

US EPA ARCHIVE DOCUMENT



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

JUL 21 1998

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Isoxaflutole: Review of Rebuttal to Terrestrial Plant Turnip Study
DP Barcode D246666

FROM: Michael Davy, Agronomist *Michael Davy*
Environmental Risk Branch II
Environmental Fate and Effects Branch (7505C)

Thru: Elizabeth M. Leovey, Chief *Betsy Leovey 7-21-98*
Environmental Risk Branch II
Environmental Fate and Effects Branch (7505C)

TO: Joanne Miller, PM-23
Registration Division (H7506)

EFED has reviewed the registrant's rebuttal of the turnip vegetative vigor data evaluation record for parent isoxaflutole. The rebuttal was submitted under DP Barcode D246666 for section 3 registration of isoxaflutole. This rebuttal was submitted in response to EFED's request to retest the vegetative vigor studies using lettuce and ryegrass (D225503, D232445). The registrant retested the lettuce and ryegrass species (D240106, MRID 44399905). Although the turnip was not requested, they also retested the turnip. All three studies were found not to be core studies.

The registrant has suggested that the original turnip study should not be used because the study provided a shallow concentration-response relationship. **EFED maintains that the original turnip study is a valid study and will continue to be used for the most sensitive phytotoxic indicators.**

EFED concluded the re-analysis in the following manner:

The registrant has stated that the original turnip study (MRID 43573242) should not be used and the cabbage species should be used instead because of the following reasons:

- 1) There was a shallow concentration-response relationship with the NOEC value higher than the EC₂₅ value.
- 2) The concentration-response study in the repeated study (MRID 44399905) was better defined with a positive slope and all of the NOEC values were below the corresponding EC₂₅ values.
- 3) The EC₂₅ values calculated from the repeated study was confirmed by another set of studies done in natural soils. These studies have not been submitted to EPA.

The EFED's responses to the registrant's rebuttal of the original turnip study are as follows:

- 1) EFED has reexamined the original turnip and cabbage studies using a continuous toxicity data model¹. The NOEC is determined by using William's test. The results are summarized below:

Turnip EC₂₅ = 2.28 x 10⁻⁵ lb ai/A (95% C.I. = 0.15 - 33.2 x 10⁻⁵ lb ai/A)
Turnip NOEC = 1.1 x 10⁻⁵ lb ai/A
Cabbage EC₂₅ = 2.97 x 10⁻⁵ lb ai/A (95% C.I. = 0.76 - 11.6 x 10⁻⁵ lb ai/A)
Cabbage NOEC = 3.4 x 10⁻⁵ lb ai/A

The registrant has indicated concerns with the NOEC value being higher than the EC₂₅ value. Because of the continuous toxicity data, the NOEC is now less than the EC₂₅.

- 2) A shallow concentration-response relationship is not a valid reason for rejecting these results. Among weed scientists, several herbicides (sulfonylurea) are noted for having a shallow concentration-response relationship². A plot of the data (attached) reveals that dose-response relationship is reasonable. It also reveals that there was some variability among replicate means, but this is common for terrestrial plant toxicity studies. The data in the controls were pooled legitimately to increase the confidence of the estimated mean response.

¹ R.D. Bruce and D.J. Versteeg. 1992. A statistical procedure for modeling continuous toxicity data. *Environ. Tox. and Chem.* 11:1485-1494.

² D.C. Thill. 1997. *Sulfonylureas and Triazolopyrimidines*, Hericide Action course, Purdue University. P. 350

3) The data provided by MRID 43573242 are completely acceptable data for estimating the EC_{25} for effects on turnip root weight. The Pesticide Reregistration Rejection Rate Analysis: Ecological Effects (EPA 738-R-94-035) states on page 155 that tier-2 plant protection studies (Guideline No. 123-1 and 123-2) "will be rejected if there is not at least one dose greater than the EC_{50} and one dose lower than the EC_{25} ." The doses used in this study were well placed for defining the EC_{25} because the highest dose (0.0047 lb ai/A) was greater than the EC_{50} (0.00017 lb ai/A) and the lowest dose (0.000011 lb ai/A) was lower than the EC_{25} . Furthermore, a goodness-of-fit test yielded a P-value of 0.41, suggesting a lack of evidence to reject a null hypothesis that the model does not fit the data. In fact, the fit of the model is better than it usually found with phytotoxicity data. In conclusion, there is no reason not to reject the data from the original turnip study.

