DP Barcode : D193959, D197369
PC Code No : 128997
EEB Out : JAN 3 1994

To: Susan Lewis/Ben Chambliss
Product Manager
Registration Division (7505C)

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch/EFED (7507C)

Attached, please find the EEB review of...

Reg./File # :
Chemical Name : Tebocunazole
Type Product : Fungicide
Product Name : Folicur
Company Name : Miles Inc.
Purpose : Review of Aquatic Plant Study

Action Code : 116, 405 Date Due : 1/1/94
Reviewer : Conchi Rodríguez Date In EEB: 12/08/93

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT	GDLN NO	MRID NO	CAT
71-1(A)			72-2(A)			72-7(A)		
71-1(B)			72-2(B)			72-7(B)		
71-2(A)			72-3(A)			122-1(A)		
71-2(B)			72-3(B)			122-1(B)		
71-3			72-3(C)			122-2		
71-4(A)			72-3(D)			123-1(A)		
71-4(B)			72-3(E)			123-1(B)		
71-5(A)			72-3(F)			123-2	428054-01	Y
71-5(B)			72-4(A)			124-1		
72-1(A)			72-4(B)			124-2		
72-1(B)			72-5			141-1		
72-1(C)			72-6			141-2		
72-1(D)						141-5		

Y=Acceptable (Study satisfied Guideline)/Concur
P=Partial (Study partially fulfilled Guideline but additional information is needed
S=Supplemental (Study provided useful information but Guideline was not satisfied)
N=Unacceptable (Study was rejected)/Nonconcur

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

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Review of Aquatic Plant Study for Folicur

FROM: Anthony F. Maciorowski, Chief
Ecological Effects Branch
7507C

JAN 3 1994

TO: Susan Lewis/Ben Chambliss
Registration Division

The Ecological Effects Branch completed the review of the Aquatic Plant Study submitted by Miles Inc. to support the registration of the fungicide Folicur. The study submitted is the following:

> Gagliano G.G., 1993. Acute Toxicity of ^{14}C to the Green Alga (*Selenastrum capricornutum*) Study No. 106218. Conducted by Miles Incorporated, Agricultural Division, Environmental Research Section, Stilwell, KS. Submitted by Miles Incorporated, Kansas City, Missouri. EPA MRID No. 429054-01.

The study is scientifically sound and fulfills the guideline requirements for Guideline 123-2 Aquatic Plant Growth Tier 2. The enclosed DER provides the necessary information regarding this study.

The registrant submitted additional information that is not presently in the system but is included as an attachment to the Data Evaluation Record. Please note the additional information and include it in the microfiche for the study.

Regarding the other aquatic plant study (MRID No. 413285-01), in a conversation between Harry Craven and Bob Graney (Miles Inc.) it was agreed that this study will not be reviewed. The data from the reviewed study (MRID 429054-01) will be used for the risk assessment.

If you have any questions please contact Conchi Rodríguez (308-2805) or Harry Craven (305-5320).

Recycled/Recyclable
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DATA EVALUATION RECORD

1. **CHEMICAL:** Folicur
Shaugnessey No. 128997

2. **TEST MATERIAL:** ^{14}C-Folicur [Ring-U-^{14}C]-α-[2-(4-Chlorophenyl)ethyl]-α-(1,1-dimethyl)-1H-1,2,4-triazole-ethanol; Folicur technical α-[2-(4-Chlorophenyl)ethyl]-α-(1,1-dimethyl)-1H-1,2,4-triazole-ethanol; Batch number 0790042/1030038; 95.8% active ingredient; a white powder.

3. **STUDY TYPE:** Growth and Reproduction of Aquatic Plants - Tier 2. Species Tested: *(Selenastrum capricornutum)*.

4. **CITATION:** Gagliano G.G., 1993. Acute Toxicity of ^{14}C to the Green Alga (*Selenastrum capricornutum*) Study No. 106218. Conducted by Miles Incorporated, Agricultural Division, Environmental Research Section, Stilwell, KS. Submitted by Miles Incorporated, Kansas City, Missouri. EPA MRID No. 429054-01.

