1.106882
3	0.5102296	0.2872956	0.2906108	0.32047	0.3168142	0.3198236
4	-3.345369	-2.263266	-2.023964	-2.275934	-2.545027	-2.334785
5	1.5643909	1.3215682	1.8177593	2.0670413	1.5028041	1.9534908
6	0.6510843	1.1152896	0.9127175	1.0421127	1.2734033	1.1003356
7	-1.471692	-0.900968	-0.957997	-1.124873	-1.057909	-1.106882
8	-0.48977	-0.275776	-0.273111	-0.301172	-0.304111	-0.301696
9	2.654631	1.7959559	2.4172455	2.7181761	2.0195403	2.5876941

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data WarfSod_hms;
input SEX$ dose resp n;
cards;
f 0.5 1 14
F 1 2 15
F 2 11 15
F 2.5 9 15
F 3 15 15
M 0.5 1 15
M 1 2 15
M 2 10 15
M 2.5 15 15
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                The PROBIT Procedure
              PROBIT Analysis on dose

Probability    dose  95% Fiducial Limits

       0.01 0.41547   0.11285    0.67656
       0.02 0.48289   0.14995    0.75304
       0.03 0.53123   0.17945    0.80656
       0.04 0.57076   0.20531    0.84970
       0.05 0.60507   0.22900    0.88678
       0.06 0.63590   0.25124    0.91988
       0.07 0.66422   0.27243    0.95014
       0.08 0.69064   0.29287    0.97829
       0.09 0.71558   0.31271    1.00481
       0.10 0.73934   0.33211    1.03005
       0.15 0.84638   0.42511    1.14403
       0.20 0.94241   0.51550    1.24784
       0.25 1.03343   0.60612    1.34901
       0.30 1.12263   0.69845    1.45214
       0.35 1.21215   0.79328    1.56104
       0.40 1.30369   0.89109    1.67955
       0.45 1.39882   0.99208    1.81204
       0.50 1.49923   1.09632    1.96387
       0.55 1.60684   1.20393    2.14183
       0.60 1.72410   1.31532    2.35479
       0.65 1.85430   1.43150    2.61496
       0.70 2.00216   1.55448    2.94016
       0.75 2.17499   1.68791    3.35871
       0.80 2.38505   1.83822    3.92025
       0.85 2.65563   2.01751    4.72433
       0.90 3.04013   2.25275    6.01516
       0.91 3.14105   2.31162    6.38192
       0.92 3.25450   2.37660    6.80779
       0.93 3.38397   2.44937    7.31129
       0.94 3.53466   2.53238    7.92059
       0.95 3.71474   2.62942    8.68123
       0.96 3.93807   2.74688    9.67334
       0.97 4.23110   2.89675   11.05639
       0.98 4.65467   3.10607   13.21699
```

```
         PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.99 5.40998   3.46182   17.53783
```

Appendix 2: Chapter 3 GENMOD and PROBIT analysis output for a resistant strain of House mouse homozygous for the VKORC1 mutation Y139C

Deviance values are highlighted

Chlorophacinone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Chloro_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.88 0 4
F 500 4 14
M 15 0 3
M 50 0 3
M 100 0 4
M 500 7 15
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                  The GENMOD Procedure
                   Model Information

   Data Set                          WORK.CHLORO_HMR
   Distribution                             Binomial
   Link Function                              PROBIT
   Response Variable (Events)                   resp
   Response Variable (Trials)                      n

         Number of Observations Read   6
         Number of Observations Used   6
         Number of Events             11
         Number of Trials             43

              Class Level Information
              Class    Levels  Values
              SEX           2  F M

                  Response Profile
        Ordered  Binary Outcome     Total
          Value                 Frequency
              1  Event                 11
              2  Nonevent              32

       Criteria For Assessing Goodness Of Fit
   Criterion                  DF     Value  Value/DF
   Deviance                    2    0.0000    0.0000
   Scaled Deviance             2    0.0000    0.0000
   Pearson Chi-Square          2    0.0000    0.0000
   Scaled Pearson X2           2    0.0000    0.0000
   Log Likelihood                 -18.7396
   Full Log Likelihood             -3.0614
   AIC (smaller is better)         14.1227
   AICC (smaller is better)        54.1227
   BIC (smaller is better)         13.2898

                  Algorithm converged.
```

```
                 Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate  Standard      Wald 95%            Wald  Pr > ChiSq
                             Error  Confidence Limits       Chi-
                                                          Square

Intercept     1 -26.0593    0.3240  -26.6944  -25.4242   6468.33      <.0001

SEX        F  1  19.1027    0.4808   18.1604   20.0450   1578.64      <.0001

SEX        M  0   0.0000    0.0000    0.0000    0.0000         .           .

Ldose*SEX  F  0   2.3678    0.0000    2.3678    2.3678         .           .

Ldose*SEX  M  0   9.6243    0.0000    9.6243    9.6243         .           .

Scale         0   1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

    Data Set                           WORK.CHLORO_HMR
    Distribution                              Binomial
    Link Function                               PROBIT
    Response Variable (Events)                    resp
    Response Variable (Trials)                       n

          Number of Observations Read   6
          Number of Observations Used   6
          Number of Events             11
          Number of Trials             43

                 Class Level Information
                 Class    Levels Values
                 SEX           2 F M

                    Response Profile
          Ordered Binary Outcome      Total
            Value                 Frequency
                1 Event                  11
                2 Nonevent               32

         Criteria For Assessing Goodness Of Fit
   Criterion                  DF     Value  Value/DF
   Deviance                    3    0.0000    0.0000
   Scaled Deviance             3    0.0000    0.0000
   Pearson Chi-Square          3    0.0000    0.0000
   Scaled Pearson X2           3    0.0000    0.0000
   Log Likelihood                 -18.7396
   Full Log Likelihood             -3.0614
   AIC (smaller is better)         12.1227
   AICC (smaller is better)        24.1227
   BIC (smaller is better)         11.4980

                  Algorithm converged.
```

```
                 Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate  Standard      Wald 95%          Wald  Pr > ChiSq
                             Error  Confidence Limits     Chi-
                                                        Square

Intercept     1 -26.0701    0.3240  -26.7052  -25.4350  6473.69     <.0001

SEX        F  1  -0.4823    0.4808   -1.4246    0.4600     1.01     0.3158

SEX        M  0   0.0000    0.0000    0.0000    0.0000        .          .

Ldose         0   9.6283    0.0000    9.6283    9.6283        .          .

Scale         0   1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                        WORK.CHLORO_HMR
      Distribution                           Binomial
      Link Function                            PROBIT
      Response Variable (Events)                 resp
      Response Variable (Trials)                    n

          Number of Observations Read   6
          Number of Observations Used   6
          Number of Events             11
          Number of Trials             43

                Class Level Information
                Class    Levels Values
                SEX           2 F M

                  Response Profile
         Ordered Binary Outcome      Total
          Value                  Frequency
              1 Event                   11
              2 Nonevent                32

                 Parameter Information
                 Parameter  Effect
                 Prm1       Intercept
                 Prm2       Ldose

       Criteria For Assessing Goodness Of Fit
     Criterion                  DF     Value  Value/DF
     Deviance                    4    1.0168    0.2542
     Scaled Deviance             4    1.0168    0.2542
     Pearson Chi-Square          4    1.0071    0.2518
     Scaled Pearson X2           4    1.0071    0.2518
     Log Likelihood                 -19.2480
     Full Log Likelihood             -3.5698
     AIC (smaller is better)         11.1396
     AICC (smaller is better)        15.1396
     BIC (smaller is better)         10.7231
```

```
                           Algorithm converged.

            Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard Wald 95% Confidence       Wald Pr > ChiSq
                           Error        Limits             Chi-
                                                         Square

Intercept  1 -25.4984     0.2368   -25.9625  -25.0343   11597.5     <.0001

Ldose      0   9.3336     0.0000     9.3336    9.3336         .          .

Scale      0   1.0000     0.0000     1.0000    1.0000

Note: The scale parameter was held fixed.

                         Observation Statistics

Observation        Raw   Pearson  Deviance       Std       Std Likelihood
              Residual  Residual  Residual  Deviance   Pearson   Residual
                                            Residual  Residual

          1  -643E-151         .         0         0         .          .

          2  -1.310345  -0.72175   -0.7363 -1.023783 -1.003553  -1.014067

          3  -1.33E-47         .         0         0         .          .

          4  -8.06E-22         .         0         0         .          .

          5  -1.68E-11 -4.104E-6 -5.804E-6 -5.804E-6 -4.104E-6  -5.804E-6

          6  1.3103448 0.6972771 0.6889802 0.9916118 1.0035531  0.9978062
```

PROBIT Dose Response data assuming a coincident response for males and females

```
data Chlorophac_hmr;
input SEX$ dose resp n;
cards;
f 0.88 0 4
F 500 4 14
M 15 0 3
M 50 0 3
M 100 0 4
M 500 7 15
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                 The PROBIT Procedure
               PROBIT Analysis on dose

    Probability      dose  95% Fiducial Limits

           0.01 302.37601           .         .
           0.02 323.62142           .         .
           0.03 337.86848           .         .
           0.04 348.99788           .         .
           0.05 358.32063           .         .
           0.06 366.45169           .         .
           0.07 373.73271           .         .
           0.08 380.37467           .         .
           0.09 386.51770           .         .
           0.10 392.26003           .         .
           0.15 416.95683           .         .
           0.20 437.68937           .         .
           0.25 456.29571           .         .
           0.30 473.67791           .         .
           0.35 490.37565           .         .
           0.40 506.76412           .         .
           0.45 523.14127           .         .
           0.50 539.77542           .         .
           0.55 556.93849           .         .
           0.60 574.93713           .         .
           0.65 594.15166           .         .
           0.70 615.09626           .         .
           0.75 638.52783           .         .
           0.80 665.67189           .         .
           0.85 698.77140           .         .
           0.90 742.76625           .         .
           0.91 753.80121           .         .
           0.92 765.97506           .         .
           0.93 779.58793           .         .
           0.94 795.07755           .         .
           0.95 813.11955           .         .
           0.96 834.84034           .         .
           0.97 862.34002           .         .
```

```
         PROBIT Analysis on dose

Probability      dose  95% Fiducial Limits

       0.98 900.30353          .         .

       0.99 963.56026          .         .
```

Coumatetralyl

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
ata Coum_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 25 0 5
F 40 0 5
F 45 0 19
F 50 0 10
F 100 7 28
M 20 2 20
M 25 7 15
M 50 10 22
M 100 19 34
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                            WORK.COUM_HMR

      Distribution                             Binomial

      Link Function                              PROBIT

      Response Variable (Events)                   resp

      Response Variable (Trials)                      n


           Number of Observations Read    9

           Number of Observations Used    9

           Number of Events              45

           Number of Trials             158


               Class Level Information

               Class    Levels Values

               SEX           2 F M


                   Response Profile

          Ordered Binary Outcome      Total
            Value                 Frequency

                1 Event                  45

                2 Nonevent              113


       Criteria For Assessing Goodness Of Fit

    Criterion                 DF     Value  Value/DF

    Deviance                   5    5.0464    1.0093

    Scaled Deviance            5    5.0464    1.0093

    Pearson Chi-Square         5    4.9120    0.9824

    Scaled Pearson X2          5    4.9120    0.9824

    Log Likelihood                -73.6235

    Full Log Likelihood           -10.9013

    AIC (smaller is better)        29.8025

    AICC (smaller is better)       39.8025

    BIC (smaller is better)        30.5914

                    Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates
Parameter     DF Estimate  Standard       Wald 95%            Wald Pr > ChiSq
                              Error  Confidence Limits        Chi-
                                                            Square

Intercept      1   -2.4601    0.8299   -4.0868   -0.8335      8.79     0.0030

SEX          F 1  -38.4191    0.8690  -40.1222  -36.7159   1954.73     <.0001

SEX          M 0    0.0000    0.0000    0.0000    0.0000         .          .

Ldose*SEX    F 0   20.1024    0.0000   20.1024   20.1024         .          .

Ldose*SEX    M 1    1.3342    0.4827    0.3881    2.2802      7.64     0.0057

Scale          0    1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

     Data Set                         WORK.COUM_HMR

     Distribution                          Binomial

     Link Function                           PROBIT

     Response Variable (Events)                resp

     Response Variable (Trials)                   n


         Number of Observations Read     9

         Number of Observations Used     9

         Number of Events               45

         Number of Trials              158


             Class Level Information

             Class    Levels Values

             SEX           2  F M


                Response Profile

        Ordered Binary Outcome      Total
          Value                 Frequency

              1 Event                  45

              2 Nonevent              113


      Criteria For Assessing Goodness Of Fit

   Criterion                  DF     Value  Value/DF

   Deviance                    6   11.3869    1.8978

   Scaled Deviance             6   11.3869    1.8978

   Pearson Chi-Square          6    9.9048    1.6508

   Scaled Pearson X2           6    9.9048    1.6508

   Log Likelihood                 -76.7937

   Full Log Likelihood            -14.0715

   AIC (smaller is better)         34.1430

   AICC (smaller is better)        38.9430

   BIC (smaller is better)         34.7347

                 Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates

Parameter     DF  Estimate   Standard       Wald 95%           Wald  Pr > ChiSq
                                Error  Confidence Limits        Chi-
                                                              Square

Intercept      1   -3.0976     0.7878   -4.6416   -1.5536     15.46      <.0001

SEX         F  1   -1.3092     0.2687   -1.8358   -0.7826     23.75      <.0001

SEX         M  0    0.0000     0.0000    0.0000    0.0000         .           .

Ldose          1    1.7094     0.4560    0.8158    2.6031     14.06      0.0002

Scale          0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

     Data Set                            WORK.COUM_HMR

     Distribution                             Binomial

     Link Function                              PROBIT

     Response Variable (Events)                   resp

     Response Variable (Trials)                      n


        Number of Observations Read    9

        Number of Observations Used    9

        Number of Events              45

        Number of Trials             158


              Class Level Information

              Class    Levels Values

              SEX           2  F M


                  Response Profile

        Ordered  Binary Outcome      Total
         Value                    Frequency

             1  Event                    45

             2  Nonevent                113


               Parameter Information

               Parameter   Effect

               Prm1        Intercept

               Prm2        Ldose


       Criteria For Assessing Goodness Of Fit

   Criterion                    DF     Value  Value/DF

   Deviance                      7   39.1044    5.5863

   Scaled Deviance               7   39.1044    5.5863

   Pearson Chi-Square            7   32.6747    4.6678

   Scaled Pearson X2             7   32.6747    4.6678

   Log Likelihood                   -90.6525

   Full Log Likelihood              -27.9303

   AIC (smaller is better)           59.8605

   AICC (smaller is better)          61.8605

   BIC (smaller is better)           60.2550
```

```
                         Algorithm converged.

           Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard      Wald 95%             Wald  Pr > ChiSq
                           Error  Confidence Limits        Chi-
                                                         Square

Intercept  1  -2.5681     0.7563   -4.0503   -1.0858      11.53      0.0007

Ldose      1   1.1478     0.4269    0.3110    1.9845       7.23      0.0072

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.