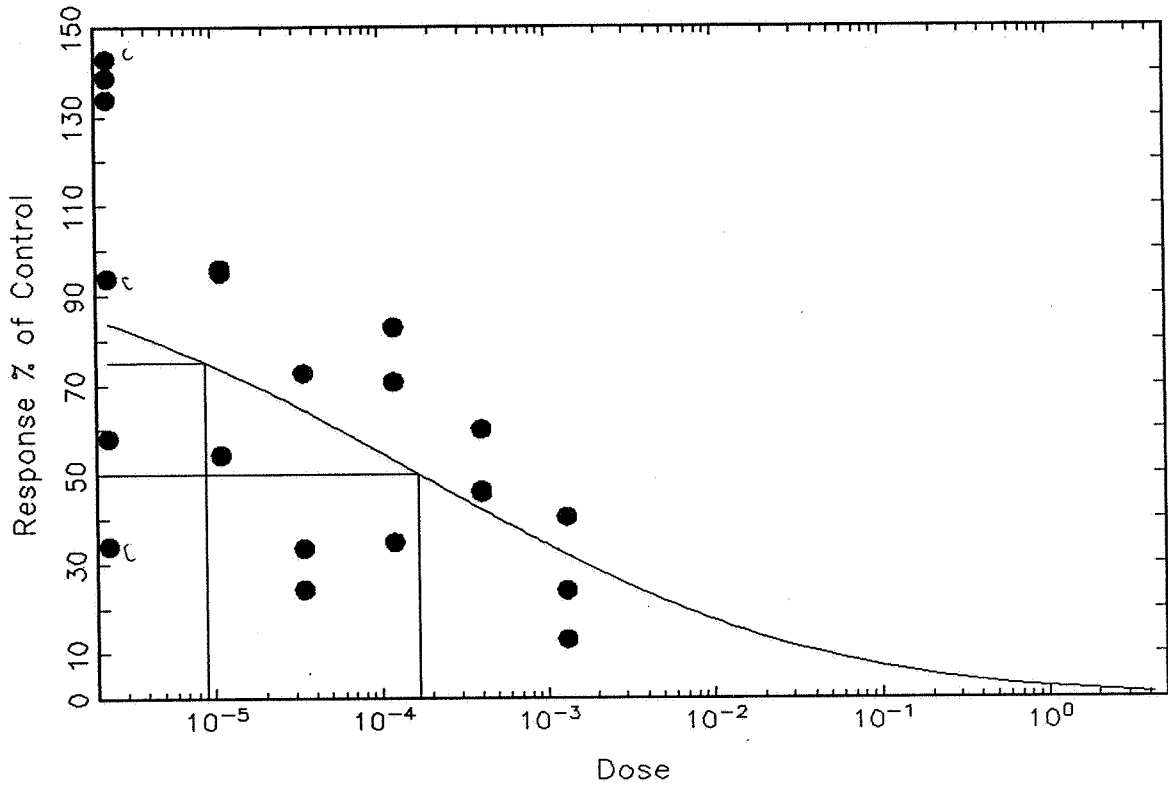
EFED believes that the true EC_{25} for the most sensitive non-target plant species is less than the 2.28×10^{-5} lb ai/A value in the above re-analysis for the following reasons:

1. The original turnip study used a high amount of water as a carrier for the isoxaflutole being applied to the vegetative foliage. The label recommends 10 gallons of water to be used on field application. The study provided an equivalent of 200 gallons per acre. Some isoxaflutole residues may have been washed off the foliage. This would underestimate the phytotoxicity. It is believed that the phytotoxicity of isoxaflutole to the turnip species is less than 2.28×10^{-5} lb ai/A.
2. The most sensitive species tested is used as a surrogate for the many thousands of non-target terrestrial plant species known in North America. If each species is tested to represent only that particular species, then several thousands of species would need to be tested. This is an unfeasible method of coming up with data to provide a risk assessment to non-target terrestrial plants. Therefore, because of this uncertainty, the most sensitive species with the most sensitive parameter is used to represent the thousands of untested non-target terrestrial plant species.
3. The cabbage species (same genus as turnip) confirms the phytotoxicity of isoxaflutole with similar EC_{25} results as the turnip.
4. The confidence interval of the re-analysis shows that the 95% lower bound EC_{25} value should be 0.15×10^{-5} lb ai/A and 0.76×10^{-5} lb ai/A for turnip and cabbage, respectively. This approach would be conceptually similar to the way 90% upper bound fate half-lives values are used in modeling. EFED would also argue that these lower values would be protective and would provide more certainty what EC_{25} value should be represented for the vast numbers of untested non-target plant species.

Because of the above cited reasons, EFED will continue to use the most sensitive EC_{25} value as 1×10^{-5} lb ai/A³ unless field data can prove the EC_{25} value otherwise.

³ This is the EC_{25} value of the original turnip study that used a probit model.

TURN_RW.DAT : isoxaflutole/ turnip/ root weight



EFFECT OF ISOXAFLUTOLE ON CABBAGE ROOT WEIGHT

105

08:14 Wednesday, April 29, 1998

OBS	CONC	LOG_CONC	Y1	Y2	Y3	Y4	Y5	Y6
1	.000000	.	0.5100	0.3398	0.5805	0.5797	0.589	0.5591
2	.000034	-4.46852	0.3484	0.5443	0.6101	.	.	.
3	.000120	-3.92082	0.2665	0.3889	0.1166	.	.	.
4	.000400	-3.39794	0.1284	0.0847	0.1477	.	.	.
5	.001300	-2.88606	0.0753	0.0433	0.0854	.	.	.
6	.004700	-2.32790	0.0336	0.0611	0.0576	.	.	.