5. **REVIEWED BY:**

Conchi Rodríguez
Biologist
Ecological Effects Branch
Environmental Fate and Effects Division

Signature: Conchi Rodríguez
Date: 12/20/93

6. **APPROVED BY:**

Harry Craven
Supervisor
Ecological Effects Branch
Environmental Fate and Effects Division

Signature: Harry Craven
Date: 12/21/93

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for a Tier 2 non-target aquatic plant study. Growth and reproduction of *S. capricornutum* was increasingly inhibited by increasing amounts of Folicur. The NOEC, EC_{25}, and EC_{50} values were 1.24, 1.66, and 2.73 mg/L, respectively.

8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:**

10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A.

11. **MATERIALS AND METHODS:**

3

A. **Test Species:** The alga used in the test, *Selenastrum capricornutum*, came from in-house cultures maintained since June 23, 1993. The culture was maintained on a 18 hour daylight photoperiod. Culture techniques were based on those by USEPA (1971).

B. **Test System:** Test vessels used were sterile 250-ml borosilicate glass erlenmeyer flasks capped with sterile borosilicate glass closures.

The test vessels were kept in an environmental chamber programmed to have a temperature of 24 ± 2°C and continuous illumination of approximately 400 foot-candles.

The water used for the culture media and vitamins was dechlorinated tap water. The water was dechlorinated with sodium metabisulfite, filtered, passed through granular activated carbon units, demineralized by conventional softeners and treated by double pass reverse osmosis. The water is constantly monitored to keep a chlorine residual concentration of 3 µg/L (ppb).

C. **Dosage:** Five-day growth and reproduction test. Based on results of preliminary test, nominal concentrations were 0.33, 0.65, 1.3, 2.6, 5.0, and 10 mg ai/L. A control and solvent control were used for the definitive test.

A 20.8688 g ai/L stock solution was prepared by diluting 0.0144 g of ^{14}C-Folicur and 10.42 g Folicur (technical) in 500 ml of acetone at 21°C. The nominal concentrations of 0.33, 0.65, 1.3, 2.6, 5.0, and 10 mg/L were prepared from the stock solution. All flasks received 1 ml of vitamins per 1 L of media.

D. **Test Design:** All replicate flasks (3 per treatment level and controls) were filled with approximately 100 ml of test solution . The test vessels were placed at random in a temperature controlled chamber. They were hand shake 2 to 3 times daily.

An aliquot of 3,000 cells/ml *S. capricornutum* cells was added. Cell density counts were performed daily using a light microscope and an Improved Neubauer hemocytometer.

Samples were taken from the test solutions and controls on days 0 and 5. Day-0 samples were obtained from the remaining solution after filling the treatment flasks.

Day-5 samples were a composite of all corresponding replicates. An aliquot of each composite was analyzed by Liquid Scintillation Counting and Thin-Layer Chromatography.

The pH of the test solutions was measured on days 0 and 5. Temperature was measured daily.

E. **Statistics:** Cell counts in the control and solvent control were t-tested for pooling. Bartlett's test was used for homogeneity of variances. Dunnett's two tailed multiple means comparison test was used to determine the NOEC (alpha level of 0.05). The EC_{50}, EC25 value and 95% confidence limits were calculated by linear regression.

12. **REPORTED RESULTS:** Mean measured concentrations in the test solutions at day 0 ranged between 89 and 99% of nominal (Table 3, attached). Day 0 pH was 7.5 for all replicates. The pH at the end of the study ranged from 7.5 to 9.6. The temperature during the 5 days ranged from 23.6 to 24.1 (Table 4). During the first 24 hours of the study only 8 automatic temperature measurements were taken because of a problem with the datalogger printer. Two additional measurements were done manually.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** "Statistical analysis of growth data for Selenastrum capricornutum after the 5-day exposure to ^{14}C FOLICUR/FOLICUR (TECH) showed no significant difference between the pooled controls and the three lowest test levels - 0.327, 0.579, and 1.24 mg/L (Table 5). The NOEC was 1.24 mg/L. The 5-day EC25 and EC50 were calculated to be 6.04 mg/L (95% C.I. 5.16 to 6.91 mg/L) and 4.73 mg/L (95% CI 3.80 to 5.13 mg/L), respectively."

A new analysis of the data by the registrant reported the following values:
EC25 = 2.63 mg/L (95% C.I. = 2.10 to 3.17 mg/L)
EC50 = 4.23 mg/L (95% C.I. = 3.55 to 4.90 mg/L)

Statements of compliance to Good Laboratory Practices and Quality Assurance were included in the report indicating compliance with 40 CFR Part 160.