                        Observation Statistics

Observation       Raw    Pearson   Deviance        Std        Std Likelihood
             Residual   Residual   Residual   Deviance    Pearson   Residual
                                              Residual   Residual

          1 -0.838221  -1.003517  -1.354604  -1.411907  -1.045968  -1.386346

          2 -1.164652  -1.232198  -1.628428   -1.66349  -1.258729  -1.648594

          3 -4.774011  -2.525092  -3.316022  -3.572842  -2.720657  -3.467259

          4 -2.682882  -1.914832  -2.499474  -2.588178  -1.982788  -2.551908

          5 -3.993542  -1.545473  -1.593568  -2.047941  -1.986133  -2.023782

          6 -0.824872  -0.529605  -0.554506  -0.723411  -0.690925  -0.710192

          7 4.4853383  3.1002799  2.6853288  3.0773908  3.5529254  3.1972698

          8 4.0976597  1.9717586  1.8693071  2.0254241  2.1364318  2.0422581

          9 5.6506993  1.9844722   1.955014  2.7086401  2.7494539  2.7282681
```

PROBIT Dose Response data assuming a separate response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Coum_hmr;
input SEX$ dose resp n;
cards;
F 25 0 5
F 40 0 5
F 45 0 19
F 50 0 10
F 100 7 28
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;


data Coum_hmr;
input SEX$ dose resp n;
cards;
M 20 2 20
M 25 7 15
M 50 10 22
M 75 7 9
M 100 19 34
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

PROBIT data response data for females

```
                The PROBIT Procedure
              PROBIT Analysis on dose
        Probability      dose  95% Fiducial Limits
               0.01   83.19127          .         .
               0.02   85.75648          .         .
               0.03   87.42489          .         .
               0.04   88.70133          .         .
               0.05   89.75334          .         .
               0.06   90.65860          .         .
               0.07   91.45984          .         .
               0.08   92.18326          .         .
               0.09   92.84615          .         .
               0.10   93.46056          .         .
               0.15   96.04793          .         .
               0.20   98.15527          .         .
               0.25  100.00000          .         .
               0.30  101.68615          .         .
               0.35  103.27399          .         .
               0.40  104.80361          .         .
               0.45  106.30510          .         .
               0.50  107.80378          .         .
               0.55  109.32360          .         .
               0.60  110.88984          .         .
               0.65  112.53227          .         .
               0.70  114.28947          .         .
               0.75  116.21656          .         .
               0.80  118.40073          .         .
               0.85  120.99851          .         .
               0.90  124.34824          .         .
               0.91  125.17111          .         .
               0.92  126.07121          .         .
               0.93  127.06840          .         .
               0.94  128.19143          .         .
               0.95  129.48438          .         .
               0.96  131.02009          .         .
```

```
         PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.97 132.93303          .         .
       0.98 135.51927          .         .
       0.99 139.69803          .         .
```

PROBIT data response data for males

```
                    The PROBIT Procedure
                  PROBIT Analysis on dose
     Probability       dose  95% Fiducial Limits
            0.01    1.61330    0.00409    6.39161
            0.02    2.47171    0.01296    8.34300
            0.03    3.24005    0.02693    9.88730
            0.04    3.97177    0.04665   11.24071
            0.05    4.68724    0.07290   12.48246
            0.06    5.39689    0.10658   13.65189
            0.07    6.10698    0.14863   14.77196
            0.08    6.82172    0.20013   15.85751
            0.09    7.54412    0.26223   16.91888
            0.10    8.27653    0.33621   17.96373
            0.15   12.14652    0.93689   23.11455
            0.20   16.47642    2.10001   28.45165
            0.25   21.40227    4.15600   34.33837
            0.30   27.06907    7.55997   41.25769
            0.35   33.65147   12.84877   50.09859
            0.40   41.37180   20.39585   62.76666
            0.45   50.52318   29.86514   83.36606
            0.50   61.50365   40.09848  119.48926
            0.55   74.87056   50.29593  183.32718
            0.60   91.43181   60.63121  295.76481
            0.65  112.40813   71.71928  497.26784
            0.70  139.74249   84.31815  872.90580
            0.75  176.74291   99.42337       1618
            0.80  229.58256  118.61187       3239
            0.85  311.42247  144.89172       7316
            0.90  457.03903  185.44390      20497
            0.91  501.41007  196.72074      26303
            0.92  554.50834  209.70957      34494
            0.93  619.40556  224.93759      46484
            0.94  700.90382  243.20174      64877
            0.95  807.02047  265.78313      94915
            0.96  952.39555  294.92100     148456
            0.97       1167  335.03509     257380
```

```
          PROBIT Analysis on dose

Probability       dose  95% Fiducial Limits

       0.98       1530  396.73150    535145

       0.99       2345  517.37619   1697868
```

Diphacinone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Diphac_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 1.24 0 5
F 500 6 14
M 15 0 3
M 50 0 4
M 100 0 4
M 500 10 16
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                 The GENMOD Procedure
                 Model Information

   Data Set                        WORK.DIPHAC_HMR

   Distribution                           Binomial

   Link Function                            PROBIT

   Response Variable (Events)                 resp

   Response Variable (Trials)                    n


         Number of Observations Read   6

         Number of Observations Used   6

         Number of Events             16

         Number of Trials             46


             Class Level Information

             Class    Levels Values

             SEX           2 F M


                Response Profile

        Ordered Binary Outcome      Total
          Value                 Frequency

              1 Event                  16

              2 Nonevent               30


     Criteria For Assessing Goodness Of Fit

  Criterion                 DF     Value Value/DF

  Deviance                   2    0.0000   0.0000

  Scaled Deviance            2    0.0000   0.0000

  Pearson Chi-Square         2    0.0000   0.0000

  Scaled Pearson X2          2    0.0000   0.0000

  Log Likelihood                -20.1457

  Full Log Likelihood            -3.1502

  AIC (smaller is better)        14.3003

  AICC (smaller is better)       54.3003

  BIC (smaller is better)        13.4674

                Algorithm converged.
```

```
                 Analysis Of Maximum Likelihood Parameter Estimates

Parameter      DF  Estimate  Standard        Wald 95%             Wald  Pr > ChiSq
                                Error  Confidence Limits          Chi-
                                                                Square

Intercept       1  -27.1277    0.3192  -27.7533   -26.5021   7223.72      <.0001

SEX          F  1   19.7650    0.4641   18.8553    20.6746   1813.59      <.0001

SEX          M  0    0.0000    0.0000    0.0000     0.0000         .           .

Ldose*SEX    F  0    2.6613    0.0000    2.6613     2.6613         .           .

Ldose*SEX    M  0   10.1692    0.0000   10.1692    10.1692         .           .

Scale           0    1.0000    0.0000    1.0000     1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                         WORK.DIPHAC_HMR

      Distribution                            Binomial

      Link Function                             PROBIT

      Response Variable (Events)                  resp

      Response Variable (Trials)                     n


          Number of Observations Read   6

          Number of Observations Used   6

          Number of Events             16

          Number of Trials             46


                Class Level Information

                Class    Levels Values

                SEX           2 F M


                   Response Profile

         Ordered Binary Outcome       Total
           Value                  Frequency

               1 Event                   16

               2 Nonevent                30


       Criteria For Assessing Goodness Of Fit

     Criterion                  DF     Value  Value/DF

     Deviance                    3    0.0000    0.0000

     Scaled Deviance             3    0.0000    0.0000

     Pearson Chi-Square          3    0.0000    0.0000

     Scaled Pearson X2           3    0.0000    0.0000

     Log Likelihood                 -20.1457

     Full Log Likelihood             -3.1502

     AIC (smaller is better)         12.3003

     AICC (smaller is better)        24.3003

     BIC (smaller is better)         11.6756

                  Algorithm converged.
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	-27.1520	0.3192	-27.7776	-26.5265	7236.68	<.0001
SEX	**F**	1	-0.4987	0.4641	-1.4083	0.4110	1.15	0.2826
SEX	**M**	0	0.0000	0.0000	0.0000	0.0000	.	.
Ldose		0	10.1782	0.0000	10.1782	10.1782	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

```
                    The GENMOD Procedure
                     Model Information

     Data Set                           WORK.DIPHAC_HMR

     Distribution                              Binomial

     Link Function                               PROBIT

     Response Variable (Events)                    resp

     Response Variable (Trials)                       n


          Number of Observations Read   6

          Number of Observations Used   6

          Number of Events             16

          Number of Trials             46


               Class Level Information

               Class    Levels Values

               SEX           2 F M


                  Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                  16

               2 Nonevent               30


        Criteria For Assessing Goodness Of Fit

   Criterion                 DF      Value   Value/DF

   Deviance                   4     1.1639     0.2910

   Scaled Deviance            4     1.1639     0.2910

   Pearson Chi-Square         4     1.1575     0.2894

   Scaled Pearson X2          4     1.1575     0.2894

   Log Likelihood                 -20.7277

   Full Log Likelihood             -3.7321

   AIC (smaller is better)         11.4643

   AICC (smaller is better)        15.4643

   BIC (smaller is better)         11.0478


                    Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard Wald 95% Confidence      Wald Pr > ChiSq
                           Error         Limits           Chi-
                                                         Square

Intercept  1 -26.5476     0.2291  -26.9967  -26.0986   13426.1     <.0001

Ldose      0   9.8672     0.0000    9.8672    9.8672         .          .

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Diphac_hmr;
input SEX$ dose resp n;
cards;
f 1.24 0 5
F 500 6 14
M 15 0 3
M 50 0 4
M 100 0 4
M 500 10 16
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                 The PROBIT Procedure
               PROBIT Analysis on dose

Probability      dose  95% Fiducial Limits

       0.01 283.38065          .          .
       0.02 302.17845          .          .
       0.03 314.74650          .          .
       0.04 324.54429          .          .
       0.05 332.73856          .          .
       0.06 339.87596          .          .
       0.07 346.25992          .          .
       0.08 352.07768          .          .
       0.09 357.45353          .          .
       0.10 362.47453          .          .
       0.15 384.02445          .          .
       0.20 402.06174          .          .
       0.25 418.20984          .          .
       0.30 433.26331          .          .
       0.35 447.69587          .          .
       0.40 461.83525          .          .
       0.45 475.94014          .          .
       0.50 490.24194          .          .
       0.55 504.97349          .          .
       0.60 520.39587          .          .
       0.65 536.83130          .          .
       0.70 554.71384          .          .
       0.75 574.68078          .          .
       0.80 597.76181          .          .
       0.85 625.83817          .          .
       0.90 663.04563          .          .
       0.91 672.35916          .          .
       0.92 682.62537          .          .
       0.93 694.09465          .          .
       0.94 707.13197          .          .
       0.95 722.30029          .          .
       0.96 740.53731          .          .
       0.97 763.58962          .          .
       0.98 795.34842          .          .
```

```
         PROBIT Analysis on dose
Probability      dose 95% Fiducial Limits
       0.99 848.10715          .         .
```

Warfarin sodium

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data WarfSod_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 300 1 15
F 400 2 16
M 200 1 16
M 280 1 15
M 300 10 15
M 500 0 2
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                 The GENMOD Procedure
                  Model Information

 Data Set                          WORK.WARFSOD_HMR

 Distribution                              Binomial

 Link Function                               PROBIT

 Response Variable (Events)                    resp

 Response Variable (Trials)                       n


        Number of Observations Read   6

        Number of Observations Used   6

        Number of Events             15

        Number of Trials             79


            Class Level Information

            Class    Levels Values

            SEX           2  F M


               Response Profile

      Ordered Binary Outcome      Total
        Value                 Frequency

            1 Event                  15

            2 Nonevent               64


     Criteria For Assessing Goodness Of Fit

Criterion                  DF      Value  Value/DF

Deviance                    2    16.8213    8.4107

Scaled Deviance             2    16.8213    8.4107

Pearson Chi-Square          2    16.1715    8.0857

Scaled Pearson X2           2    16.1715    8.0857

Log Likelihood                  -35.0753

Full Log Likelihood             -14.0917

AIC (smaller is better)          36.1834

AICC (smaller is better)         76.1834

BIC (smaller is better)          35.3505

                 Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate  Standard     Wald 95%          Wald Pr > ChiSq
                             Error Confidence Limits     Chi-
                                                       Square

Intercept     1  -9.9912    5.2462  -20.2737   0.2912    3.63     0.0569

SEX        F  1   1.5362   14.0907  -26.0810  29.1534    0.01     0.9132

SEX        M  0   0.0000    0.0000    0.0000   0.0000       .          .

Ldose*SEX  F  1   2.8073    5.1213   -7.2303  12.8449    0.30     0.5836

Ldose*SEX  M  1   3.8308    2.1482   -0.3796   8.0411    3.18     0.0745

Scale         0   1.0000    0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                  The GENMOD Procedure
                   Model Information

  Data Set                          WORK.WARFSOD_HMR
  Distribution                              Binomial
  Link Function                               PROBIT
  Response Variable (Events)                    resp
  Response Variable (Trials)                       n

        Number of Observations Read   6
        Number of Observations Used   6
        Number of Events             15
        Number of Trials             79

             Class Level Information
             Class    Levels Values
             SEX           2 F M

                Response Profile
        Ordered Binary Outcome      Total
          Value                 Frequency
              1 Event                  15
              2 Nonevent               64

      Criteria For Assessing Goodness Of Fit
 Criterion                 DF     Value  Value/DF
 Deviance                   3   16.8550    5.6183
 Scaled Deviance            3   16.8550    5.6183
 Pearson Chi-Square         3   16.1700    5.3900
 Scaled Pearson X2          3   16.1700    5.3900
 Log Likelihood               -35.0921
 Full Log Likelihood          -14.1086
 AIC (smaller is better)       34.2171
 AICC (smaller is better)      46.2171
 BIC (smaller is better)       33.5924

                 Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate  Standard      Wald 95%         Wald  Pr > ChiSq
                              Error  Confidence Limits    Chi-
                                                        Square

Intercept     1   -9.6224    4.8396  -19.1079   -0.1369    3.95      0.0468

SEX        F  1   -1.0607    0.4382   -1.9195   -0.2019    5.86      0.0155

SEX        M  0    0.0000    0.0000    0.0000    0.0000       .           .

Ldose         1    3.6796    1.9820   -0.2050    7.5642    3.45      0.0634

Scale         0    1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                               WORK.WARFSOD_HMR

 Distribution                                   Binomial

 Link Function                                    PROBIT

 Response Variable (Events)                         resp

 Response Variable (Trials)                            n


        Number of Observations Read   6

        Number of Observations Used   6

        Number of Events             15

        Number of Trials             79


               Class Level Information

               Class    Levels Values

               SEX           2 F M


                  Response Profile

       Ordered Binary Outcome       Total
         Value                  Frequency

             1 Event                   15

             2 Nonevent                64


                Parameter Information

                Parameter  Effect

                Prm1       Intercept

                Prm2       Ldose


      Criteria For Assessing Goodness Of Fit

 Criterion                    DF      Value  Value/DF

 Deviance                      4    23.1261    5.7815

 Scaled Deviance               4    23.1261    5.7815

 Pearson Chi-Square            4    27.3301    6.8325

 Scaled Pearson X2             4    27.3301    6.8325

 Log Likelihood                    -38.2276

 Full Log Likelihood               -17.2441

 AIC (smaller is better)            38.4882

 AICC (smaller is better)           42.4882

 BIC (smaller is better)            38.0717
```

```
                    Algorithm converged.

        Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate  Standard      Wald 95%        Wald Pr > ChiSq
                          Error Confidence Limits    Chi-
                                                   Square

Intercept  1  -3.2562    4.1053  -11.3024  4.7900    0.63     0.4277

Ldose      1   0.9621    1.6578   -2.2871  4.2113    0.34     0.5617

Scale      0   1.0000    0.0000    1.0000  1.0000

Note: The scale parameter was held fixed.

                    Observation Statistics

Observation      Raw   Pearson  Deviance       Std       Std Likelihood
            Residual  Residual  Residual  Deviance   Pearson   Residual
                                          Residual  Residual

          1 -1.869995 -1.227482 -1.380538 -1.535554 -1.365312   -1.50441

          2 -1.612604 -0.964245 -1.030268 -1.556715 -1.456956  -1.501467

          3 -1.377765 -0.968337 -1.076143 -1.924509 -1.731716  -1.794226

          4 -1.753634 -1.169575    -1.312 -1.467013  -1.30776   -1.43655

          5 7.1300053 4.6802003 4.0128613 4.4634538 5.2057264  4.6150155

          6  -0.50954 -0.826883  -1.08455 -1.188373 -0.906039  -1.146046
```