5

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Dependent Variable COUNT		Method: Gauss-Newton		
Iter	LOG_EC50	SIGMA	CO	Weighted SS
0	-3.380000	0.960000	0.530000	0.837494
1	-3.924109	1.136186	0.553234	0.567017
2	-3.837963	0.897470	0.541256	0.544245
3	-3.899491	0.970315	0.549550	0.538147
4	-3.878023	0.948324	0.545768	0.537683
5	-3.885162	0.955603	0.546866	0.537807
6	-3.882830	0.953211	0.546494	0.537762
7	-3.883599	0.953999	0.546615	0.537776
8	-3.883346	0.953740	0.546576	0.537771
9	-3.883430	0.953825	0.546589	0.537773
10	-3.883402	0.953797	0.546584	0.537772
11	-3.883411	0.953806	0.546586	0.537773
12	-3.883408	0.953803	0.546585	0.537773
13	-3.883409	0.953804	0.546585	0.537773
14	-3.883409	0.953804	0.546585	0.537773
15	-3.883409	0.953804	0.546585	0.537773

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	6.1500000000	2.0500000000
Residual	18	0.5377725349	0.0298762519
Uncorrected Total	21	6.6877725349	
(Corrected Total)	20	4.0632985729	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC50	-3.883408958	0.18834656031	-4.2791077828	-3.4877101325
SIGMA	0.953803736	0.17108610664	0.5943675389	1.3132399333
CO	0.546585399	0.05152402093	0.4383381629	0.6548326347

Asymptotic Correlation Matrix

Corr	LOG_EC50	SIGMA	CO
LOG_EC50	1	-0.694420986	-0.659319542
SIGMA	-0.694420986	1	0.359710113
CO	-0.659319542	0.359710113	1

6

SUMMARY OF NONLINEAR REGRESSION

107

08:14 Wednesday, April 29, 1998

OBS	LOG_EC50	SIGMA	C0	RESID_SS	EC50	SLOPE
1	-3.88341	0.95380	0.54659	0.53777	.00013079	1.04843

95% CI : 0.0000526 - 0.000325

7

MODEL: YOUNG = C0 * PROB NORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)

WEIGHTED REGRESSION

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Dependent Variable COUNT Method: Gauss-Newton

Iter	LOG_EC25	SIGMA	C0	Weighted SS
0	-4.000000	0.960000	0.530000	0.875015
1	-4.701687	1.153318	0.553459	0.573858
2	-4.435779	0.891439	0.540943	0.546271
3	-4.556479	0.971817	0.549878	0.538192
4	-4.516816	0.947818	0.545696	0.537676
5	-4.529979	0.955768	0.546893	0.537810
6	-4.525671	0.953157	0.546486	0.537761
7	-4.527091	0.954016	0.546618	0.537777
8	-4.526624	0.953734	0.546575	0.537771
9	-4.526778	0.953827	0.546589	0.537773
10	-4.526727	0.953796	0.546584	0.537772
11	-4.526744	0.953806	0.546586	0.537773
12	-4.526739	0.953803	0.546585	0.537773
13	-4.526740	0.953804	0.546585	0.537773
14	-4.526740	0.953804	0.546585	0.537773
15	-4.526740	0.953804	0.546585	0.537773

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics

Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	6.150000000	2.050000000
Residual	18	0.5377725350	0.0298762519
Uncorrected Total	21	6.6877725350	
(Corrected Total)	20	4.0632985713	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC25	-4.526740044	0.28102722476	-5.1171524328	-3.9363276545
SIGMA	0.953803739	0.17108610712	0.5943675403	1.3132399367
C0	0.546585399	0.05152402096	0.4383381632	0.6548326352

Asymptotic Correlation Matrix

Corr	LOG_EC25	SIGMA	C0
LOG_EC25	1	-0.87602784	-0.589585685
SIGMA	-0.87602784	1	0.3597101122
C0	-0.589585685	0.3597101122	1

SUMMARY OF NONLINEAR REGRESSION

109

MODEL: YOUNG = C0 * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)

SUMMARY OF NONLINEAR REGRESSION

08:14 Wednesday, April 29, 1998

OBS	LOG_EC25	SIGMA	C0	RESID_SS	EC25	SLOPE
1	-4.52674	0.95380	0.54659	0.53777	.000029734	1.04843

MODEL: YOUNG = CO * PROB NORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

WEIGHTED REGRESSION

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Iter	Dependent Variable	COUNT	Method: Gauss-Newton	CO	Weighted SS
0	LOG_EC05	SIGMA		CO	Weighted SS
0	-5.000000	1.900000		0.400000	2.079129
1	-8.995537	1.991459		0.547029	4.415071
2	-3.702678	0.415889		0.537752	1.715002
3	-4.745734	0.811355		0.471778	0.704355
4	-5.813598	1.126754		0.555732	0.567039
5	-5.302462	0.894236		0.540960	0.543273
6	-5.498657	0.971561		0.549792	0.538124
7	-5.436870	0.947925		0.545711	0.537678
8	-5.457375	0.955733		0.546887	0.537810
9	-5.450655	0.953168		0.546488	0.537761
10	-5.452868	0.954013		0.546618	0.537776
11	-5.452140	0.953735		0.546575	0.537771
12	-5.452380	0.953826		0.546589	0.537773
13	-5.452301	0.953796		0.546584	0.537772
14	-5.452327	0.953806		0.546586	0.537773
15	-5.452319	0.953803		0.546585	0.537773
16	-5.452321	0.953804		0.546585	0.537773
17	-5.452320	0.953804		0.546585	0.537773
18	-5.452321	0.953804		0.546585	0.537773