14. **REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS:**

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A. **Test Procedure:** The test procedure and the report were generally in accordance with the SEP and Subdivision J guidelines, the following are deviations:

In the report it was not clear if the solvent used was DMF or acetone.

The temperature and light intensity of the primary culture was not specified.

B. **Statistical Analysis:** The reviewer used a statistical procedure for continuous data develop by Bruce and Versteeg (1992) to determine the EC50 and the EC25. To determine the NOEC value, the control and solvent control data was subject to t-test and pooled. Then Dunnett's test was used to determine the NOEC from the day-5 cell density data. The reviewer obtained different values for the EC25 and EC50.

C. **Discussion/Results:** Additional information from the registrant indicates that the solvent used was acetone and not DMF (see attached information).

The EC25 and EC50 values reported by the author are not clear. The author is reporting and EC25 (6.04 mg/L) value higher than the EC50 (4.47 mg/L). After conversations with the registrant, they submitted new calculations for the EC25 and EC50 (see attached information). Their first calculations were wrong. The reviewer calculated the EC25 and EC50 value using the method develop by Bruce and Versteeg (1992) for continuous data. The EC50 value was 2.73 mg/L with a 95% confidence interval values of 2.33 - 3.19 mg/L. The EC25 value was 1.66 mg/L with a 95% confidence interval values of 1.31 - 2.09 mg/L. These values are more conservative than the registrant values.

The NOEC value calculated by Dunnett's test was 1.24 mg/L. This value correspond with the author's value.

This study is scientifically sound and meets the guideline requirements for a Tier 2 non-target aquatic plant study. Growth and reproduction of *S. capricornutum* was increasingly inhibited by increasing amounts of Folicur. The NOEC, EC_{25}, and EC_{50} values were 1.24, 1.66, and 2.73 mg/L, respectively.

D. **Adequacy of the Study:**

(1) **Classification:** Core

(2) **Rationale:** N/A

(3) **Repairability:** N/A

15. **COMPLETION OF ONE-LINER:** Yes

16. **Reference:**

Bruce, R. B. and D.J. Versteeg, 1992. A Statistical Procedure for Modeling Continuous Toxicity Data. Environmental Toxicology and Chemistry 11:1485-1494.

7

Page_____ is not included in this copy.

Pages 8 through 13 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Effect of Folicur on Selenastrum
2:19 Wednesday, December 15, 1993

OBS	CONC	LOG_CONC	Y1	Y2	Y3
1	0.000	.	13.56	16.25	12.19
2	0.327	-0.48545	13.31	17.81	14.69
3	0.579	-0.23732	13.25	15.75	15.88
4	1.240	0.09342	12.94	13.00	12.50
5	2.210	0.34439	10.94	9.06	8.81
6	4.850	0.68574	3.38	2.31	2.31
7	8.900	0.94939	1.13	0.88	1.13

Effect of Folicur on Selenastrum
MODEL: COUNT = C0 * PROBNORM ((LOG_EC50 - LOG_CONC) / SIGMA)
WEIGHTED REGRESSION
2:19 Wednesday, December 15, 1993

Non-Linear Least Squares Iterative Phase
Dependent Variable COUNT Method: Gauss-Newton

Iter	LOG_EC50	SIGMA	C0	Weighted SS
0	0.540000	0.240000	14.000000	5.402221
1	0.439736	0.326991	14.774918	3.010017
2	0.436885	0.320043	14.888688	2.986795
3	0.436405	0.320564	14.894350	2.985788
4	0.436471	0.320499	14.893626	2.985882
5	0.436462	0.320507	14.893720	2.985869
6	0.436463	0.320506	14.893708	2.985871
7	0.436463	0.320506	14.893710	2.985871
8	0.436463	0.320506	14.893710	2.985871

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	211.08000000	70.36000000
Residual	18	2.98587084	0.16588171
Uncorrected Total	21	214.06587084	
(Corrected Total)	20	134.40531594	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval Lower	Upper
LOG_EC50	0.43646304	0.03267708498	0.367811482	0.505114591
SIGMA	0.32050618	0.02829163864	0.261068045	0.379944314
C0	14.89370956	0.54643263549	13.745704773	16.041714337