PROBIT Dose Response data assuming a parallel response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data WarfSod_hmr_f;
input SEX$ dose resp n;
cards;
F 300 1 15
F 400 2 16
M 200 1 16
M 280 1 15
M 300 10 15
M 500 0 2

;
proc PROBIT log10 inversecl lackfit hprob=0.05;
class sex;
model resp/n=sex dose;
run;
```

PROBIT data response data for females

```
                 The PROBIT Procedure
               PROBIT Analysis on dose
Probability       dose  95% Fiducial Limits
       0.01  186.67932           .         .
       0.02  221.40116           .         .
       0.03  246.70821           .         .
       0.04  267.63486           .         .
       0.05  285.95952           .         .
       0.06  302.54183           .         .
       0.07  317.87060           .         .
       0.08  332.25357           .         .
       0.09  345.89862           .         .
       0.10  358.95370           .         .
       0.15  418.45978           .         .
       0.20  472.71288           .         .
       0.25  524.82973           .         .
       0.30  576.51138           .         .
       0.35  628.93446           .         .
       0.40  683.07994           .         .
       0.45  739.89900           .         .
       0.50  800.42966           .         .
       0.55  865.91230           .         .
       0.60  937.93948           .         .
       0.65       1019           .         .
       0.70       1111           .         .
       0.75       1221           .         .
       0.80       1355           .         .
       0.85       1531           .         .
       0.90       1785           .         .
       0.91       1852           .         .
       0.92       1928           .         .
       0.93       2016           .         .
       0.94       2118           .         .
       0.95       2240           .         .
       0.96       2394           .         .
       0.97       2597           .         .
```

```
         PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.98      2894          .         .
       0.99      3432          .         .
```

PROBIT data response data for males

```
                The PROBIT Procedure
              PROBIT Analysis on dose
    Probability      dose  95% Fiducial Limits
           0.01   96.12570         .         .
           0.02  114.00481         .         .
           0.03  127.03603         .         .
           0.04  137.81166         .         .
           0.05  147.24747         .         .
           0.06  155.78611         .         .
           0.07  163.67926         .         .
           0.08  171.08540         .         .
           0.09  178.11157         .         .
           0.10  184.83395         .         .
           0.15  215.47506         .         .
           0.20  243.41130         .         .
           0.25  270.24753         .         .
           0.30  296.85966         .         .
           0.35  323.85357         .         .
           0.40  351.73439         .         .
           0.45  380.99190         .         .
           0.50  412.16060         .         .
           0.55  445.87920         .         .
           0.60  482.96773         .         .
           0.65  524.54682         .         .
           0.70  572.24468         .         .
           0.75  628.59543         .         .
           0.80  697.89842         .         .
           0.85  788.38060         .         .
           0.90  919.07555         .         .
           0.91  953.76377         .         .
           0.92  992.93312         .         .
           0.93       1038         .         .
           0.94       1090         .         .
           0.95       1154         .         .
           0.96       1233         .         .
           0.97       1337         .         .
```

```
         PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.98      1490           .        .
       0.99      1767           .        .
```

Brodifacoum

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Brod_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.45 0 11
F 0.6 7 16
F 0.85 7 10
M 0.55 8 24
M 0.75 18 34
M 0.9 17 20
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                    The GENMOD Procedure

                     Model Information

          Data Set                          WORK.BROD_HMR
          Distribution                           Binomial
          Link Function                            PROBIT
          Response Variable (Events)                 resp
          Response Variable (Trials)                    n

            Number of Observations Read     6
            Number of Observations Used     6
            Number of Events               57
            Number of Trials              115

                 Class Level Information

                 Class    Levels  Values
                 SEX           2  F M

                    Response Profile

            Ordered  Binary Outcome      Total
              Value                  Frequency
                  1  Event                  57
                  2  Nonevent               58

          Criteria For Assessing Goodness Of Fit

       Criterion                  DF      Value   Value/DF
       Deviance                    2     4.6072     2.3036
       Scaled Deviance             2     4.6072     2.3036
       Pearson Chi-Square          2     3.8388     1.9194
       Scaled Pearson X2           2     3.8388     1.9194
       Log Likelihood                  -66.6159
       Full Log Likelihood             -10.4230
       AIC (smaller is better)          28.8460
       AICC (smaller is better)         68.8460
       BIC (smaller is better)          28.0131

                   Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard     Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits    Chi-
                                                         Square

Intercept     1    1.0230     0.3153    0.4051    1.6409  10.53      0.0012

SEX        F  1    0.3109     0.6375   -0.9385    1.5603   0.24      0.6258

SEX        M  0    0.0000     0.0000    0.0000    0.0000      .           .

Ldose*SEX  F  1    8.0631     2.5761    3.0140   13.1122   9.80      0.0017

Ldose*SEX  M  1    6.0258     1.8628    2.3749    9.6768  10.46      0.0012

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                         The GENMOD Procedure
                          Model Information

              Data Set                          WORK.BROD_HMR

              Distribution                           Binomial

              Link Function                            PROBIT

              Response Variable (Events)                 resp

              Response Variable (Trials)                    n


                  Number of Observations Read    6

                  Number of Observations Used    6

                  Number of Events              57

                  Number of Trials             115


                      Class Level Information

                      Class    Levels Values

                      SEX           2  F M


                         Response Profile

                  Ordered  Binary Outcome      Total
                    Value                  Frequency

                        1  Event                  57

                        2  Nonevent               58


             Criteria For Assessing Goodness Of Fit

          Criterion                   DF      Value  Value/DF

          Deviance                     3     5.0272    1.6757

          Scaled Deviance              3     5.0272    1.6757

          Pearson Chi-Square           3     3.9465    1.3155

          Scaled Pearson X2            3     3.9465    1.3155

          Log Likelihood                   -66.8260

          Full Log Likelihood              -10.6330

          AIC (smaller is better)           27.2660

          AICC (smaller is better)          39.2660

          BIC (smaller is better)           26.6413

                         Algorithm converged.
```

```
           Analysis Of Maximum Likelihood Parameter Estimates
Parameter     DF Estimate  Standard      Wald 95%           Wald  Pr > ChiSq
                              Error Confidence Limits       Chi-
                                                          Square

Intercept      1   1.1323    0.2684    0.6061   1.6584     17.79      <.0001

SEX          F 1  -0.0543    0.2848   -0.6124   0.5038      0.04      0.8487

SEX          M 0   0.0000    0.0000    0.0000   0.0000         .           .

Ldose          1   6.7574    1.4910    3.8351   9.6798     20.54      <.0001

Scale          0   1.0000    0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                  The GENMOD Procedure
                   Model Information

      Data Set                          WORK.BROD_HMR

      Distribution                           Binomial

      Link Function                            PROBIT

      Response Variable (Events)                 resp

      Response Variable (Trials)                    n


         Number of Observations Read    6

         Number of Observations Used    6

         Number of Events              57

         Number of Trials             115


             Class Level Information

             Class    Levels Values

             SEX           2  F M


                Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                  57

               2 Nonevent               58


       Criteria For Assessing Goodness Of Fit

    Criterion                  DF      Value  Value/DF

    Deviance                    4     5.0636    1.2659

    Scaled Deviance             4     5.0636    1.2659

    Pearson Chi-Square          4     3.9285    0.9821

    Scaled Pearson X2           4     3.9285    0.9821

    Log Likelihood                  -66.8441

    Full Log Likelihood             -10.6512

    AIC (smaller is better)          25.3024

    AICC (smaller is better)         29.3024

    BIC (smaller is better)          24.8859

                 Algorithm converged.
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter	DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept	1	1.1281	0.2673	0.6043	1.6520	17.82	<.0001
Ldose	1	6.8303	1.4396	4.0088	9.6519	22.51	<.0001
Scale	0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Brod_hmr;
input SEX$ dose resp n;
cards;
f 0.45 0 11
F 0.6 7 16
F 0.85 7 10
M 0.55 8 24
M 0.75 18 34
M 0.9 17 20
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
             The PROBIT Procedure
          PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.01 0.31207   0.17744    0.39695
       0.02 0.34210   0.20724    0.42419
       0.03 0.36264   0.22865    0.44252
       0.04 0.37890   0.24617    0.45689
       0.05 0.39266   0.26138    0.46896
       0.06 0.40477   0.27504    0.47953
       0.07 0.41569   0.28758    0.48903
       0.08 0.42572   0.29928    0.49772
       0.09 0.43505   0.31031    0.50580
       0.10 0.44382   0.32080    0.51338
       0.15 0.48205   0.36787    0.54640
       0.20 0.51478   0.40964    0.57489
       0.25 0.54461   0.44858    0.60139
       0.30 0.57288   0.48583    0.62734
       0.35 0.60038   0.52192    0.65386
       0.40 0.62769   0.55701    0.68206
       0.45 0.65530   0.59099    0.71316
       0.50 0.68365   0.62367    0.74847
       0.55 0.71324   0.65500    0.78933
       0.60 0.74461   0.68527    0.83698
       0.65 0.77848   0.71516    0.89283
       0.70 0.81585   0.74565    0.95882
       0.75 0.85819   0.77802    1.03818
       0.80 0.90793   0.81404    1.13665
       0.85 0.96956   0.85660    1.26553
       0.90 1.05308   0.91180    1.45108
       0.91 1.07431   0.92548    1.50012
       0.92 1.09786   0.94051    1.55538
       0.93 1.12435   0.95725    1.61861
       0.94 1.15469   0.97623    1.69240
       0.95 1.19029   0.99824    1.78082
       0.96 1.23352   1.02464    1.89082
       0.97 1.28883   1.05792    2.03565
       0.98 1.36621   1.10366    2.24588
```

```
          PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.99 1.49771   1.17942    2.62298
```

Bromadiolone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Brom_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 25 2 16
F 35 8 15
F 60 14 15
F 100 5 5
M 15 2 14
M 25 12 24
M 60 18 24
M 100 22 29
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT
run;
```

```
                  The GENMOD Procedure
                   Model Information

   Data Set                          WORK.BROM_HMR
   Distribution                           Binomial
   Link Function                            PROBIT
   Response Variable (Events)                 resp
   Response Variable (Trials)                    n

        Number of Observations Read     8
        Number of Observations Used     8
        Number of Events               83
        Number of Trials              142

              Class Level Information
              Class    Levels Values
              SEX           2 F M

                  Response Profile
        Ordered Binary Outcome      Total
          Value                 Frequency
              1 Event                  83
              2 Nonevent               59

     Criteria For Assessing Goodness Of Fit
  Criterion                 DF     Value  Value/DF
  Deviance                   4    3.2091    0.8023
  Scaled Deviance            4    3.2091    0.8023
  Pearson Chi-Square         4    3.0677    0.7669
  Scaled Pearson X2          4    3.0677    0.7669
  Log Likelihood               -73.5711
  Full Log Likelihood          -11.9142
  AIC (smaller is better)       31.8284
  AICC (smaller is better)      45.1617
  BIC (smaller is better)       32.1462

                  Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate  Standard     Wald 95%          Wald  Pr > ChiSq
                              Error  Confidence Limits    Chi-
                                                         Square

Intercept     1   -2.7440    0.7783   -4.2694  -1.2186    12.43      0.0004

SEX        F  1   -8.0949    2.7310  -13.4476  -2.7422     8.79      0.0030

SEX        M  0    0.0000    0.0000    0.0000   0.0000        .           .

Ldose*SEX  F  1    7.0023    1.6942    3.6817  10.3230    17.08      <.0001

Ldose*SEX  M  1    1.8144    0.4667    0.8996   2.7291    15.11      0.0001

Scale         0    1.0000    0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                  The GENMOD Procedure
                   Model Information

       Data Set                         WORK.BROM_HMR
       Distribution                          Binomial
       Link Function                           PROBIT
       Response Variable (Events)                resp
       Response Variable (Trials)                   n

          Number of Observations Read    8
          Number of Observations Used    8
          Number of Events              83
          Number of Trials             142

               Class Level Information
               Class    Levels Values
               SEX           2 F M

                  Response Profile
        Ordered  Binary Outcome      Total
          Value                  Frequency
              1  Event                  83
              2  Nonevent               59

        Criteria For Assessing Goodness Of Fit
     Criterion                  DF     Value  Value/DF
     Deviance                    5   15.2203    3.0441
     Scaled Deviance             5   15.2203    3.0441
     Pearson Chi-Square          5   13.4103    2.6821
     Scaled Pearson X2           5   13.4103    2.6821
     Log Likelihood                 -79.5767
     Full Log Likelihood            -17.9198
     AIC (smaller is better)         41.8396
     AICC (smaller is better)        47.8396
     BIC (smaller is better)         42.0779

                 Algorithm converged.
```

```
                Analysis Of Maximum Likelihood Parameter Estimates

Parameter     DF  Estimate   Standard       Wald 95%           Wald  Pr > ChiSq
                                Error  Confidence Limits       Chi-
                                                             Square

Intercept      1   -3.7440     0.7384  -5.1912  -2.2968       25.71      <.0001

SEX          F 1    0.0496     0.2391  -0.4190   0.5182        0.04      0.8358

SEX          M 0    0.0000     0.0000   0.0000   0.0000           .           .

Ldose          1    2.4243     0.4418   1.5584   3.2901       30.11      <.0001

Scale          0    1.0000     0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

      Data Set                          WORK.BROM_HMR

      Distribution                           Binomial

      Link Function                            PROBIT

      Response Variable (Events)                 resp

      Response Variable (Trials)                    n


         Number of Observations Read    8

         Number of Observations Used    8

         Number of Events              83

         Number of Trials             142


            Class Level Information

            Class    Levels  Values

            SEX           2  F M


               Response Profile

        Ordered  Binary Outcome      Total
          Value                  Frequency

              1  Event                  83

              2  Nonevent               59


             Parameter Information

             Parameter  Effect

             Prm1       Intercept

             Prm2       Ldose


       Criteria For Assessing Goodness Of Fit

    Criterion                  DF      Value  Value/DF

    Deviance                    6    15.2633    2.5439

    Scaled Deviance             6    15.2633    2.5439

    Pearson Chi-Square          6    13.4282    2.2380

    Scaled Pearson X2           6    13.4282    2.2380

    Log Likelihood                  -79.5982

    Full Log Likelihood             -17.9413

    AIC (smaller is better)          39.8826

    AICC (smaller is better)         42.2826

    BIC (smaller is better)          40.0415
```

```
                          Algorithm converged.

            Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard      Wald 95%           Wald Pr > ChiSq
                           Error  Confidence Limits      Chi-
                                                       Square

Intercept  1  -3.7114     0.7203  -5.1230   -2.2997     26.55      <.0001

Ldose      1   2.4154     0.4392   1.5545    3.2763     30.24      <.0001

Scale      0   1.0000     0.0000   1.0000    1.0000
```

PROBIT Dose Response data assuming a separate response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Brom_Hmr;
input SEX$ dose resp n;
cards;
F 25 2 16
F 35 8 15
F 60 14 15
F 100 5 5
M 15 2 14
M 25 12 24
M 60 18 24
M 100 22 29
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
by sex;
run;
```

PROBIT data response data for females

```
                         The PROBIT Procedure
                               SEX=F

                       PROBIT Analysis on dose

              Probability     dose  95% Fiducial Limits

                     0.01 16.43144   8.15107   21.49266

                     0.02 17.97236   9.63099   22.92356

                     0.03 19.02413  10.70101   23.89236

                     0.04 19.85571  11.57981   24.65614

                     0.05 20.55887  12.34451   25.30173

                     0.06 21.17695  13.03233   25.86990

                     0.07 21.73416  13.66442   26.38333

                     0.08 22.24551  14.25403   26.85604

                     0.09 22.72099  14.81011   27.29737

                     0.10 23.16766  15.33900   27.71390

                     0.15 25.11235  17.70605   29.55935

                     0.20 26.77369  19.79085   31.19874

                     0.25 28.28630  21.71345   32.76860

                     0.30 29.71737  23.52859   34.34759

                     0.35 31.10801  25.26389   35.99487

                     0.40 32.48772  26.93396   37.76336

                     0.45 33.88083  28.54785   39.70520

                     0.50 35.31015  30.11417   41.87493

                     0.55 36.79978  31.64484   44.33290

                     0.60 38.37779  33.15778   47.15131

                     0.65 40.07993  34.67867   50.42510

                     0.70 41.95549  36.24320   54.29142

                     0.75 44.07811  37.90194   58.96601

                     0.80 46.56836  39.73201   64.81982

                     0.85 49.64916  41.86747   72.56991

                     0.90 53.81670  44.59347   83.88495

                     0.91 54.87466  45.26228   86.90292

                     0.92 56.04758  45.99447   90.31601

                     0.93 57.36622  46.80689   94.23659

                     0.94 58.87565  47.72401   98.83167

                     0.95 60.64569  48.78356  104.36445

                     0.96 62.79337  50.04821  111.28458

                     0.97 65.53818  51.63447  120.45539
```

```
        PROBIT Analysis on dose
Probability      dose 95% Fiducial Limits
       0.98  69.37356  53.80123  133.87668
       0.99  75.87936  57.36342  158.23782
```

PROBIT data response data for males

```
                    The PROBIT Procedure
                           SEX=M

                  PROBIT Analysis on dose

  Probability       dose  95% Fiducial Limits

         0.01    1.69905    0.06032    5.23448

         0.02    2.40133    0.12068    6.61668

         0.03    2.99073    0.18726    7.68158

         0.04    3.52767    0.26051    8.59733

         0.05    4.03476    0.34067    9.42480

         0.06    4.52341    0.42796   10.19391

         0.07    5.00032    0.52261   10.92195

         0.08    5.46985    0.62488   11.61993

         0.09    5.93505    0.73505   12.29544

         0.10    6.39816    0.85342   12.95394

         0.15    8.73280    1.58035   16.10983

         0.20   11.18216    2.57047   19.22043

         0.25   13.82425    3.88779   22.44361

         0.30   16.72493    5.61323   25.90675

         0.35   19.95352    7.84607   29.75312

         0.40   23.59161   10.70206   34.18008

         0.45   27.74167   14.30288   39.49439

         0.50   32.53807   18.74880   46.20744

         0.55   38.16374   24.07220   55.19454

         0.60   44.87722   30.20571   67.92685

         0.65   53.05961   37.04530   86.78666

         0.70   63.30224   44.61993  115.66884

         0.75   76.58469   53.24086  161.55891

         0.80   94.67989   63.61191  238.81221

         0.85  121.23554   77.13468  382.18715

         0.90  165.47360   97.07715  699.34498

         0.91  178.38534  102.48453  810.31221

         0.92  193.55648  108.65379  951.31678

         0.93  211.73141  115.81460       1135

         0.94  234.05458  124.31196       1384

         0.95  262.40097  134.69642       1735

         0.96  300.12060  147.92234       2265

         0.97  354.00188  165.85495       3146
```

```
          PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.98 440.89098 192.91465       4872
       0.99 623.12650 244.39348       9726
```

Difenacoum

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Difen_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 1 0 5
F 1.3 5 16
F 1.35 5 16
F 1.4 8 16
F 1.5 9 15
F 2.5 4 5
F 5 5 5
M 0.5 0 14
M 0.8 2 6
M 1 6 21
M 1.1 9 15
M 1.2 9 10
M 1.3 6 9
M 1.4 5 5
M 1.5 4 5
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
             The GENMOD Procedure
              Model Information

  Data Set                    WORK.DIFEN_HMR

  Distribution                      Binomial

  Link Function                       PROBIT

  Response Variable (Events)            resp

  Response Variable (Trials)               n

       Number of Observations Read   15

       Number of Observations Used   15

       Number of Events              77

       Number of Trials             163

           Class Level Information

           Class    Levels Values

           SEX           2  F M

               Response Profile

       Ordered Binary Outcome     Total
         Value                Frequency

             1 Event                 77

             2 Nonevent              86

    Criteria For Assessing Goodness Of Fit

Criterion                 DF     Value  Value/DF

Deviance                  11   11.9217    1.0838

Scaled Deviance           11   11.9217    1.0838

Pearson Chi-Square        11   10.6453    0.9678

Scaled Pearson X2         11   10.6453    0.9678

Log Likelihood                -87.4826

Full Log Likelihood           -20.6575

AIC (smaller is better)        49.3149

AICC (smaller is better)       53.3149

BIC (smaller is better)        52.1471

             Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard       Wald 95%             Wald  Pr > ChiSq
                               Error  Confidence Limits         Chi-
                                                              Square

Intercept     1   -0.1841     0.1794   -0.5358    0.1676        1.05      0.3049

SEX        F  1   -0.9622     0.4196   -1.7846   -0.1397        5.26      0.0219

SEX        M  0    0.0000     0.0000    0.0000    0.0000           .           .

Ldose*SEX  F  1    6.3983     2.3464    1.7994   10.9972        7.44      0.0064

Ldose*SEX  M  1    8.3841     2.1523    4.1658   12.6025       15.18      <.0001

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                            WORK.DIFEN_HMR

      Distribution                              Binomial

      Link Function                               PROBIT

      Response Variable (Events)                    resp

      Response Variable (Trials)                       n


           Number of Observations Read   15

           Number of Observations Used   15

           Number of Events              77

           Number of Trials             163


               Class Level Information

               Class    Levels Values

               SEX           2  F M


                  Response Profile

          Ordered Binary Outcome      Total
            Value                 Frequency

                1 Event                  77

                2 Nonevent               86


        Criteria For Assessing Goodness Of Fit

    Criterion                  DF     Value  Value/DF

    Deviance                   12   12.3073    1.0256

    Scaled Deviance            12   12.3073    1.0256

    Pearson Chi-Square         12   11.6897    0.9741

    Scaled Pearson X2          12   11.6897    0.9741

    Log Likelihood                 -87.6753

    Full Log Likelihood            -20.8502

    AIC (smaller is better)         47.7005

    AICC (smaller is better)        49.8823

    BIC (smaller is better)         49.8246


                    Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                              Error  Confidence Limits     Chi-
                                                         Square

Intercept     1  -0.1528     0.1668  -0.4796    0.1741     0.84      0.3597

SEX        F  1  -1.1656     0.2786  -1.7118   -0.6195    17.50      <.0001

SEX        M  0   0.0000     0.0000   0.0000    0.0000        .           .

Ldose         1   7.5675     1.5587   4.5125   10.6225    23.57      <.0001

Scale         0   1.0000     0.0000   1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

     Data Set                          WORK.DIFEN_HMR

     Distribution                            Binomial

     Link Function                             PROBIT

     Response Variable (Events)                  resp

     Response Variable (Trials)                     n


          Number of Observations Read   15

          Number of Observations Used   15

          Number of Events              77

          Number of Trials             163


              Class Level Information

              Class    Levels Values

              SEX           2  F M


                 Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                  77

               2 Nonevent               86


       Criteria For Assessing Goodness Of Fit

   Criterion                  DF      Value  Value/DF

   Deviance                   13    31.5551    2.4273

   Scaled Deviance            13    31.5551    2.4273

   Pearson Chi-Square         13    26.6320    2.0486

   Scaled Pearson X2          13    26.6320    2.0486

   Log Likelihood                  -97.2993

   Full Log Likelihood             -30.4742

   AIC (smaller is better)          64.9483

   AICC (smaller is better)         65.9483

   BIC (smaller is better)          66.3644

                 Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates

Parameter  DF  Estimate    Standard       Wald 95%              Wald  Pr > ChiSq
                              Error  Confidence Limits          Chi-
                                                              Square

Intercept   1   -0.4295      0.1354   -0.6949    -0.1641       10.06      0.0015

Ldose       1    4.1941      0.9655    2.3018     6.0864       18.87      <.0001

Scale       0    1.0000      0.0000    1.0000     1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a parallel response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Difen_hmr;
input SEX$ dose resp n;
cards;
F 1 0 5
F 1.3 5 16
F 1.35 5 16
F 1.4 8 16
F 1.5 9 15
F 2.5 4 5
F 5 5 5
M 0.5 0 14
M 0.8 2 6
M 1 6 21
M 1.1 9 15
M 1.2 9 10
M 1.3 6 9
M 1.4 5 5
M 1.5 4 5
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
class sex;
model resp/n=sex dose;
run;
```

PROBIT response data for females

```
           The PROBIT Procedure
          PROBIT Analysis on dose
Probability     dose  95% Fiducial Limits
       0.01 0.73588   0.46808   0.90005
       0.02 0.79952   0.53675   0.95696
       0.03 0.84272   0.58525   0.99525
       0.04 0.87675   0.62446   1.02529
       0.05 0.90545   0.65816   1.05059
       0.06 0.93061   0.68818   1.07277
       0.07 0.95324   0.71553   1.09275
       0.08 0.97398   0.74084   1.11109
       0.09 0.99323   0.76456   1.12817
       0.10 1.01128   0.78697   1.14425
       0.15 1.08959   0.88571   1.21501
       0.20 1.15613   0.97068   1.27735
       0.25 1.21644   1.04736   1.33677
       0.30 1.27328   1.11818   1.39648
       0.35 1.32832   1.18428   1.45883
       0.40 1.38275   1.24633   1.52579
       0.45 1.43752   1.30491   1.59907
       0.50 1.49355   1.36074   1.68015
       0.55 1.55177   1.41479   1.77055
       0.60 1.61324   1.46822   1.87208
       0.65 1.67934   1.52237   1.98731
       0.70 1.75193   1.57884   2.12013
       0.75 1.83379   1.63968   2.27683
       0.80 1.92946   1.70795   2.46823
       0.85 2.04729   1.78892   2.71507
       0.90 2.20582   1.89384   3.06495
       0.91 2.24592   1.91979   3.15651
       0.92 2.29030   1.94827   3.25926
       0.93 2.34012   1.97995   3.37632
       0.94 2.39704   2.01580   3.51227
       0.95 2.46365   2.05733   3.67430
       0.96 2.54427   2.10702   3.87460
```

```
          PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.97 2.64702   2.16949   4.13635
       0.98 2.79005   2.25504   4.51265
       0.99 3.03134   2.39603   5.17804
```

PROBIT data response data for males

```
                  The PROBIT Procedure
                PROBIT Analysis on dose
      Probability    dose  95% Fiducial Limits
             0.01 0.51615   0.30692   0.64895
             0.02 0.56079   0.35213   0.68961
             0.03 0.59109   0.38412   0.71688
             0.04 0.61496   0.41003   0.73821
             0.05 0.63508   0.43234   0.75611
             0.06 0.65273   0.45225   0.77175
             0.07 0.66861   0.47041   0.78580
             0.08 0.68315   0.48727   0.79865
             0.09 0.69665   0.50308   0.81057
             0.10 0.70931   0.51807   0.82175
             0.15 0.76424   0.58455   0.87036
             0.20 0.81091   0.64265   0.91213
             0.25 0.85321   0.69620   0.95075
             0.30 0.89308   0.74703   0.98821
             0.35 0.93169   0.79613   1.02593
             0.40 0.96986   0.84405   1.06514
             0.45 1.00828   0.89105   1.10710
             0.50 1.04758   0.93726   1.15321
             0.55 1.08841   0.98276   1.20503
             0.60 1.13153   1.02777   1.26434
             0.65 1.17789   1.07278   1.33328
             0.70 1.22881   1.11869   1.41460
             0.75 1.28623   1.16695   1.51246
             0.80 1.35333   1.21983   1.63383
             0.85 1.43597   1.28128   1.79214
             0.90 1.54717   1.35959   2.01839
             0.91 1.57529   1.37880   2.07780
             0.92 1.60642   1.39983   2.14455
             0.93 1.64136   1.42317   2.22067
             0.94 1.68129   1.44953   2.30916
             0.95 1.72801   1.47998   2.41472
             0.96 1.78456   1.51634   2.54532
             0.97 1.85662   1.56196   2.71612
```