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics

Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	6.1500000000	2.0500000000
Residual	18	0.5377725350	0.0298762519
Uncorrected Total	21	6.6877725350	
(Corrected Total)	20	4.0632985716	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC05	-5.452320728	0.43391948689	-6.3639457182	-4.5406957382
SIGMA	0.953803738	0.17108610702	0.5943675400	1.3132399360
CO	0.546585399	0.05152402095	0.4383381631	0.6548326351

10

SUMMARY OF NONLINEAR REGRESSION

111

MODEL: YOUNG = CO * PROBNORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

WEIGHTED REGRESSION

08:14 Wednesday, April 29, 1998

Asymptotic Correlation Matrix

Corr	LOG_EC05	SIGMA	CO
LOG_EC05	1	-0.949971952	-0.519474299
SIGMA	-0.949971952	1	0.3597101124
CO	-0.519474299	0.3597101124	1

11

SUMMARY OF NONLINEAR REGRESSION

112

MODEL: YOUNG = CO * PROBNORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

SUMMARY OF NONLINEAR REGRESSION

08:14 Wednesday, April 29, 1998

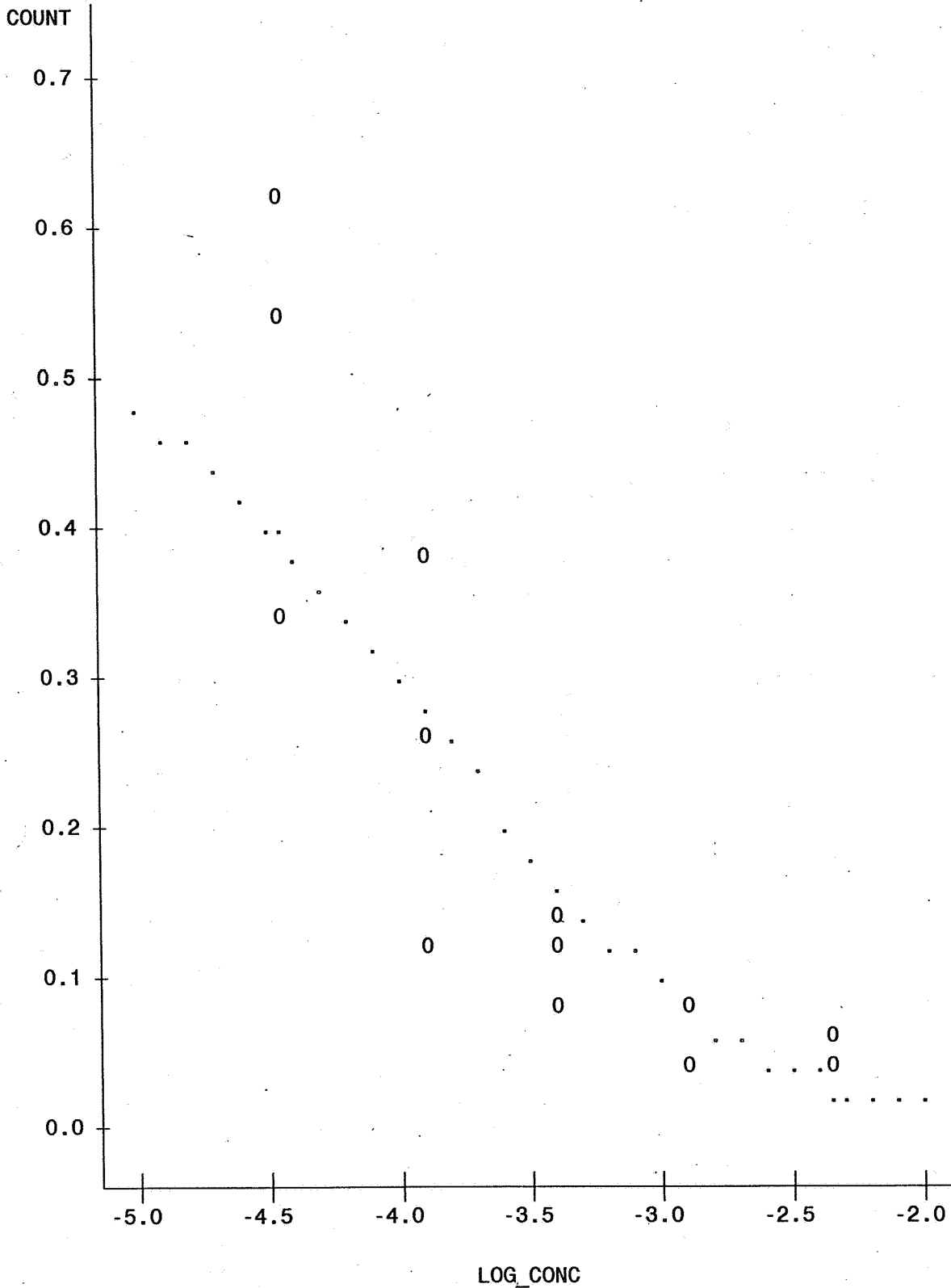
OBS	LOG_EC05	SIGMA	CO	RESID_SS	EC05	SLOPE
1	-5.45232	0.95380	0.54659	0.53777	.0000035292	1.04843