Asymptotic Correlation Matrix

Corr	LOG_EC50	SIGMA	C0
LOG_EC50	1	-0.690739933	-0.644803584
SIGMA	-0.690739933	1	0.4598838239
C0	-0.644803584	0.4598838239	1

SUMMARY OF NONLINEAR REGRESSION

2:19 Wednesday, December 15, 1993

OBS	CONC	LOG_EC50	SIGMA	C0	RESID_SS	EC50
1	0	0.43646	0.32051	14.8937	2.98587	2.73189

SUMMARY OF NONLINEAR REGRESSION
MODEL: YOUNG = C0 * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
WEIGHTED REGRESSION
2:19 Wednesday, December 15, 1993

Non-Linear Least Squares Iterative Phase
Dependent Variable COUNT Method: Gauss-Newton

Iter	LOG_EC25	SIGMA	C0	Weighted SS
0	0.360000	0.240000	14.000000	5.392602
1	0.216884	0.326177	14.816417	2.999069
2	0.221167	0.319966	14.887938	2.986821
3	0.220170	0.320574	14.894465	2.985773
4	0.220300	0.320497	14.893611	2.985884
5	0.220283	0.320507	14.893722	2.985869
6	0.220285	0.320506	14.893708	2.985871
7	0.220285	0.320506	14.893710	2.985871
8	0.220285	0.320506	14.893710	2.985871
9	0.220285	0.320506	14.893710	2.985871

NOTE: Convergence criterion met.

Non-Linear Least Squares Summary Statistics Dependent Variable COUNT

Source	DF	Weighted SS	Weighted MS
Regression	3	211.08000000	70.36000000
Residual	18	2.98587083	0.16588171
Uncorrected Total	21	214.06587083	
(Corrected Total)	20	134.40531565	

Parameter	Estimate	Asymptotic Std. Error	Asymptotic 95 % Confidence Interval Lower	Upper
LOG_EC25	0.22028482	0.04788907915	0.119674262	0.320895376
SIGMA	0.32050618	0.02829163881	0.261068047	0.379944317
C0	14.89370958	0.54643263785	13.745704795	16.041714368

Asymptotic Correlation Matrix

Corr	LOG_EC25	SIGMA	C0
LOG_EC25	1	-0.86979737	-0.623231893
SIGMA	-0.86979737	1	0.4598838263
C0	-0.623231893	0.4598838263	1