```
        PROBIT Analysis on dose
Probability    dose 95% Fiducial Limits
       0.98 1.95694   1.62430   2.96186
       0.99 2.12618   1.72679   3.39673
```

Difethialone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Difeth_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.4 0 11
F 0.5 0 20
F 0.75 2 6
F 1 12 25
F 1.2 4 16
M 0.4 0 15
M 0.5 3 20
M 1 5 15
M 1.2 4 8
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                     The GENMOD Procedure
                      Model Information

          Data Set                      WORK.DIFETH_HMR

          Distribution                         Binomial

          Link Function                          PROBIT

          Response Variable (Events)               resp

          Response Variable (Trials)                  n


                Number of Observations Read    9

                Number of Observations Used    9

                Number of Events              30

                Number of Trials             136


                    Class Level Information

                    Class    Levels Values

                    SEX           2 F M


                       Response Profile

               Ordered Binary Outcome      Total
                 Value                 Frequency

                     1 Event                  30

                     2 Nonevent              106


            Criteria For Assessing Goodness Of Fit

        Criterion                 DF      Value  Value/DF

        Deviance                   5    10.7915    2.1583

        Scaled Deviance            5    10.7915    2.1583

        Pearson Chi-Square         5     9.4118    1.8824

        Scaled Pearson X2          5     9.4118    1.8824

        Log Likelihood                 -59.0679

        Full Log Likelihood            -14.0944

        AIC (smaller is better)         36.1889

        AICC (smaller is better)        46.1889

        BIC (smaller is better)         36.9778


                      Algorithm converged.
```

```
                Analysis Of Maximum Likelihood Parameter Estimates

Parameter     DF  Estimate   Standard      Wald 95%            Wald  Pr > ChiSq
                                Error  Confidence Limits       Chi-
                                                             Square

Intercept      1   -0.3264     0.2436   -0.8039   0.1511       1.79      0.1804

SEX         F  1   -0.0996     0.3022   -0.6919   0.4926       0.11      0.7416

SEX         M  0    0.0000     0.0000    0.0000   0.0000          .           .

Ldose*SEX   F  1    4.4639     1.3905    1.7386   7.1891      10.31      0.0013

Ldose*SEX   M  1    3.3081     1.1249    1.1033   5.5129       8.65      0.0033

Scale          0    1.0000     0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                              WORK.DIFETH_HMR
      Distribution                                 Binomial
      Link Function                                  PROBIT
      Response Variable (Events)                       resp
      Response Variable (Trials)                          n

            Number of Observations Read     9
            Number of Observations Used     9
            Number of Events               30
            Number of Trials              136

                  Class Level Information
                  Class    Levels  Values
                  SEX           2  F M

                      Response Profile
            Ordered  Binary Outcome      Total
              Value                  Frequency
                  1  Event                  30
                  2  Nonevent              106

        Criteria For Assessing Goodness Of Fit
    Criterion                 DF        Value    Value/DF
    Deviance                   6      11.2236      1.8706
    Scaled Deviance            6      11.2236      1.8706
    Pearson Chi-Square         6       9.7138      1.6190
    Scaled Pearson X2          6       9.7138      1.6190
    Log Likelihood                   -59.2840
    Full Log Likelihood              -14.3105
    AIC (smaller is better)           34.6210
    AICC (smaller is better)          39.4210
    BIC (smaller is better)           35.2127

                    Algorithm converged.
```

```
             Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits     Chi-
                                                          Square

Intercept     1   -0.2693     0.2269   -0.7141   0.1755     1.41      0.2353

SEX        F  1   -0.1790     0.2751   -0.7181   0.3601     0.42      0.5152

SEX        M  0    0.0000     0.0000    0.0000   0.0000        .           .

Ldose         1    3.8047     0.8535    2.1318   5.4775    19.87      <.0001

Scale         0    1.0000     0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
             The GENMOD Procedure

              Model Information
  Data Set                   WORK.DIFETH_HMR
  Distribution                      Binomial
  Link Function                       PROBIT
  Response Variable (Events)            resp
  Response Variable (Trials)               n

       Number of Observations Read    9
       Number of Observations Used    9
       Number of Events              30
       Number of Trials             136

           Class Level Information
           Class    Levels Values
           SEX           2 F M

               Response Profile
       Ordered Binary Outcome     Total
         Value                Frequency
             1 Event                 30
             2 Nonevent             106

    Criteria For Assessing Goodness Of Fit
Criterion                DF    Value Value/DF
Deviance                  7  11.6482   1.6640
Scaled Deviance           7  11.6482   1.6640
Pearson Chi-Square        7   9.9977   1.4282
Scaled Pearson X2         7   9.9977   1.4282
Log Likelihood              -59.4963
Full Log Likelihood         -14.5228
AIC (smaller is better)      33.0456
AICC (smaller is better)     35.0456
BIC (smaller is better)      33.4400

             Algorithm converged.
```

```
             Analysis Of Maximum Likelihood Parameter Estimates
Parameter DF Estimate   Standard       Wald 95%           Wald Pr > ChiSq
                           Error  Confidence Limits       Chi-
                                                        Square

Intercept  1  -0.3842     0.1437   -0.6658   -0.1026      7.15     0.0075

Ldose      1   3.6941     0.8299    2.0676    5.3206     19.81     <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Difeth_hmr;
input SEX$ dose resp n;
cards;
f 0.45 0 11
F 0.5 0 20
F 0.75 2 6
F 1 12 25
F 1.2 4 16
M 0.4 0 15
M 0.5 3 20
M 1 5 15
M 1.2 4 8
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                  The PROBIT Procedure
                PROBIT Analysis on dose

Probability    dose  95% Fiducial Limits
       0.01 0.30222   0.13000    0.42641
       0.02 0.35759   0.17474    0.48161
       0.03 0.39787   0.21059    0.52080
       0.04 0.43114   0.24215    0.55279
       0.05 0.46024   0.27110    0.58061
       0.06 0.48655   0.29829    0.60574
       0.07 0.51086   0.32420    0.62899
       0.08 0.53365   0.34911    0.65091
       0.09 0.55526   0.37324    0.67185
       0.10 0.57592   0.39672    0.69208
       0.15 0.66998   0.50689    0.78838
       0.20 0.75558   0.60742    0.88659
       0.25 0.83768   0.69848    0.99589
       0.30 0.91898   0.78015    1.12203
       0.35 1.00135   0.85416    1.26807
       0.40 1.08633   0.92316    1.43607
       0.45 1.17540   0.98972    1.62876
       0.50 1.27019   1.05598    1.85050
       0.55 1.37262   1.12376    2.10786
       0.60 1.48517   1.19486    2.41056
       0.65 1.61120   1.27126    2.77312
       0.70 1.75561   1.35553    3.21804
       0.75 1.92600   1.45135    3.78221
       0.80 2.13528   1.56470    4.53148
       0.85 2.40809   1.70663    5.59880
       0.90 2.80139   1.90190    7.31246
       0.91 2.90564   1.95210    7.80052
       0.92 3.02330   2.00805    8.36808
       0.93 3.15818   2.07132    9.04034
       0.94 3.31595   2.14424    9.85571
       0.95 3.50552   2.23040   10.87644
       0.96 3.74214   2.33589   12.21242
       0.97 4.05502   2.47220   14.08315
       0.98 4.51182   2.66542   17.02328
```

```
        PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.99 5.33850   3.00028   22.95837
```

Flocoumafen

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Floc_hmr;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.25 0 15
F 0.3 0 15
F 0.4 0 16
F 0.45 3 13
F 0.5 17 26
F 0.65 7 10
F 1 17 17
M 0.25 0 5
M 0.3 2 5
M 0.4 6 15
M 0.45 8 15
M 0.5 10 13
M 0.8 5 10
M 1 9 9
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                    The GENMOD Procedure
                     Model Information

       Data Set                          WORK.FLOC_HMR

       Distribution                           Binomial

       Link Function                            PROBIT

       Response Variable (Events)                 resp

       Response Variable (Trials)                    n


            Number of Observations Read   14

            Number of Observations Used   14

            Number of Events              84

            Number of Trials             184


                Class Level Information

                Class    Levels Values

                SEX           2  F M


                   Response Profile

           Ordered Binary Outcome      Total
             Value                 Frequency

                 1 Event                  84

                 2 Nonevent              100


        Criteria For Assessing Goodness Of Fit

    Criterion                  DF     Value  Value/DF

    Deviance                   10   22.3893    2.2389

    Scaled Deviance            10   22.3893    2.2389

    Pearson Chi-Square         10   20.3119    2.0312

    Scaled Pearson X2          10   20.3119    2.0312

    Log Likelihood                 -78.8750

    Full Log Likelihood            -22.7010

    AIC (smaller is better)         53.4021

    AICC (smaller is better)        57.8465

    BIC (smaller is better)         55.9583

                   Algorithm converged.
```

```
             Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate   Standard      Wald 95%          Wald Pr > ChiSq
                              Error Confidence Limits      Chi-
                                                         Square

Intercept     1   1.1409     0.3566  0.4419    1.8399     10.23     0.0014

SEX         F 1   2.2489     0.8989  0.4872    4.0107      6.26     0.0124

SEX         M 0   0.0000     0.0000  0.0000    0.0000         .          .

Ldose*SEX   F 1  11.5797     2.5885  6.5064   16.6531     20.01     <.0001

Ldose*SEX   M 1   3.2426     1.0210  1.2415    5.2437     10.09     0.0015

Scale         0   1.0000     0.0000  1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

     Data Set                         WORK.FLOC_HMR

     Distribution                          Binomial

     Link Function                           PROBIT

     Response Variable (Events)                resp

     Response Variable (Trials)                   n


         Number of Observations Read   14

         Number of Observations Used   14

         Number of Events              84

         Number of Trials             184


             Class Level Information

             Class    Levels Values

             SEX           2  F M


                Response Profile

        Ordered Binary Outcome      Total
          Value                 Frequency

              1 Event                  84

              2 Nonevent              100


       Criteria For Assessing Goodness Of Fit

   Criterion                 DF     Value  Value/DF

   Deviance                  11   36.7823    3.3438

   Scaled Deviance           11   36.7823    3.3438

   Pearson Chi-Square        11   42.9805    3.9073

   Scaled Pearson X2         11   42.9805    3.9073

   Log Likelihood                -86.0715

   Full Log Likelihood           -29.8975

   AIC (smaller is better)        65.7951

   AICC (smaller is better)       68.1951

   BIC (smaller is better)        67.7123

                 Algorithm converged.
```

```
             Analysis Of Maximum Likelihood Parameter Estimates

Parameter     DF  Estimate   Standard        Wald 95%           Wald  Pr > ChiSq
                                Error  Confidence Limits        Chi-
                                                              Square

Intercept      1    1.9801     0.3152     1.3623    2.5979     39.46      <.0001

SEX          F 1   -0.3851     0.2210    -0.8183    0.0481      3.04      0.0814

SEX          M 0    0.0000     0.0000     0.0000    0.0000         .           .

Ldose          1    5.8759     0.8330     4.2434    7.5085     49.76      <.0001

Scale          0    1.0000     0.0000     1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

      Data Set                           WORK.FLOC_HMR

      Distribution                            Binomial

      Link Function                             PROBIT

      Response Variable (Events)                  resp

      Response Variable (Trials)                     n


          Number of Observations Read   14

          Number of Observations Used   14

          Number of Events              84

          Number of Trials             184


              Class Level Information

              Class    Levels Values

              SEX           2  F M


                 Response Profile

         Ordered Binary Outcome      Total
           Value                 Frequency

               1 Event                  84

               2 Nonevent              100


       Criteria For Assessing Goodness Of Fit

    Criterion                  DF    Value  Value/DF

    Deviance                   12  39.8354    3.3196

    Scaled Deviance            12  39.8354    3.3196

    Pearson Chi-Square         12  39.8039    3.3170

    Scaled Pearson X2          12  39.8039    3.3170

    Log Likelihood                -87.5981

    Full Log Likelihood           -31.4241

    AIC (smaller is better)        66.8481

    AICC (smaller is better)       67.9390

    BIC (smaller is better)        68.1262

                    Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard       Wald 95%       Wald Chi- Pr > ChiSq
                           Error  Confidence Limits      Square

Intercept  1   1.7722     0.2885    1.2067    2.3377      37.73     <.0001

Ldose      1   5.8963     0.8280    4.2734    7.5191      50.71     <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a separate response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Floc_Hmr;
input SEX$ dose resp n;
cards;
F 0.25 0 15
F 0.3 0 15
F 0.4 0 16
F 0.45 3 13
F 0.5 17 26
F 0.65 7 10
F 1 17 17
M 0.25 0 5
M 0.3 2 5
M 0.4 6 15
M 0.45 8 15
M 0.5 10 13
M 0.8 5 10
M 1 9 9
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
by sex;
run;
```

PROBIT response data for females

```
                   The PROBIT Procedure
                         SEX=F
                 PROBIT Analysis on dose
        Probability    dose  95% Fiducial Limits
               0.01  0.32090   0.22875   0.36894
               0.02  0.33877   0.25150   0.38375
               0.03  0.35062   0.26702   0.39355
               0.04  0.35981   0.27928   0.40116
               0.05  0.36746   0.28963   0.40751
               0.06  0.37411   0.29870   0.41304
               0.07  0.38003   0.30686   0.41800
               0.08  0.38541   0.31433   0.42252
               0.09  0.39037   0.32125   0.42672
               0.10  0.39499   0.32772   0.43065
               0.15  0.41472   0.35557   0.44782
               0.20  0.43110   0.37871   0.46277
               0.25  0.44567   0.39899   0.47690
               0.30  0.45917   0.41722   0.49103
               0.35  0.47205   0.43382   0.50569
               0.40  0.48460   0.44905   0.52133
               0.45  0.49706   0.46310   0.53830
               0.50  0.50964   0.47621   0.55687
               0.55  0.52253   0.48866   0.57731
               0.60  0.53597   0.50074   0.59992
               0.65  0.55022   0.51277   0.62516
               0.70  0.56565   0.52510   0.65373
               0.75  0.58279   0.53817   0.68676
               0.80  0.60248   0.55258   0.72620
               0.85  0.62628   0.56936   0.77572
               0.90  0.65756   0.59065   0.84363
               0.91  0.66534   0.59584   0.86101
               0.92  0.67391   0.60151   0.88032
               0.93  0.68345   0.60777   0.90210
               0.94  0.69427   0.61482   0.92711
               0.95  0.70682   0.62292   0.95654
               0.96  0.72185   0.63253   0.99237
```

```
         PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.97  0.74077   0.64449   1.03836
       0.98  0.76669   0.66066   1.10294
       0.99  0.80939   0.68683   1.21326
```

PROBIT response data for males