MODEL: YOUNG = CO * PROBNORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

08:14 Wednesday, April 29, 1998

Plot of COUNT*LOG_CONC. Symbol used is '0'.

Plot of PRED*LOG_CONC. Symbol used is '.'.



NOTE: 58 obs had missing values. 31 obs hidden.

13

SUMMARY OF NONLINEAR REGRESSION
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

114

08:14 Wednesday, April 29, 1998

General Linear Models Procedure
Class Level Information

Class	Levels	Values
DOSE	6	0 0.0004 0.0013 0.0047 0.00012 0.000034

Number of observations in data set = 36

NOTE: Due to missing values, only 21 observations can be used in this analysis.

14

SUMMARY OF NONLINEAR REGRESSION
 COMPARISON OF MEANS FOR NOEL DETERMINATION
 TEST IF TREATMENT IS LESS THAN CONTROL

115

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Dependent Variable: RESPONSE

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	0.87765443	0.17553089	21.30	0.0001
Error	15	0.12360642	0.00824043		
Corrected Total	20	1.00126085			

R-Square	C.V.	Root MSE	RESPONSE Mean
0.876549	30.99696	0.090777	0.292857

Source	DF	Type I SS	Mean Square	F Value	Pr > F
DOSE	5	0.87765443	0.17553089	21.30	0.0001

Source	DF	Type III SS	Mean Square	F Value	Pr > F
DOSE	5	0.87765443	0.17553089	21.30	0.0001

15

SUMMARY OF NONLINEAR REGRESSION
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

116

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Level of DOSE	N	-----RESPONSE-----	
		Mean	SD
0	6	0.52635000	0.09575412
0.0004	3	0.12026667	0.03227791
0.0013	3	0.06800000	0.02197885
0.0047	3	0.05076667	0.01496941
0.00012	3	0.25733333	0.13638124
0.000034	3	0.50093333	0.13613311

16

SUMMARY OF NONLINEAR REGRESSION
 COMPARISON OF MEANS FOR NOEL DETERMINATION
 TEST IF TREATMENT IS LESS THAN CONTROL

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

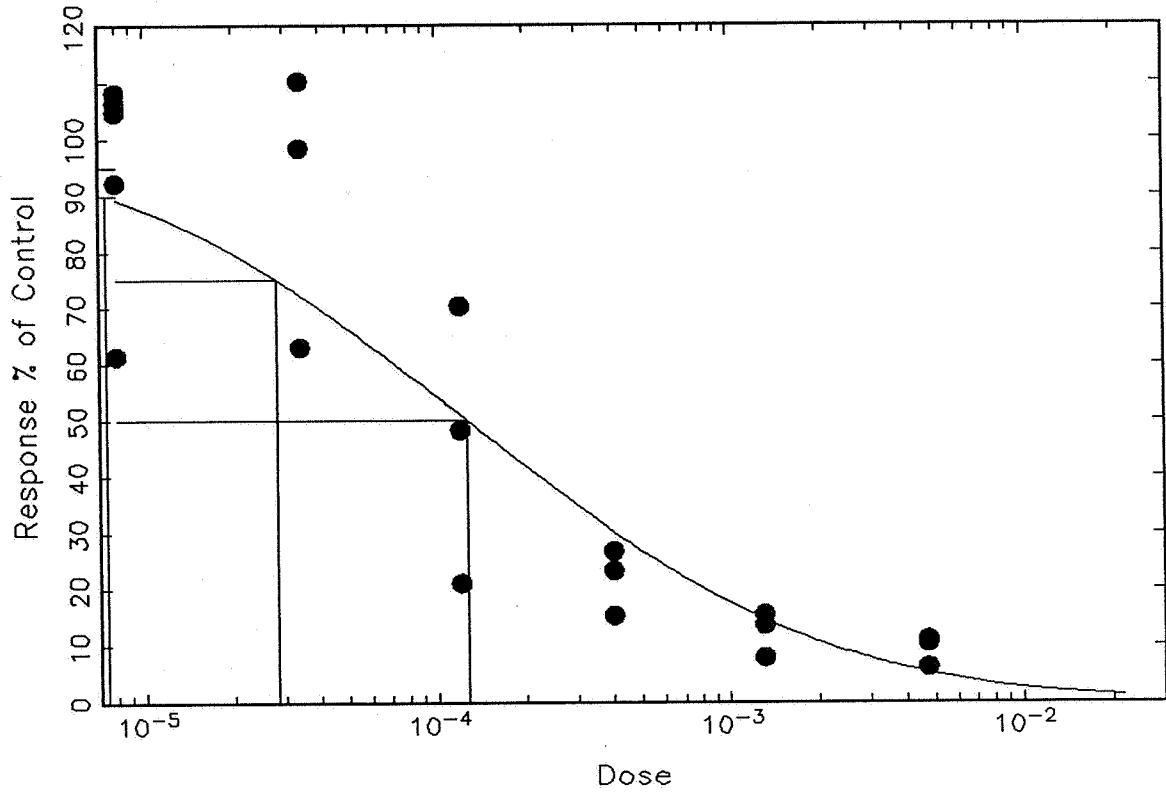
NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 15 MSE= 0.00824
 Critical Value of Dunnett's T= 2.506