SUMMARY OF NONLINEAR REGRESSION

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

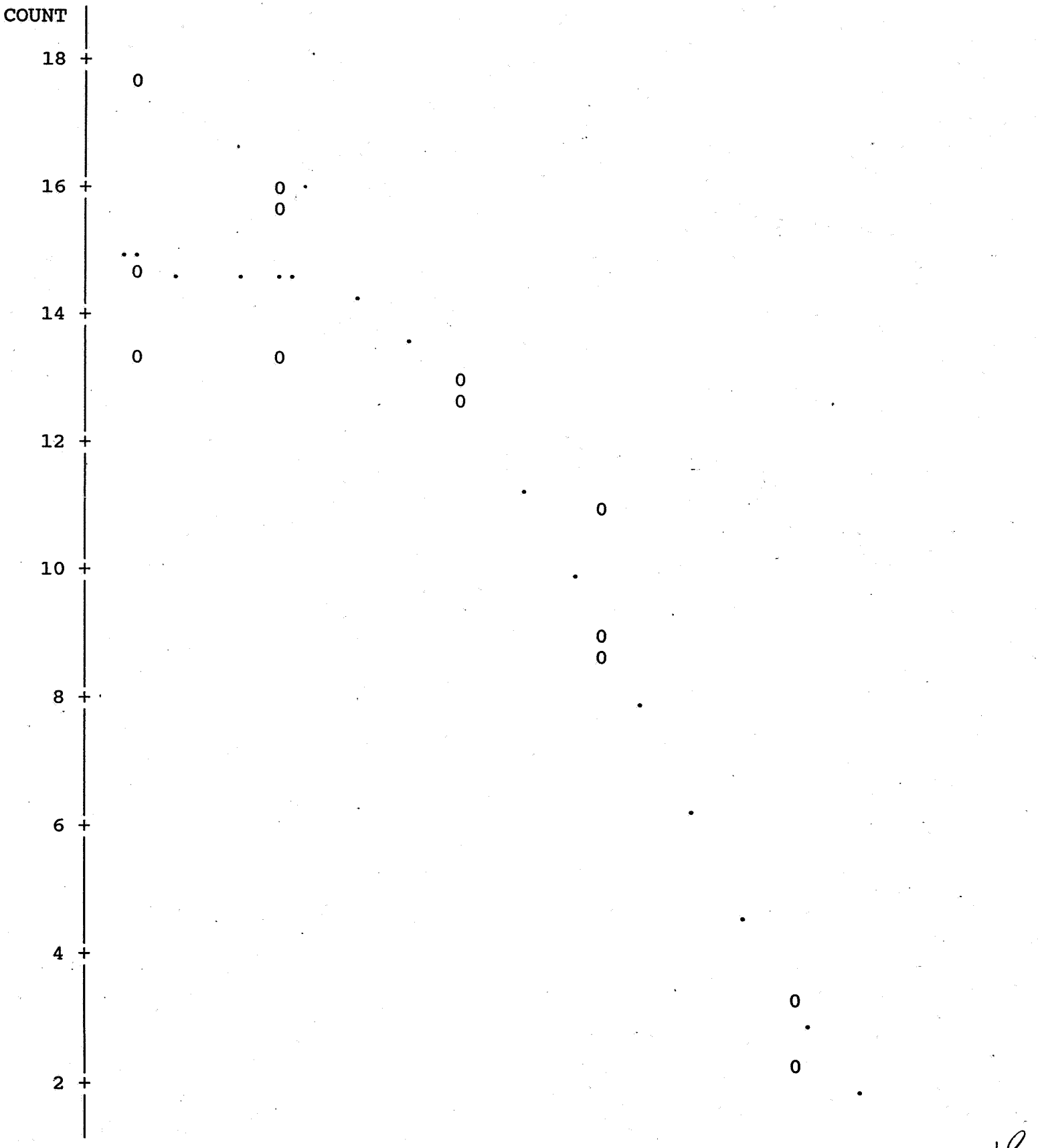
SUMMARY OF NONLINEAR REGRESSION

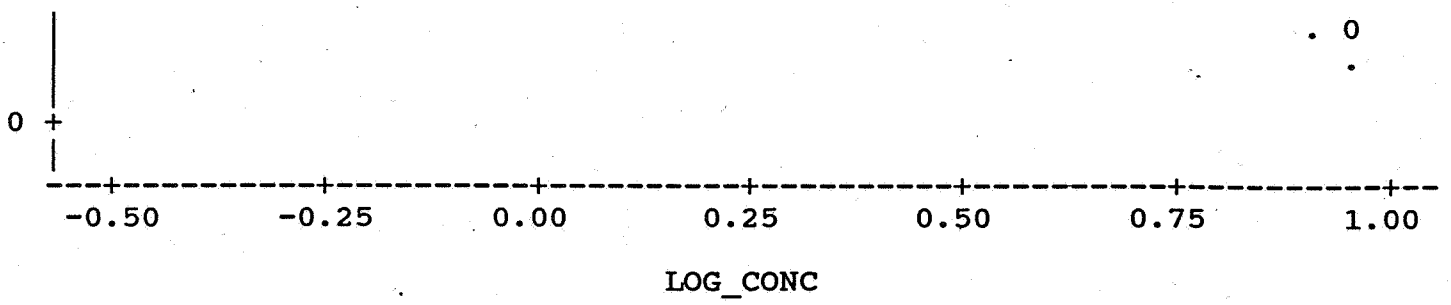
2:19 Wednesday, December 15, 1993

OBS	CONC	LOG_EC25	SIGMA	C0	RESID_SS	EC25
1	0	0.22028	0.32051	14.8937	2.98587	1.66068

SUMMARY OF NONLINEAR REGRESSION
MODEL: YOUNG = C0 * PROBNORM ((LOG_EC25 - LOG_CONC) / SIGMA - 0.67449)
2:19 Wednesday, December 15, 1993

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





NOTE: 18 obs had missing values. 20 obs hidden.

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

Chi-square test for normality: actual and expected frequencies

INTERVAL	<-1.5	-1.5 to <-0.5	-0.5 to 0.5	>0.5 to 1.5	>1.5
EXPECTED	1.608	5.808	9.168	5.808	1.608
OBSERVED	0	9	6	8	1

Calculated Chi-Square goodness of fit test statistic = 5.5142
Table Chi-Square value (alpha = 0.01) = 13.277

Data PASS normality test. Continue analysis.