```
                    The PROBIT Procedure
                           SEX=M
                   PROBIT Analysis on dose
       Probability    dose  95% Fiducial Limits
              0.01 0.08526   0.00506    0.16920
              0.02 0.10346   0.00836    0.19123
              0.03 0.11698   0.01150    0.20675
              0.04 0.12831   0.01462    0.21930
              0.05 0.13832   0.01776    0.23012
              0.06 0.14746   0.02095    0.23978
              0.07 0.15597   0.02422    0.24862
              0.08 0.16400   0.02757    0.25685
              0.09 0.17166   0.03102    0.26459
              0.10 0.17903   0.03457    0.27196
              0.15 0.21307   0.05406    0.30517
              0.20 0.24468   0.07692    0.33527
              0.25 0.27552   0.10381    0.36450
              0.30 0.30650   0.13538    0.39437
              0.35 0.33832   0.17227    0.42640
              0.40 0.37155   0.21491    0.46262
              0.45 0.40682   0.26318    0.50632
              0.50 0.44479   0.31570    0.56310
              0.55 0.48630   0.36951    0.64182
              0.60 0.53246   0.42136    0.75437
              0.65 0.58477   0.47019    0.91503
              0.70 0.64547   0.51756    1.14365
              0.75 0.71806   0.56638    1.47454
              0.80 0.80855   0.62036    1.97522
              0.85 0.92850   0.68502    2.79655
              0.90 1.10504   0.77149    4.35689
              0.91 1.15248   0.79346    4.85239
              0.92 1.20634   0.81788    5.45587
              0.93 1.26847   0.84542    6.20771
              0.94 1.34164   0.87707    7.17216
              0.95 1.43026   0.91439    8.45840
              0.96 1.54189   0.95999   10.27019
```

PROBIT Analysis on dose

Probability	**dose**	**95% Fiducial Limits**	
0.97	1.69114	1.01883	13.04229
0.98	1.91213	1.10214	17.92717
0.99	2.32052	1.24647	29.62260

APPENDIX 3 Chapter 4 GENMOD and PROBIT analysis output for a resistant strain of House mouse heterozygous for the *VKORC1* mutation Y139C

Deviances are highlighted

Brodifacoum

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Brod_wildHh;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.38 0 20
F 0.45 3 12
F 0.6 14 15
M 0.38 1 12
M 0.6 7 12
M 1 16 20
M 1.3 15 15
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                          WORK.BROD_WILDHH

 Distribution                              Binomial

 Link Function                               PROBIT

 Response Variable (Events)                    resp

 Response Variable (Trials)                       n


       Number of Observations Read    7

       Number of Observations Used    7

       Number of Events              56

       Number of Trials             106


            Class Level Information

            Class    Levels Values

            SEX           2  F M


               Response Profile

       Ordered Binary Outcome      Total
         Value                 Frequency

             1 Event                  56

             2 Nonevent               50


     Criteria For Assessing Goodness Of Fit

Criterion                  DF     Value  Value/DF

Deviance                    3    3.5053    1.1684

Scaled Deviance             3    3.5053    1.1684

Pearson Chi-Square          3    2.8028    0.9343

Scaled Pearson X2           3    2.8028    0.9343

Log Likelihood               -33.7750

Full Log Likelihood           -8.0282

AIC (smaller is better)       24.0564

AICC (smaller is better)      44.0564

BIC (smaller is better)       23.8400

                  Algorithm converged.
```

```
             Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF  Estimate   Standard     Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits    Chi-
                                                         Square
Intercept     1    1.1383     0.2673    0.6143    1.6622   18.13     <.0001
SEX        F  1    4.7721     1.4126    2.0035    7.5407   11.41     0.0007
SEX        M  0    0.0000     0.0000    0.0000    0.0000       .          .
Ldose*SEX  F  1   19.4446     4.2981   11.0204   27.8688   20.47     <.0001
Ldose*SEX  M  1    5.5088     1.1831    3.1900    7.8276   21.68     <.0001
Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                     The GENMOD Procedure
                      Model Information

 Data Set                              WORK.BROD_WILDHH
 Distribution                                  Binomial
 Link Function                                   PROBIT
 Response Variable (Events)                        resp
 Response Variable (Trials)                           n

       Number of Observations Read    7
       Number of Observations Used    7
       Number of Events              56
       Number of Trials             106

                 Class Level Information
                 Class    Levels Values
                 SEX           2  F M

                    Response Profile
        Ordered Binary Outcome       Total
          Value                  Frequency
              1 Event                   56
              2 Nonevent                50

     Criteria For Assessing Goodness Of Fit
Criterion                   DF     Value  Value/DF
Deviance                     4   17.9915    4.4979
Scaled Deviance              4   17.9915    4.4979
Pearson Chi-Square           4   14.9786    3.7447
Scaled Pearson X2            4   14.9786    3.7447
Log Likelihood                  -41.0181
Full Log Likelihood             -15.2713
AIC (smaller is better)          36.5426
AICC (smaller is better)         44.5426
BIC (smaller is better)          36.3803

                   Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates
Parameter    DF Estimate  Standard     Wald 95%          Wald Pr > ChiSq
                             Error Confidence Limits     Chi-
                                                       Square

Intercept     1   1.4320    0.2955    0.8529   2.0111   23.49     <.0001

SEX        F  1   0.6838    0.3868   -0.0743   1.4418    3.13     0.0771

SEX        M  0   0.0000    0.0000    0.0000   0.0000       .          .

Ldose         1   7.5530    1.2637    5.0763  10.0297   35.73     <.0001

Scale         0   1.0000    0.0000    1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

    Data Set                           WORK.BROD_WILDHH
    Distribution                               Binomial
    Link Function                                PROBIT
    Response Variable (Events)                     resp
    Response Variable (Trials)                        n

          Number of Observations Read    7
          Number of Observations Used    7
          Number of Events              56
          Number of Trials             106

                 Class Level Information
                 Class    Levels  Values
                 SEX           2  F M

                     Response Profile
          Ordered  Binary Outcome     Total
            Value                 Frequency
                1  Event                 56
                2  Nonevent              50

        Criteria For Assessing Goodness Of Fit
   Criterion                  DF     Value  Value/DF
   Deviance                    5   21.3369    4.2674
   Scaled Deviance             5   21.3369    4.2674
   Pearson Chi-Square          5   18.4740    3.6948
   Scaled Pearson X2           5   18.4740    3.6948
   Log Likelihood                 -42.6908
   Full Log Likelihood            -16.9440
   AIC (smaller is better)         37.8879
   AICC (smaller is better)        40.8879
   BIC (smaller is better)         37.7798

                   Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates
Parameter DF Estimate   Standard      Wald 95%       Wald Chi- Pr > ChiSq
                           Error  Confidence Limits     Square

Intercept  1   1.5043     0.2923    0.9314    2.0772     26.49      <.0001

Ldose      1   6.3561     1.0125    4.3716    8.3406     39.41      <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a separate response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Brod_WildHh;
input SEX$ dose resp n;
cards;
F 0.38 0 20
F 0.45 3 12
F 0.6 14 15
M 0.38 1 12
M 0.6 7 12
M 1 16 20
M 1.3 15 15
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
by sex;
run;
```

PROBIT response data for females

```
                The PROBIT Procedure
                       SEX=F

              PROBIT Analysis on dose

        Probability     dose  95% Fiducial Limits

               0.01 0.377052  0.305200  0.415056
               0.02 0.389422  0.322259  0.425602
               0.03 0.397480  0.333464  0.432572
               0.04 0.403652  0.342079  0.437982
               0.05 0.408742  0.349196  0.442501
               0.06 0.413126  0.355326  0.446439
               0.07 0.417008  0.360752  0.449969
               0.08 0.420515  0.365646  0.453194
               0.09 0.423730  0.370125  0.456185
               0.10 0.426711  0.374267  0.458991
               0.15 0.439278  0.391569  0.471211
               0.20 0.449530  0.405381  0.481757
               0.25 0.458515  0.417160  0.491531
               0.30 0.466737  0.427599  0.500982
               0.35 0.474488  0.437090  0.510386
               0.40 0.481961  0.445889  0.519940
               0.45 0.489304  0.454181  0.529809
               0.50 0.496640  0.462115  0.540145
               0.55 0.504085  0.469820  0.551113
               0.60 0.511765  0.477424  0.562906
               0.65 0.519826  0.485063  0.575775
               0.70 0.528458  0.492899  0.590069
               0.75 0.537934  0.501148  0.606317
               0.80 0.548687  0.510129  0.625386
               0.85 0.561491  0.520396  0.648877
               0.90 0.578028  0.533111  0.680324
               0.91 0.582095  0.536161  0.688232
               0.92 0.586545  0.539468  0.696961
               0.93 0.591478  0.543099  0.706725
               0.94 0.597036  0.547149  0.717834
               0.95 0.603439  0.551767  0.730770
               0.96 0.611049  0.557192  0.746332
               0.97 0.620536  0.563871  0.766006
```

```
          PROBIT Analysis on dose
Probability     dose  95% Fiducial Limits
       0.98 0.633376  0.572776  0.793098
       0.99 0.654155  0.586909  0.838028
```

PROBIT response data for males

```
                    The PROBIT Procedure
                           SEX=M

                  PROBIT Analysis on dose

        Probability    dose  95% Fiducial Limits

               0.01 0.23500    0.10080    0.33779

               0.02 0.26337    0.12233    0.36716

               0.03 0.28311    0.13826    0.38725

               0.04 0.29893    0.15157    0.40318

               0.05 0.31245    0.16330    0.41669

               0.06 0.32444    0.17398    0.42861

               0.07 0.33533    0.18389    0.43939

               0.08 0.34539    0.19322    0.44932

               0.09 0.35480    0.20210    0.45858

               0.10 0.36369    0.21062    0.46732

               0.15 0.40293    0.24960    0.50585

               0.20 0.43711    0.28522    0.53955

               0.25 0.46874    0.31933    0.57112

               0.30 0.49909    0.35286    0.60198

               0.35 0.52896    0.38641    0.63314

               0.40 0.55896    0.42038    0.66549

               0.45 0.58961    0.45507    0.69991

               0.50 0.62140    0.49073    0.73744

               0.55 0.65491    0.52758    0.77933

               0.60 0.69082    0.56586    0.82726

               0.65 0.72999    0.60589    0.88346

               0.70 0.77369    0.64820    0.95113

               0.75 0.82378    0.69372    1.03512

               0.80 0.88339    0.74421    1.14346

               0.85 0.95833    0.80311    1.29151

               0.90 1.06172    0.87825    1.51499

               0.91 1.08832    0.89670    1.57581

               0.92 1.11798    0.91692    1.64511

               0.93 1.15152    0.93939    1.72538

               0.94 1.19017    0.96481    1.82028

               0.95 1.23583    0.99426    1.93565

               0.96 1.29173    1.02954    2.08151

               0.97 1.36392    1.07403    2.27727
```

```
        PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.98  1.46617   1.13526   2.56831
       0.99  1.64312   1.23720   3.10872
```

Bromadiolone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Brom_wildHh;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 5 1 14
F 15 11 15
F 20 14 15
F 23.3 15 15
M 5 0 9
M 10 5 15
M 20 14 14
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                            WORK.BROM_WILDHH
 Distribution                                Binomial
 Link Function                                 PROBIT
 Response Variable (Events)                      resp
 Response Variable (Trials)                         n

        Number of Observations Read    7
        Number of Observations Used    7
        Number of Events              60
        Number of Trials              97

               Class Level Information
               Class    Levels  Values
               SEX           2  F M

                    Response Profile
          Ordered  Binary Outcome      Total
            Value                  Frequency
                1  Event                  60
                2  Nonevent               37

      Criteria For Assessing Goodness Of Fit
 Criterion                    DF      Value  Value/DF
 Deviance                      3     1.5060    0.5020
 Scaled Deviance               3     1.5060    0.5020
 Pearson Chi-Square            3     1.0272    0.3424
 Scaled Pearson X2             3     1.0272    0.3424
 Log Likelihood                    -26.2758
 Full Log Likelihood                -5.7024
 AIC (smaller is better)            19.4049
 AICC (smaller is better)           39.4049
 BIC (smaller is better)            19.1885

                   Algorithm converged.
```

```
                 Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate  Standard       Wald 95%           Wald Pr > ChiSq
                             Error  Confidence Limits       Chi-
                                                          Square

Intercept     1 -24.9464    0.3348  -25.6025  -24.2903   5553.51      <.0001

SEX        F  1  19.7716    1.2593   17.3033   22.2398    246.49      <.0001

SEX        M  0   0.0000    0.0000    0.0000    0.0000         .           .

Ldose*SEX  F  1   5.1162    1.0487    3.0608    7.1716     23.80      <.0001

Ldose*SEX  M  0  24.5157    0.0000   24.5157   24.5157         .           .

Scale         0   1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                     The GENMOD Procedure
                      Model Information

  Data Set                              WORK.BROM_WILDHH

  Distribution                                  Binomial

  Link Function                                   PROBIT

  Response Variable (Events)                        resp

  Response Variable (Trials)                           n


         Number of Observations Read    7

         Number of Observations Used    7

         Number of Events              60

         Number of Trials              97


               Class Level Information

               Class    Levels  Values

               SEX           2  F M


                  Response Profile

          Ordered  Binary Outcome      Total
            Value                  Frequency

                1  Event                  60

                2  Nonevent               37


      Criteria For Assessing Goodness Of Fit

 Criterion                    DF      Value  Value/DF

 Deviance                      4     4.5214    1.1303

 Scaled Deviance               4     4.5214    1.1303

 Pearson Chi-Square            4     3.6895    0.9224

 Scaled Pearson X2             4     3.6895    0.9224

 Log Likelihood                    -27.7835

 Full Log Likelihood                -7.2101

 AIC (smaller is better)            20.4203

 AICC (smaller is better)           28.4203

 BIC (smaller is better)            20.2580

                     Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard       Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits      Chi-
                                                           Square

Intercept     1   -6.2699     1.0968   -8.4197   -4.1202    32.68      <.0001

SEX         F 1    0.0887     0.3900   -0.6757    0.8532     0.05      0.8200

SEX         M 0    0.0000     0.0000    0.0000    0.0000        .           .

Ldose         1    5.9963     1.0113    4.0141    7.9785    35.15      <.0001

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                              WORK.BROM_WILDHH
 Distribution                                  Binomial
 Link Function                                   PROBIT
 Response Variable (Events)                        resp
 Response Variable (Trials)                           n

         Number of Observations Read    7
         Number of Observations Used    7
         Number of Events              60
         Number of Trials              97

               Class Level Information

               Class    Levels Values

               SEX           2 F M

                    Response Profile

        Ordered Binary Outcome       Total
          Value                  Frequency

              1 Event                   60
              2 Nonevent                37

       Criteria For Assessing Goodness Of Fit

Criterion                   DF      Value  Value/DF

Deviance                     5     4.5728    0.9146
Scaled Deviance              5     4.5728    0.9146
Pearson Chi-Square           5     4.0504    0.8101
Scaled Pearson X2            5     4.0504    0.8101
Log Likelihood                   -27.8092
Full Log Likelihood               -7.2358
AIC (smaller is better)           18.4717
AICC (smaller is better)          21.4717
BIC (smaller is better)           18.3635

                   Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard      Wald 95%           Wald  Pr > ChiSq
                           Error  Confidence Limits      Chi-
                                                       Square

Intercept  1  -6.2939     1.1045   -8.4588   -4.1291    32.47      <.0001

Ldose      1   6.0613     0.9841    4.1325    7.9901    37.94      <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Brom_WildHh;
input SEX$ dose resp n;
cards;
f 5 1 14
F 15 11 15
F 20 14 15
F 23.3 15 15
M 5 0 9
M 10 5 15
M 20 14 14
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                 The PROBIT Procedure
              PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.01   4.51414    2.70089   5.96898
       0.02   5.00667    3.13487   6.47542
       0.03   5.34667    3.44464   6.82091
       0.04   5.61757    3.69697   7.09425
       0.05   5.84802    3.91525   7.32569
       0.06   6.05160    4.11070   7.52947
       0.07   6.23592    4.28967   7.71352
       0.08   6.40572    4.45616   7.88278
       0.09   6.56415    4.61284   8.04053
       0.10   6.71346    4.76162   8.18907
       0.15   7.36861    5.42605   8.84091
       0.20   7.93462    6.01278   9.40650
       0.25   8.45472    6.55955   9.93093
       0.30   8.95079    7.08540  10.43765
       0.35   9.43641    7.60199  10.94210
       0.40   9.92155    8.11754  11.45660
       0.45  10.41466    8.63860  11.99265
       0.50  10.92388    9.17105  12.56245
       0.55  11.45799    9.72085  13.18026
       0.60  12.02747   10.29475  13.86405
       0.65  12.64583   10.90135  14.63788
       0.70  13.33192   11.55268  15.53592
       0.75  14.11414   12.26726  16.61022
       0.80  15.03931   13.07621  17.94738
       0.85  16.19452   14.03817  19.71038
       0.90  17.77492   15.28451  22.27131
       0.91  18.17921   15.59277  22.95143
       0.92  18.62885   15.93127  23.71896
       0.93  19.13610   16.30808  24.59840
       0.94  19.71896   16.73500  25.62603
       0.95  20.40541   17.23025  26.85883
       0.96  21.24250   17.82427  28.39369
       0.97  22.31880   18.57388  30.41572
       0.98  23.83444   19.60613  33.35086
```