Comparisons significant at the 0.05 level are indicated by '***'.

DOSE Comparison	Simultaneous		Simultaneous	
	Lower Confidence Limit	Difference Between Means	Upper Confidence Limit	
0.000034 - 0	-0.18629	-0.02542	0.13546	
0.00012 - 0	-0.42989	-0.26902	-0.10814	***
0.0004 - 0	-0.56696	-0.40608	-0.24521	***
0.0013 - 0	-0.61922	-0.45835	-0.29748	***
0.0047 - 0	-0.63646	-0.47558	-0.31471	***

CABB_RW.DAT : isoxaflutole / cabbage weight



EFFECT OF ISOXAFLUTOLE ON TURNIP ROOT WEIGHT

93

08:14 Wednesday, April 29, 1998

OBS	CONC	LOG_CONC	Y1	Y2	Y3	Y4	Y5	Y6
1	.000000	.	0.3735	0.5700	0.1353	0.5339	0.5534	0.2314
2	.000011	-4.95861	0.3784	0.3819	0.2165	.	.	.
3	.000034	-4.46852	0.0966	0.2894	0.1331	.	.	.
4	.000120	-3.92082	0.3302	0.2815	0.1386	.	.	.
5	.000400	-3.39794	0.1847	0.1827	0.2395	.	.	.
6	.001300	-2.88606	0.0523	0.1609	0.0954	.	.	.
7	.004700	-2.32790	0.0108	0.0617	0.0203	.	.	.

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Iter	LOG_EC50	SIGMA	C0	Weighted SS
0	-3.800000	1.900000	0.400000	0.998320
1	-3.822572	1.278424	0.394484	0.989861
2	-3.760929	1.310697	0.387926	0.978189
3	-3.759683	1.310142	0.388010	0.977613
4	-3.759508	1.309902	0.387991	0.977622
5	-3.759456	1.309834	0.387985	0.977625
6	-3.759442	1.309814	0.387983	0.977626
7	-3.759437	1.309809	0.387983	0.977626
8	-3.759436	1.309807	0.387983	0.977626
9	-3.759436	1.309806	0.387983	0.977626
10	-3.759436	1.309806	0.387983	0.977626

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	5.6520000000	1.8840000000
Residual	21	0.9776258586	0.0465536123
Uncorrected Total	24	6.6296258586	
(Corrected Total)	23	3.0871161028	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC50	-3.759435696	0.35509761374	-4.4978958485	-3.0209755435
SIGMA	1.309806330	0.39018277094	0.4983831680	2.1212294919
C0	0.387982821	0.05365975780	0.2763921162	0.4995735254

Asymptotic Correlation Matrix

Corr	LOG_EC50	SIGMA	C0
LOG_EC50	1	-0.632069979	-0.75403796
SIGMA	-0.632069979	1	0.4543874619
C0	-0.75403796	0.4543874619	1

SUMMARY OF NONLINEAR REGRESSION

95

08:14 Wednesday, April 29, 1998

OBS	LOG_EC50	SIGMA	CO	RESID_SS	EC50	SLOPE
1	-3.75944	1.30981	0.38798	0.97763	.00017401	0.76347

95% C.I.: 0.0000318 - 0.000953

MODEL: YOUNG = CO * PROB NORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)

WEIGHTED REGRESSION

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Iter	Dependent Variable	COUNT	Method: Gauss-Newton	CO	Weighted SS
0	LOG_EC25	SIGMA		0.400000	0.999110
1	-5.100000	1.900000		0.394504	0.987908
2	-4.679938	1.277582		0.387875	0.978194
3	-4.643830	1.309836		0.387990	0.977622
4	-4.643020	1.309902		0.387985	0.977625
5	-4.642926	1.309834		0.387983	0.977626
6	-4.642898	1.309814		0.387983	0.977626
7	-4.642890	1.309809		0.387983	0.977626
8	-4.642888	1.309807		0.387983	0.977626
9	-4.642887	1.309806		0.387983	0.977626
9	-4.642887	1.309806		0.387983	0.977626

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics

Source	DF	Weighted SS	Weighted MS
Regression	3	5.6520000000	1.8840000000
Residual	21	0.9776258587	0.0465536123
Uncorrected Total	24	6.6296258587	
(Corrected Total)	23	3.0871161033	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC25	-4.642886966	0.55990376432	-5.8072615023	-3.4785124305
SIGMA	1.309806329	0.39018277073	0.4983831677	2.1212294907
CO	0.387982821	0.05365975779	0.2763921161	0.4995735254