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

Hartley test for homogeneity of variance

Calculated H statistic (max Var/min Var) = 255.11
Closest, conservative, Table H statistic = 1705.0 (alpha = 0.01)

Used for Table H ==> R (# groups) = 7, df (# reps-1) = 2
Actual values ==> R (# groups) = 7, df (# avg reps-1) = 2.43
(average df used)

Data PASS homogeneity test. Continue analysis.

NOTE: This test requires equal replicate sizes. If they are unequal but do not differ greatly, the Hartley test may still be used as an approximate test (average df are used).

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

t-test of Solvent and Blank Controls Ho:GRP1 MEAN = GRP2 MEAN

GRP1 (SOLVENT CRTL) MEAN =	14.0000	CALCULATED t VALUE =	2.1868
GRP2 (BLANK CRTL) MEAN =	11.3133	DEGREES OF FREEDOM =	4
DIFFERENCE IN MEANS =	2.6867		

TABLE t VALUE (0.05 (2), 4) = 2.776 NO significant difference at alpha=0.05
TABLE t VALUE (0.01 (2), 4) = 4.604 NO significant difference at alpha=0.01

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

ANOVA TABLE

SOURCE	DF	SS	MS	F
Between	6	624.457	104.076	45.869
Within (Error)	17	38.573	2.269	
Total	23	663.030		

Critical F value = 2.70 (0.05,6,17)
Since F > Critical F REJECT Ho:All groups equal

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

DUNNETTS TEST

****** WARNING ******

This data set has unequal replicates. The Bonferroni T-test should be used instead of the Dunnetts test.

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 1 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	GRPS 1&2 POOLED	12.657	12.657		
2	0.327	15.270	15.270	-2.454	
3	0.579	14.960	14.960	-2.162	
4	1.24	12.813	12.813	-0.147	
5	2.21	9.603	9.603	2.867	*
6	4.85	2.667	2.667	9.379	*
7	8.90	1.047	1.047	10.900	*

Dunnett table value = 2.49 (1 Tailed Value, P=0.05, df=17,6)

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 2 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	REPS	(IN ORIG. UNITS)	CONTROL	FROM CONTROL
1	GRPS 1&2 POOLED	6			
2	0.327	3	2.652	21.0	-2.613
3	0.579	3	2.652	21.0	-2.303
4	1.24	3	2.652	21.0	-0.157
5	2.21	3	2.652	21.0	3.053
6	4.85	3	2.652	21.0	9.990
7	8.90	3	2.652	21.0	11.610

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

ANOVA TABLE

SOURCE	DF	SS	MS	F
Between	6	624.457	104.076	45.869
Within (Error)	17	38.573	2.269	
Total	23	663.030		

Critical F value = 2.70 (0.05,6,17)
Since F > Critical F REJECT Ho:All groups equal

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

BONFERRONI T-TEST - TABLE 1 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	GRPS 1&2 POOLED	12.657	12.657		
2	0.327	15.270	15.270	-2.454	
3	0.579	14.960	14.960	-2.162	
4	1.24	12.813	12.813	-0.147	
5	2.21	9.603	9.603	2.867	*
6	4.85	2.667	2.667	9.379	*
7	8.90	1.047	1.047	10.900	*

Bonferroni T table value = 2.65 (1 Tailed Value, P=0.05, df=17,6)

Cell Density
File: a:\algstat Transform: NO TRANSFORMATION

BONFERRONI T-TEST - TABLE 2 OF 2 Ho:Control<Treatment

GROUP	IDENTIFICATION	NUM OF REPS	Minimum Sig Diff (IN ORIG. UNITS)	% of CONTROL	DIFFERENCE FROM CONTROL
1	GRPS 1&2 POOLED	6			
2	0.327	3	2.828	22.3	-2.613
3	0.579	3	2.828	22.3	-2.303
4	1.24	3	2.828	22.3	-0.157
5	2.21	3	2.828	22.3	3.053
6	4.85	3	2.828	22.3	9.990
7	8.90	3	2.828	22.3	11.610

RAPIFAX FROM:

R. L. Graney
Miles Incorporated
Miles Research Park
17745 S. Metcalf
Stilwell, Kansas 66085

FAX Number: 913-897-5215
Phone Number: 913-897-9132

IMPORTANT

Please deliver the following document(s) immediately:

DATE: 12/16/93

TO: Conchi Rodriques

FROM: Bob Graney

COPY: H. Craven

NUMBER OF PAGES: 6

Attached is a response to the questions you had concerning the FOLICUR Green Alga study. Hopefully this clarifies the situation. Also attached are copies of corrected pages which can be inserted into the report (I assume).