```
              PROBIT Analysis on dose

Probability      dose  95% Fiducial Limits

       0.99  26.43495   21.32454   38.61003
```

Difenacoum

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Difen_wildHh;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.65 0 9
F 0.72 15 28
F 0.8 15 20
F 0.99 12 12
M 0.83 2 20
M 0.93 12 15
M 1.05 15 15
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                  The GENMOD Procedure
                   Model Information

 Data Set                            WORK.DIFEN_WILDHH
 Distribution                                 Binomial
 Link Function                                  PROBIT
 Response Variable (Events)                       resp
 Response Variable (Trials)                          n

      Number of Observations Read    7
      Number of Observations Used    7
      Number of Events              71
      Number of Trials             119

          Class Level Information
          Class    Levels Values
          SEX           2 F M

              Response Profile
     Ordered Binary Outcome      Total
       Value                 Frequency
           1 Event                  71
           2 Nonevent               48

   Criteria For Assessing Goodness Of Fit
Criterion                  DF     Value  Value/DF
Deviance                    3    3.9359    1.3120
Scaled Deviance             3    3.9359    1.3120
Pearson Chi-Square          3    2.8439    0.9480
Scaled Pearson X2           3    2.8439    0.9480
Log Likelihood                 -46.5590
Full Log Likelihood             -8.1045
AIC (smaller is better)         24.2090
AICC (smaller is better)        44.2090
BIC (smaller is better)         23.9926

                  Algorithm converged.
```

```
           Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate  Standard       Wald 95%            Wald  Pr > ChiSq
                              Error  Confidence Limits        Chi-
                                                            Square

Intercept     1    2.2204    0.6225    1.0003    3.4406      12.72      0.0004

SEX        F  1    0.8621    1.0420   -1.1802    2.9044       0.68      0.4081

SEX        M  0    0.0000    0.0000    0.0000    0.0000          .           .

Ldose*SEX  F  1   22.6516    6.2132   10.4740   34.8291      13.29      0.0003

Ldose*SEX  M  1   43.3600   10.3160   23.1411   63.5789      17.67      <.0001

Scale         0    1.0000    0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

 Data Set                            WORK.DIFEN_WILDHH

 Distribution                                 Binomial

 Link Function                                  PROBIT

 Response Variable (Events)                       resp

 Response Variable (Trials)                          n


        Number of Observations Read    7

        Number of Observations Used    7

        Number of Events              71

        Number of Trials             119


            Class Level Information

            Class    Levels Values

            SEX           2  F M


                Response Profile

        Ordered  Binary Outcome     Total
         Value                  Frequency

             1  Event                  71

             2  Nonevent               48


    Criteria For Assessing Goodness Of Fit

Criterion                  DF    Value  Value/DF

Deviance                    4   7.2068    1.8017

Scaled Deviance             4   7.2068    1.8017

Pearson Chi-Square          4   6.8876    1.7219

Scaled Pearson X2           4   6.8876    1.7219

Log Likelihood                -48.1944

Full Log Likelihood            -9.7399

AIC (smaller is better)        25.4799

AICC (smaller is better)       33.4799

BIC (smaller is better)        25.3176


                 Algorithm converged.
```

```
            Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard       Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits      Chi-
                                                           Square

Intercept     1    1.5194     0.3570    0.8196    2.2192    18.11      <.0001

SEX        F  1    2.5615     0.5151    1.5520    3.5710    24.73      <.0001

SEX        M  0    0.0000     0.0000    0.0000    0.0000        .           .

Ldose         1   30.2513     5.2392   19.9826   40.5199    33.34      <.0001

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

   Data Set                              WORK.DIFEN_WILDHH
   Distribution                                   Binomial
   Link Function                                    PROBIT
   Response Variable (Events)                         resp
   Response Variable (Trials)                            n

           Number of Observations Read     7
           Number of Observations Used     7
           Number of Events               71
           Number of Trials              119

                  Class Level Information
                  Class    Levels Values
                  SEX           2 F M

                     Response Profile
          Ordered Binary Outcome       Total
            Value                  Frequency
                1 Event                   71
                2 Nonevent                48

        Criteria For Assessing Goodness Of Fit
  Criterion                   DF     Value  Value/DF
  Deviance                     5   40.2920    8.0584
  Scaled Deviance              5   40.2920    8.0584
  Pearson Chi-Square           5   35.9146    7.1829
  Scaled Pearson X2            5   35.9146    7.1829
  Log Likelihood                  -64.7370
  Full Log Likelihood             -26.2825
  AIC (smaller is better)          56.5651
  AICC (smaller is better)         59.5651
  BIC (smaller is better)          56.4569

                   Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates
Parameter DF Estimate   Standard        Wald 95%       Wald Chi- Pr > ChiSq
                           Error  Confidence Limits      Square
Intercept  1   1.2774     0.2545   0.7786    1.7763       25.19     <.0001
Ldose      1  11.9195     2.3893   7.2366   16.6025       24.89     <.0001
Scale      0   1.0000     0.0000   1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a parallel response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Difen_wildHh;
input SEX$ dose resp n;
cards;
F 0.65 0 9
F 0.72 15 28
F 0.8 15 20
F 0.99 12 12
M 0.83 2 20
M 0.93 12 15
M 1.05 15 15
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
class sex;
model resp/n=sex dose;
run;
```

PROBIT data response data for females

```
                 The PROBIT Procedure
               PROBIT Analysis on dose
         Probability     dose  95% Fiducial Limits
                0.01 0.614042  0.554889  0.647432
                0.02 0.626916  0.572208  0.657984
                0.03 0.635224  0.583428  0.664823
                0.04 0.641546  0.591982  0.670049
                0.05 0.646735  0.599009  0.674357
                0.06 0.651184  0.605037  0.678067
                0.07 0.655111  0.610356  0.681355
                0.08 0.658647  0.615143  0.684329
                0.09 0.661879  0.619516  0.687059
                0.10 0.664868  0.623557  0.689595
                0.15 0.677389  0.640415  0.700366
                0.20 0.687508  0.653908  0.709295
                0.25 0.696310  0.665487  0.717286
                0.30 0.704311  0.675833  0.724782
                0.35 0.711806  0.685323  0.732055
                0.40 0.718992  0.694194  0.739299
                0.45 0.726014  0.702607  0.746671
                0.50 0.732992  0.710687  0.754316
                0.55 0.740036  0.718539  0.762379
                0.60 0.747264  0.726270  0.771017
                0.65 0.754808  0.733998  0.780421
                0.70 0.762841  0.741869  0.790840
                0.75 0.771606  0.750088  0.802637
                0.80 0.781484  0.758961  0.816394
                0.85 0.793158  0.769023  0.833177
                0.90 0.808095  0.781391  0.855311
                0.91 0.811745  0.784345  0.860814
                0.92 0.815729  0.787544  0.866857
                0.93 0.820132  0.791050  0.873580
                0.94 0.825077  0.794956  0.881181
                0.95 0.830753  0.799401  0.889969
                0.96 0.837473  0.804615  0.900449
                0.97 0.845807  0.811020  0.913562
```

```
        PROBIT Analysis on dose
Probability      dose  95% Fiducial Limits
       0.98  0.857016  0.819538  0.931374
       0.99  0.874984  0.833005  0.960317
```

PROBIT data response data for males

```
               The PROBIT Procedure
              PROBIT Analysis on dose
      Probability     dose  95% Fiducial Limits
             0.01 0.746229  0.675622  0.787572
             0.02 0.761874  0.696407  0.800757
             0.03 0.771970  0.709832  0.809342
             0.04 0.779653  0.720042  0.815927
             0.05 0.785959  0.728412  0.821373
             0.06 0.791367  0.735577  0.826077
             0.07 0.796139  0.741888  0.830256
             0.08 0.800436  0.747558  0.834046
             0.09 0.804364  0.752728  0.837534
             0.10 0.807997  0.757498  0.840781
             0.15 0.823213  0.777308  0.854647
             0.20 0.835511  0.793050  0.866237
             0.25 0.846207  0.806475  0.876667
             0.30 0.855930  0.818409  0.886483
             0.35 0.865039  0.829316  0.896011
             0.40 0.873772  0.839493  0.905477
             0.45 0.882306  0.849152  0.915062
             0.50 0.890785  0.858456  0.924927
             0.55 0.899346  0.867550  0.935235
             0.60 0.908130  0.876573  0.946168
             0.65 0.917298  0.885675  0.957950
             0.70 0.927060  0.895040  0.970885
             0.75 0.937712  0.904912  0.985414
             0.80 0.949717  0.915664  1.002253
             0.85 0.963904  0.927940  1.022705
             0.90 0.982057  0.943104  1.049607
             0.91 0.986492  0.946733  1.056289
             0.92 0.991333  0.950663  1.063627
             0.93 0.996684  0.954973  1.071789
             0.94 1.002694  0.959775  1.081018
             0.95 1.009592  0.965239  1.091687
             0.96 1.017758  0.971648  1.104415
             0.97 1.027887  0.979519  1.120342
```

```
        PROBIT Analysis on dose

Probability     dose  95% Fiducial Limits

       0.98 1.041508  0.989979  1.141986

       0.99 1.063344  1.006500  1.177179
```

Difethialone

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Difeth_wildHh;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.8 9 15
F 1.2 9 13
F 1.5 12 15
F 1.8 15 15
M 0.5 0 15
M 0.8 3 5
M 1.5 12 15
M 1.9 6 6
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                  The GENMOD Procedure
                   Model Information

Data Set                          WORK.DIFETH_WILDHH

Distribution                                Binomial

Link Function                                 PROBIT

Response Variable (Events)                      resp

Response Variable (Trials)                         n


         Number of Observations Read   8

         Number of Observations Used   8

         Number of Events             66

         Number of Trials             99


             Class Level Information

             Class    Levels Values

             SEX           2 F M


                 Response Profile

        Ordered Binary Outcome      Total
          Value                 Frequency

              1 Event                  66

              2 Nonevent               33


     Criteria For Assessing Goodness Of Fit

Criterion                  DF     Value  Value/DF

Deviance                    4    7.8804    1.9701

Scaled Deviance             4    7.8804    1.9701

Pearson Chi-Square          4    6.2497    1.5624

Scaled Pearson X2           4    6.2497    1.5624

Log Likelihood                 -40.4366

Full Log Likelihood            -10.8030

AIC (smaller is better)         29.6060

AICC (smaller is better)        42.9393

BIC (smaller is better)         29.9237


                  Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter      DF  Estimate    Standard      Wald 95%           Wald  Pr > ChiSq
                                  Error  Confidence Limits      Chi-
                                                              Square

Intercept       1    0.0430      0.2779   -0.5016    0.5877     0.02      0.8769

SEX          F  1    0.4232      0.3517   -0.2661    1.1125     1.45      0.2289

SEX          M  0    0.0000      0.0000    0.0000    0.0000        .           .

Ldose*SEX    F  1    3.6931      1.4643    0.8232    6.5629     6.36      0.0117

Ldose*SEX    M  1    5.9924      1.3820    3.2836    8.7011    18.80      <.0001

Scale           0    1.0000      0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                 The GENMOD Procedure
                  Model Information

Data Set                               WORK.DIFETH_WILDHH

Distribution                                     Binomial

Link Function                                      PROBIT

Response Variable (Events)                           resp

Response Variable (Trials)                              n

       Number of Observations Read    8

       Number of Observations Used    8

       Number of Events              66

       Number of Trials              99

           Class Level Information

           Class    Levels  Values

           SEX           2  F M

              Response Profile

      Ordered  Binary Outcome       Total
        Value                   Frequency

            1  Event                   66

            2  Nonevent                33

    Criteria For Assessing Goodness Of Fit

Criterion                  DF      Value  Value/DF

Deviance                    5     9.2220    1.8444

Scaled Deviance             5     9.2220    1.8444

Pearson Chi-Square          5     7.4372    1.4874

Scaled Pearson X2           5     7.4372    1.4874

Log Likelihood                  -41.1075

Full Log Likelihood             -11.4738

AIC (smaller is better)          28.9476

AICC (smaller is better)         34.9476

BIC (smaller is better)          29.1860

                 Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard      Wald 95%             Wald  Pr > ChiSq
                               Error  Confidence Limits        Chi-
                                                             Square

Intercept     1    0.0646     0.2561  -0.4373   0.5664        0.06      0.8009

SEX         F 1    0.3225     0.3259  -0.3163   0.9613        0.98      0.3225

SEX         M 0    0.0000     0.0000   0.0000   0.0000           .           .

Ldose         1    5.0144     0.9495   3.1534   6.8754       27.89      <.0001

Scale         0    1.0000     0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                     The GENMOD Procedure
                      Model Information

Data Set                               WORK.DIFETH_WILDHH

Distribution                                     Binomial

Link Function                                      PROBIT

Response Variable (Events)                           resp

Response Variable (Trials)                              n


       Number of Observations Read   8

       Number of Observations Used   8

       Number of Events             66

       Number of Trials             99


          Class Level Information

          Class    Levels  Values

          SEX           2  F M


             Response Profile

     Ordered  Binary Outcome      Total
       Value                  Frequency

           1  Event                  66

           2  Nonevent               33


    Criteria For Assessing Goodness Of Fit

Criterion                  DF      Value  Value/DF

Deviance                    6    10.1919    1.6987

Scaled Deviance             6    10.1919    1.6987

Pearson Chi-Square          6     7.9410    1.3235

Scaled Pearson X2           6     7.9410    1.3235

Log Likelihood                  -41.5924

Full Log Likelihood             -11.9588

AIC (smaller is better)          27.9175

AICC (smaller is better)         30.3175

BIC (smaller is better)          28.0764

                     Algorithm converged.
```

Analysis Of Maximum Likelihood Parameter Estimates

Parameter	DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept	1	0.2629	0.1588	-0.0483	0.5741	2.74	0.0978
Ldose	1	5.1621	0.9187	3.3615	6.9627	31.57	<.0001
Scale	0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Difeth_WildHh;
input SEX$ dose resp n;
cards;
f 0.8 9 15
F 1.2 9 13
F 1.5 12 15
F 1.8 15 15
M 0.5 0 15
M 0.8 3 5
M 1.5 12 15
M 1.9 6 6
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                  The PROBIT Procedure
                PROBIT Analysis on dose

Probability    dose  95% Fiducial Limits

       0.01 0.31508    0.15962    0.44234
       0.02 0.35581    0.19196    0.48515
       0.03 0.38435    0.21575    0.51455
       0.04 0.40732    0.23553    0.53793
       0.05 0.42701    0.25292    0.55779
       0.06 0.44451    0.26870    0.57533
       0.07 0.46045    0.28333    0.59120
       0.08 0.47521    0.29708    0.60583
       0.09 0.48904    0.31014    0.61949
       0.10 0.50213    0.32265    0.63237
       0.15 0.56014    0.37979    0.68911
       0.20 0.61099    0.43188    0.73859
       0.25 0.65828    0.48173    0.78468
       0.30 0.70386    0.53080    0.82941
       0.35 0.74891    0.58002    0.87419
       0.40 0.79432    0.63008    0.92017
       0.45 0.84088    0.68151    0.96853
       0.50 0.88936    0.73479    1.02060
       0.55 0.94063    0.79036    1.07801
       0.60 0.99576    0.84869    1.14293
       0.65 1.05614    0.91038    1.21832
       0.70 1.12373    0.97631    1.30842
       0.75 1.20154    1.04805    1.41958
       0.80 1.29454    1.12850    1.56229
       0.85 1.41206    1.22353    1.75624
       0.90 1.57521    1.34651    2.04697
       0.91 1.61736    1.37701    2.12569
       0.92 1.66443    1.41057    2.21521
       0.93 1.71777    1.44801    2.31863
       0.94 1.77937    1.49056    2.44059
       0.95 1.85232    1.54009    2.58840
       0.96 1.94186    1.59977    2.77463
       0.97 2.05789    1.67550    3.02349
       0.98 2.22294    1.78058    3.39146
```

```
          PROBIT Analysis on dose
Probability    dose  95% Fiducial Limits
       0.99  2.51036   1.95744   4.06916
```