Asymptotic Correlation Matrix

Corr	LOG_EC25	SIGMA	CO
LOG_EC25	1	-0.870901304	-0.691797845
SIGMA	-0.870901304	1	0.4543874621
CO	-0.691797845	0.4543874621	1

SUMMARY OF NONLINEAR REGRESSION

97

MODEL: YOUNG = CO * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)

SUMMARY OF NONLINEAR REGRESSION

08:14 Wednesday, April 29, 1998

OBS	LOG_EC25	SIGMA	CO	RESID_SS	EC25	SLOPE
1	-4.64289	1.30981	0.38798	0.97763	.000022757	0.76347

95% C.I.: 0.00000156 - 0.000332

MODEL: YOUNG = C0 * PROB NORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

WEIGHTED REGRESSION

08:14 Wednesday, April 29, 1998

Non-Linear Least Squares Iterative Phase

Dependent Variable COUNT Method: Gauss-Newton

Iter	LOG_EC05	SIGMA	C0	Weighted SS
0	-6.900000	1.900000	0.400000	0.997913
1	-5.933583	1.279760	0.394455	0.992572
2	-5.919708	1.311925	0.387999	0.978178
3	-5.915547	1.310480	0.388039	0.977600
4	-5.914399	1.310000	0.387999	0.977619
5	-5.914069	1.309862	0.387987	0.977624
6	-5.913974	1.309822	0.387984	0.977625
7	-5.913947	1.309811	0.387983	0.977626
8	-5.913939	1.309808	0.387983	0.977626
9	-5.913937	1.309807	0.387983	0.977626
10	-5.913936	1.309806	0.387983	0.977626
11	-5.913936	1.309806	0.387983	0.977626

E: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	5.652000000	1.884000000
Residual	21	0.9776258595	0.0465536124
Uncorrected Total	24	6.6296258595	
(Corrected Total)	23	3.0871161185	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval	
			Lower	Upper
LOG_EC05	-5.913936073	0.90891214043	-7.8041075976	-4.0237645489
SIGMA	1.309806307	0.39018276465	0.4983831582	2.1212294559
C0	0.387982819	0.05365975759	0.2763921147	0.4995735231

Asymptotic Correlation Matrix

Corr	LOG_EC05	SIGMA	C0
LOG_EC05	1	-0.953071403	-0.615448088
SIGMA	-0.953071403	1	0.4543874678
C0	-0.615448088	0.4543874678	1