I apologize for the errors and truly appreciate your contacting us directly so the situation could be resolved immediately. I think this represents an example of how, by communicating, problems can be resolved quickly and efficiently without the need for extensive paperwork etc. Please call if you have any questions or need additional input. Hope your Holidays are enjoyable.

Bob

Bob Graney

RESPONSE TO USEPA REVIEWER QUESTIONS
FOR FOLICUR *SELENASTRUM* ACUTE TOXICITY STUDY
MRID 42905401

Reviewer Question: What carrier solvent was used? Both DMF and acetone are listed on page 9 of the report.

Miles Inc. Response: The solvent used for the study was acetone. The reference to dimethylformamide is a typographical error.

Review Question: What is the correct EC50 value? The value given on page 7 and page 11 are different. Why is the EC25 value greater than the EC50?

Miles Inc. Response: The EC50 value on page 7 is the calculated EC50 whereas the EC50 value on page 11 is a typographical error. The EC25 value was incorrectly calculated. Upon re-examination of the statistical analysis an error was found and the EC50 and EC25 values were re-calculated. Originally, the regression analysis was conducted using the mean of control and solvent control Day 5 growth data. However, it is more appropriate to use the data from the individual control replicates. Therefore, the regression analysis was rerun using these data (statistical output attached). The output shows that the regression line fits the data well (R^2 = 82.5%). The predictive equation derived from the regression analysis is:

Concentration in mg/L = 7.43 - (0.506 X Cells/ml)

The cells/ml value for the EC25 and EC50 were determined as follows:

The cell/ml data for the control and solvent control were determined to be poolable via a t-test. The data were pooled to yield a mean of 12.66×10^5 cells/ml. An EC50 would be predicted from a cell/ml value that is 50% of the control mean, i.e. $(12.66 \times 10^5) \times 50\% = 6.33 \times 10^5$ cells/ml. Likewise an EC25 would be predicted from a cell/ml value that shows 25% inhibition (100% - 25% = 75%). So, $(12.66 \times 10^5) \times 75\% = 9.495 \times 10^5$ cells/ml. These cells/ml values were then plugged into the formula to solve for the unknown concentration term. The statistics program computed this value and it's associated 95% confidence intervals automatically.

The results are more conservative than the previously reported EC25 and EC50. Based on this re-analysis of the data the reported EC values are given below:

5-day EC25 = 2.63 mg/L (95% C.I. = 2.10 to 3.17 mg/L)
5-day EC50 = 4.23 mg/L (95% C.I. = 3.55 to 4.90 mg/L)

```
MTB > read 'folicur.dat' c1 c2
     24 ROWS READ

 ROW      C1      C2

   1   0.000   10.75
   2   0.000   11.75
   3   0.000   11.44
   4   0.000   13.56
   .   .   .

MTB > name c1 'CONC' c2 'CELLS/ml'
MTB > regr c1 1 c2;
SUBC> predict 9.495;
SUBC> predict 6.33.

The regression equation is
CONC = 7.43 - 0.506 CELLS/ml

Predictor        Coef       Stdev    t-ratio        p
Constant       7.4291      0.5712      13.01    0.000
CELLS/ml    -0.50600     0.04974     -10.17    0.000

s = 1.281       R-sq = 82.5%     R-sq(adj) = 81.7%

Analysis of Variance

SOURCE        DF          SS          MS          F        p
Regression     1      169.76      169.76     103.48    0.000
Error         22       36.09        1.64
Total         23      205.85


     Fit  Stdev.Fit          95% C.I.          95% P.I.
   2.625      0.264   (  2.077,  3.172)  ( -0.088,  5.337)

   4.226      0.325   (  3.552,  4.900)  (  1.485,  6.967)


MTB > plot c1 c1
```

Page_____ is not included in this copy.

Pages 30 through 32 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.