Flocoumafen

Comparison of male and female PROBIT Response

SAS data input file (sex; dose; responders; number tested)

```
data Floc_wildHh;
input SEX$ dose resp n;
Ldose=Log10(dose);
cards;
F 0.45 3 15
F 0.5 10 15
F 0.55 19 20
M 0.35 0 12
M 0.4 2 20
M 0.5 15 20
M 0.6 14 15
;
proc GENMOD;
class sex;
model resp/n=sex sex*Ldose / dist=b link=PROBIT;
proc GENMOD;
class sex;
model resp/n=sex Ldose / dist=b link=PROBIT;
Proc GENMOD;
class sex;
model resp/n=Ldose / dist=b link=PROBIT;
run;
```

```
                    The GENMOD Procedure
                     Model Information

   Data Set                             WORK.FLOC_WILDHH
   Distribution                                 Binomial
   Link Function                                  PROBIT
   Response Variable (Events)                       resp
   Response Variable (Trials)                          n

         Number of Observations Read    7
         Number of Observations Used    7
         Number of Events              63
         Number of Trials             117

                 Class Level Information
                 Class    Levels  Values
                 SEX           2  F M

                     Response Profile
         Ordered  Binary Outcome      Total
           Value                  Frequency
               1  Event                  63
               2  Nonevent               54

          Criteria For Assessing Goodness Of Fit
   Criterion                    DF     Value  Value/DF
   Deviance                      3    1.2402    0.4134
   Scaled Deviance               3    1.2402    0.4134
   Pearson Chi-Square            3    1.2475    0.4158
   Scaled Pearson X2             3    1.2475    0.4158
   Log Likelihood                   -43.0665
   Full Log Likelihood               -8.3391
   AIC (smaller is better)           24.6783
   AICC (smaller is better)          44.6783
   BIC (smaller is better)           24.4619

                    Algorithm converged.
```

```
           Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF Estimate   Standard     Wald 95%          Wald Pr > ChiSq
                              Error Confidence Limits     Chi-
                                                        Square

Intercept     1   5.7869     1.1189   3.5940   7.9798    26.75     <.0001

SEX         F 1   3.2219     2.3644  -1.4123   7.8561     1.86     0.1730

SEX         M 0   0.0000     0.0000   0.0000   0.0000        .          .

Ldose*SEX   F 1  28.4352     6.7242  15.2560  41.6144    17.88     <.0001

Ldose*SEX   M 1  17.6111     3.3451  11.0548  24.1674    27.72     <.0001

Scale         0   1.0000     0.0000   1.0000   1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

 Data Set                            WORK.FLOC_WILDHH
 Distribution                                Binomial
 Link Function                                 PROBIT
 Response Variable (Events)                      resp
 Response Variable (Trials)                         n

      Number of Observations Read    7
      Number of Observations Used    7
      Number of Events              63
      Number of Trials             117

                Class Level Information
                Class    Levels Values
                SEX           2 F M

                    Response Profile
           Ordered Binary Outcome      Total
             Value                 Frequency
                 1 Event                  63
                 2 Nonevent               54

         Criteria For Assessing Goodness Of Fit
Criterion                  DF      Value  Value/DF
Deviance                    4     3.4265    0.8566
Scaled Deviance             4     3.4265    0.8566
Pearson Chi-Square          4     4.2944    1.0736
Scaled Pearson X2           4     4.2944    1.0736
Log Likelihood                  -44.1596
Full Log Likelihood              -9.4323
AIC (smaller is better)          24.8646
AICC (smaller is better)         32.8646
BIC (smaller is better)          24.7023

                    Algorithm converged.
```

```
              Analysis Of Maximum Likelihood Parameter Estimates

Parameter    DF  Estimate   Standard      Wald 95%          Wald  Pr > ChiSq
                               Error  Confidence Limits     Chi-
                                                          Square

Intercept     1    6.6401     1.0669    4.5489    8.7312   38.73      <.0001

SEX        F  1   -0.1528     0.3105   -0.7614    0.4559    0.24      0.6228

SEX        M  0    0.0000     0.0000    0.0000    0.0000       .           .

Ldose         1   20.2169     3.1962   13.9524   26.4814   40.01      <.0001

Scale         0    1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

```
                    The GENMOD Procedure
                     Model Information

          Data Set                          WORK.FLOC_WILDHH
          Distribution                              Binomial
          Link Function                               PROBIT
          Response Variable (Events)                    resp
          Response Variable (Trials)                       n

          Number of Observations Read    7
          Number of Observations Used    7
          Number of Events              63
          Number of Trials             117

                 Class Level Information
                 Class    Levels Values
                 SEX           2 F M

                     Response Profile
          Ordered Binary Outcome      Total
            Value                 Frequency
                1 Event                  63
                2 Nonevent               54

           Criteria For Assessing Goodness Of Fit
         Criterion                  DF     Value  Value/DF
         Deviance                    5    3.6701    0.7340
         Scaled Deviance             5    3.6701    0.7340
         Pearson Chi-Square          5    3.9999    0.8000
         Scaled Pearson X2           5    3.9999    0.8000
         Log Likelihood                 -44.2814
         Full Log Likelihood             -9.5541
         AIC (smaller is better)         23.1082
         AICC (smaller is better)        26.1082
         BIC (smaller is better)         23.0000

                   Algorithm converged.
```

```
               Analysis Of Maximum Likelihood Parameter Estimates

Parameter DF Estimate   Standard      Wald 95%            Wald Pr > ChiSq
                           Error  Confidence Limits       Chi-
                                                        Square

Intercept  1   6.4606     0.9983    4.5041    8.4172     41.89     <.0001

Ldose      1  19.9094     3.1386   13.7578   26.0610     40.24     <.0001

Scale      0   1.0000     0.0000    1.0000    1.0000

Note: The scale parameter was held fixed.
```

PROBIT Dose Response data assuming a coincident response for males and females

SAS data input file (sex; dose; responders; number tested)

```
data Floc_WildHh;
input SEX$ dose resp n;
cards;
f 0.45 3 15
F 0.5 10 15
F 0.55 19 20
M 0.35 0 12
M 0.4 2 20
M 0.5 15 20
M 0.6 14 15
;
proc PROBIT log10 inversecl lackfit hprob=0.05;
model resp/n=dose;
run;
```

```
                   The PROBIT Procedure
                PROBIT Analysis on dose
Probability     dose 95% Fiducial Limits
       0.01 0.361952  0.315613  0.390256
       0.02 0.373545  0.330112  0.400053
       0.03 0.381093  0.339626  0.406430
       0.04 0.386870  0.346944  0.411316
       0.05 0.391635  0.352999  0.415352
       0.06 0.395736  0.358224  0.418831
       0.07 0.399367  0.362859  0.421918
       0.08 0.402647  0.367050  0.424711
       0.09 0.405653  0.370896  0.427278
       0.10 0.408441  0.374463  0.429663
       0.15 0.420185  0.389503  0.439793
       0.20 0.429759  0.401733  0.448184
       0.25 0.438147  0.412378  0.455680
       0.30 0.445819  0.422015  0.462697
       0.35 0.453048  0.430966  0.469490
       0.40 0.460016  0.439433  0.476248
       0.45 0.466860  0.447554  0.483128
       0.50 0.473694  0.455430  0.490276
       0.55 0.480629  0.463151  0.497847
       0.60 0.487779  0.470805  0.506009
       0.65 0.495281  0.478497  0.514964
       0.70 0.503312  0.486366  0.524974
       0.75 0.512125  0.494617  0.536415
       0.80 0.522120  0.503567  0.549887
       0.85 0.534018  0.513779  0.566487
       0.90 0.549373  0.526437  0.588630
       0.91 0.553147  0.529479  0.594176
       0.92 0.557277  0.532782  0.600285
       0.93 0.561854  0.536412  0.607102
       0.94 0.567010  0.540469  0.614838
       0.95 0.572948  0.545103  0.623818
       0.96 0.580004  0.550560  0.634578
       0.97 0.588797  0.557295  0.648118
       0.98 0.600693  0.566308  0.666645
```

```
          PROBIT Analysis on dose
Probability     dose  95% Fiducial Limits
       0.99 0.619933  0.580683  0.697079
```

APPENDIX 4: Chapter 5 House mouse *VKORC1* gene exon sequences

A text version of the *VKORC1* gene sequence can be obtained from the National Centre for Biotechnology Information (NCBI) website; the link for the sequence for House mice is https://www.ncbi.nim.nih.gov/gene/27973.

The gene sequence can be viewed as text, the bases are red and green in colour and the exons are red highlighted sections. Exons 1 and 3 are the areas of the gene sequence where single nucleotide polymorphisms (SNPs) which cause anticoagulant resistance occur. Exon 1 is the area where the *Spretus* mutations are found, exon 3 is the area where first generation and second generation anticoagulant active ingredient mutations are found. The primers are produced using the website http://primer3.ut.ee/. The exon sequence is pasted into the page and the primer sequence is given as the output which shows a left (forward) and right (reverse) primer

Exon 1

atgggcaccacctggaggagccctggactcgtg**cgg**cttgcactgtgcctcgctggcttagccctctcactgtac**gca**ctgcacgtgaaggcggcgcgcgcccgcgatgaaaattaccgcgcgctctgcgatgtgggcacg**gcc**atcagctgttcc**cgc**gtcttctcctctcg

Left primer: ctggactcgtgcggcttg (highlighted yellow)

Right primer: gagaggagaagacgcggg (highlighted blue)

Exon 3

gattcttccctcctgtccctgggctgtactgtcgacatgggcaccacctggaggagccctggactcgtgcggctt
gcactgtgcctcgctggcttagccctctcactgtacgcactgcacgtgaaggcggcgcgcccgcgatgaaaat
taccgcgcgctctgcgatgtgggcacggccatcagctgttcccgcgtcttctcctctcggtggggccggggcttt
gggctggtggagcacatgctaggagcggacagcgtcctcaaccaatccaacagcatatttggttgcctgttctac
accttacagctgttgttaggttgcttgaggggacgttgggcctctatcctactggtgctgagttccctgggtgtcc
gtcgctggttccgtgtacctggcctggatcctgttctttgtg**tta**tatgatttctgcattgtgtgcattaccacc
tatgccatcaatgtgggtctgatgttgcttagcttccagaaggtaccagaacacaagaccaaaaagcactgagtt
cccacctcatgccagactaacctaacttgctttgccttggcacatgacccttgcccaagtgtgtgggttcctaga
aggccctacccacatcattcaaaccccctccataaccacacacagagaaatgaccaaacgtgcctctaagttct
gttcccatgggctgcattctgctgttggttaaagagaaggattttgaacaataaatttttctatgttggtcaaaa
aaaaaaaaaaaaaa

Left primer: tactggtgctgagttccctg (highlighted yellow)

Right primer: ttagtctggcatgaggtggg (highlighted blue)

The base letters in bold on both exons are the original wild-type codons for the *VKORC1* gene.

Table A4.1: Codon sequences for *VKORC1* mutations on exon 1 and exon 3 in House mice

Mutation	Wild-type Codon	Codon Sequence	New Codon
Exon 1			
R12W	CGG	GTG-**CGG**-CTT	TGG
A26S	GCA	TAC-**GCA**-CTG	TCA
A48T	GCC	ACG-**GCC**-ATC	ACC
R61L	CGC	TCC-**CGC**-GTC	CTC
Exon 3			
L128S	TTA	TTT-GTG-**TTA**-TAT	TCA
Y139C	TAT	ACC-ACC-**TAT**-GCC	TGT

APPENDIX 5: Chapter 6 INR values of House mice homozygous for the VKORC1 mutation Y139C selected for breeding

Male House mice received a dose equivalent to 32.5mg.kg^{-1}, females received a dose equivalent to 35.3mg.kg^{-1} bromadiolone via oral gavage.

Generation 0

Male House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	52.3	0.52	4.0	Y
2	46.4	0.46	4.8	N
3	39.9	0.40	2.9	Y
4	51.7	0.52	7.2	N
5	49.9	0.50	4.0	Y

Female House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	53.7	0.54	4.0	Y
2	31.7	0.32	5.6	N
3	31.7	0.32	-	N
4	45.5	0.46	3.5	Y
5	51.9	0.52	1.8	Y

Generation 1

Male House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	45.0	0.45	7.2	N
2	49.6	0.50	5.6	N
3	40.3	0.40	4.8	N
4	46.3	0.46	4.4	Y
5	45.3	0.45	4.0	Y
6	43.3	0.43	5.3	N
7	42.4	0.42	4.2	Y
8	44.8	0.45	3.2	Y
9	43.9	0.44	6.7	N
10	42.8	0.43	5.3	N
11	43.9	0.44	3.9	Y
12	43.4	0.43	7.0	N
13	49.9	0.50	6.8	N

Female House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	44.0	0.44	2.8	Y
2	40.3	0.40	2.4	Y
3	46.6	0.47	1.7	Y
4	40.2	0.40	3.9	N
5	37.0	0.37	1.9	Y
6	39.9	0.40	1.8	Y
7	42.2	0.42	2.9	Y

Generation 2

Male House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	39.0	0.39	5.6	N
2	38.2	0.38	>8.0	N
3	39.1	0.39	1.6	Y
4	41.6	0.42	3.2	Y
5	42.8	0.43	2.4	Y

Female House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	35.5	0.36	1.2	N
2	27.7	0.28	1.5	N
3	31.6	0.32	1.1	N
4	33.0	0.33	1.2	N
5	30.0	0.30	2.4	N
6	35.0	0.35	1.8	Y
7	34.6	0.35	2.1	Y
8	30.1	0.30	1.2	Y

Generation 3

Male House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	47.6	0.48	5.2	Y
2	43.2	0.43	4.9	Y
3	43.6	0.44	>8.0	N
4	45.7	0.46	3.5	Y
5	48.1	0.48	5.5	Y

Female House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	32.7	0.33	1.3	Y
2	38.4	0.38	1.3	Y
3	35.5	0.36	4.2	N
4	38.4	0.38	2.4	Y
5	42.2	0.42	2.2	Y
6	39.6	0.40	2.3	Y

Generation 4

Male House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	43.9	0.44	>8.0	N
2	49.2	0.49	>8.0	N
3	45.2	0.45	>8.0	N
4	41.2	0.41	>8.0	N
5	40.2	0.40	>8.0	N
6	39.6	0.40	>8.0	N

Female House mice

Mouse	Body Wt (g)	Volume of dose (ml)	INR	Selected for breeding Y/N
1	39.4	0.39	4.9	N
2	39.1	0.39	3.5	N
3	35.7	0.36	7.6	N
4	34.8	0.35	>8.0	N