24

SUMMARY OF NONLINEAR REGRESSION

99

MODEL: YOUNG = CO * PROBNORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

SUMMARY OF NONLINEAR REGRESSION

08:14 Wednesday, April 29, 1998

OBS	LOG_EC05	SIGMA	CO	RESID_SS	EC05	SLOPE
1	-5.91394	1.30981	0.38798	0.97763	.0000012192	0.76347

25

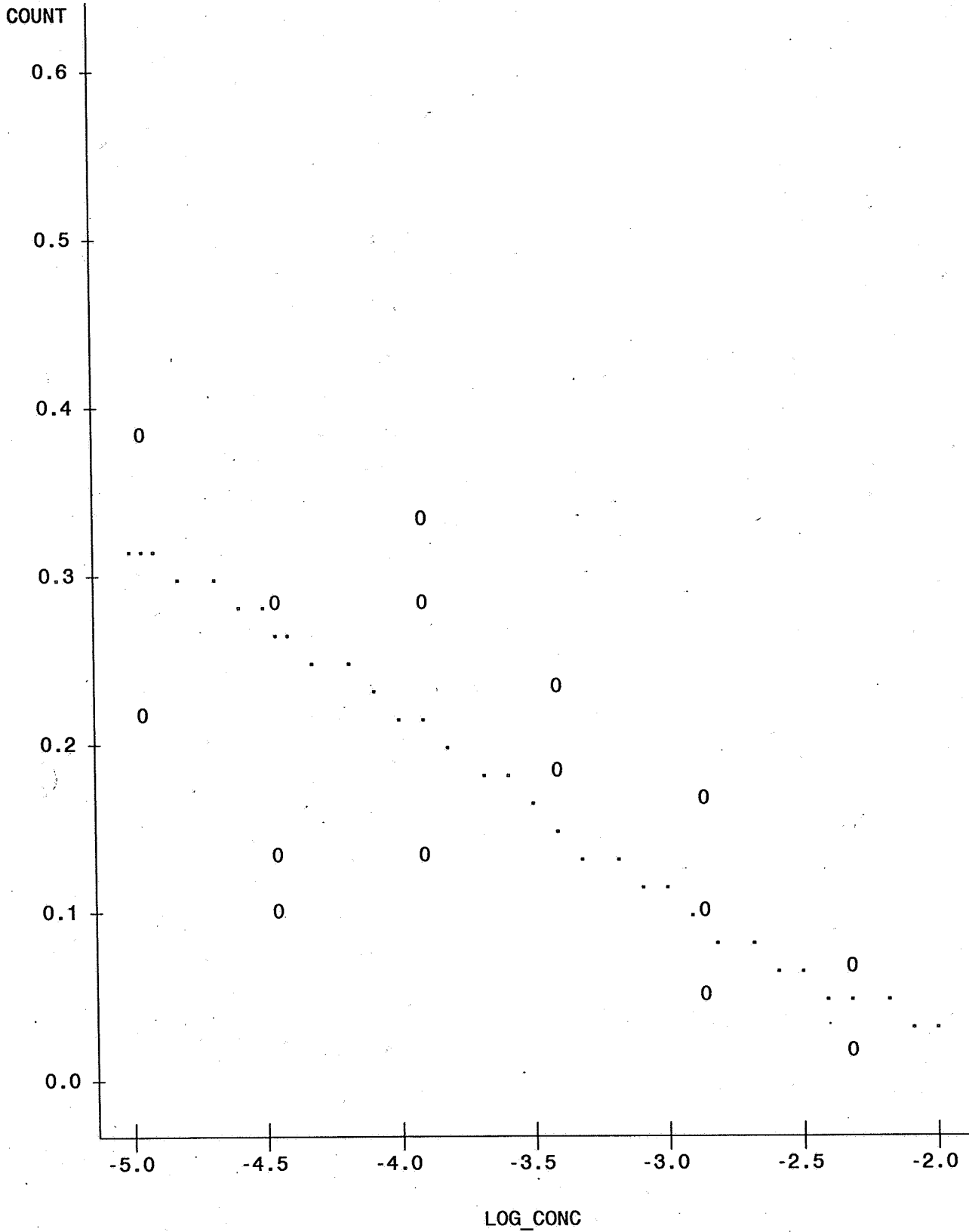
SUMMARY OF NONLINEAR REGRESSION

100

MODEL: YOUNG = CO * PROBNORM ((LOG_EC05 - LOG_CONC) / SIGMA - 1.6449)

08:14 Wednesday, April 29, 1998

Plot of COUNT*LOG_CONC. Symbol used is '0'.
 Plot of PRED*LOG_CONC. Symbol used is '.'.



NOTE: 61 obs had missing values. 37 obs hidden.

26

SUMMARY OF NONLINEAR REGRESSION
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

101

08:14 Wednesday, April 29, 1998

General Linear Models Procedure
Class Level Information

Class	Levels	Values
DOSE	7	0 0.0004 0.0013 0.0047 0.00012 0.000011 0.000034

Number of observations in data set = 42

NOTE: Due to missing values, only 24 observations can be used in this analysis.

SUMMARY OF NONLINEAR REGRESSION
 COMPARISON OF MEANS FOR NOEL DETERMINATION
 TEST IF TREATMENT IS LESS THAN CONTROL

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Dependent Variable: RESPONSE

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	6	0.37986389	0.06331065	4.53	0.0064
Error	17	0.23774989	0.01398529		
Corrected Total	23	0.61761378			

R-Square	C.V.	Root MSE	RESPONSE Mean
0.615051	50.21631	0.118259	0.235500

Source	DF	Type I SS	Mean Square	F Value	Pr > F
DOSE	6	0.37986389	0.06331065	4.53	0.0064

Source	DF	Type III SS	Mean Square	F Value	Pr > F
DOSE	6	0.37986389	0.06331065	4.53	0.0064

SUMMARY OF NONLINEAR REGRESSION
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

103

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Level of DOSE	N	-----RESPONSE-----	
		Mean	SD
0	6	0.39958333	0.18414887
0.0004	3	0.20230000	0.03223166
0.0013	3	0.10286667	0.05468367
0.0047	3	0.03093333	0.02706480
0.00012	3	0.25010000	0.09958469
0.000011	3	0.32560000	0.09449958
0.000034	3	0.17303333	0.10241564

SUMMARY OF NONLINEAR REGRESSION
COMPARISON OF MEANS FOR NOEL DETERMINATION
TEST IF TREATMENT IS LESS THAN CONTROL

104

08:14 Wednesday, April 29, 1998

General Linear Models Procedure

Dunnett's One-tailed T tests for variable: RESPONSE

NOTE: This tests controls the type I experimentwise error for comparisons of all treatments against a control.

Alpha= 0.05 Confidence= 0.95 df= 17 MSE= 0.013985
Critical Value of Dunnett's T= 2.554

Comparisons significant at the 0.05 level are indicated by '***'.

DOSE Comparison	Simultaneous		Simultaneous	
	Lower Confidence Limit	Difference Between Means	Upper Confidence Limit	
0.000011 - 0	-0.28756	-0.07398	0.13959	
0.00012 - 0	-0.36306	-0.14948	0.06409	
0.0004 - 0	-0.41086	-0.19728	0.01629	
0.000034 - 0	-0.44012	-0.22655	-0.01298	***
0.0013 - 0	-0.51029	-0.29672	-0.08314	***
0.0047 - 0	-0.58222	-0.36865	-0.15508	***

30