5-24-83
128201

DATA EVALUATION RECORD

1. CHEMICAL: DPX-Y6202 or C.A.: 2-[4-[(6-chloro-2-quinoxalinyl)oxy]phenoxy]propionic acid, ethyl ester.

2. FORMULATION: Technical 99.1% (see memo dated 1-11-89 attached to Report #3)

3. CITATION: McDougall, J. (1982) The determination of the acute toxicity (LD_{50}) of NC 302 to birds single oral administration (capsule), IRI Project No. 130194, Report No. 2457, (Unpublished study received May 2, 1983 Under 352-EUP-112; submitted by E.I. duPont de Nemours and Company (Inc.) Wilmington, Delaware; CDL: 250071)

MRID = 00128210

4. REVIEWED BY: Dennis J. McLane
Wildlife Biologist
EEB/HED

5. DATE REVIEWED: 5-24-83

6. TEST TYPE: Avian acute LD_{50} for both mallard duck and bobwhite quail

7. REPORTED RESULTS:

After a 7-day acclimatization period a single oral dose of NC 302 was administered by gavage to adult mallard ducks and bobwhite quail. Following a 14-day observation and recovery period surviving birds were sacrificed.

At the maximum dose level, 2000 mg. kg^{-1} body weight, no LD_{50} value for NC 302 to mallard ducks or bobwhite quail could be established.

8. REVIEWER'S CONCLUSION

This study is scientifically sound. However, it does not satisfy the guideline requirements. The LD_{50} of >2000 mg/l indicates the material is practically non-toxic to these birds.

ASSURE

Page_____ is not included in this copy.

Pages 2 through 12 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.

Body Weights

Group mean body weights are presented in Table 3.

Analysis of variance revealed a significant difference (P=0.001) in the group mean body weights. Individual comparisions of the body weight values of Groups 3, 4, 5 and 6 with that of the control group demonstrated a significant difference (P=0.01).

Food Consumption

Group mean food consumption is recorded in Table 4. The food consumption of all groups receiving NC 302 was reduced in a dose related manner over the 24 h period following dosing. Such reductions ranged from ca 30% (Group 2,500 mg/kg^{-1}) to >80% (Group 6, 2000 $mg.kg^{-1}$). During the subsequent 24 h period food intake in Groups 5 (1500 mg/kg^{-1}) and 6 remained reduced by 30% and 50% respectively, other groups showing recovery. Subsequently, food consumption was found to be unaffected by NC 302 administration.

Gross Pathology

Gross pathology findings for individual animals are presented in Appendix 6. No significant pathological changes were found in any animal as a result of NC 302 administration.

Conclusion

NC 302 has been administered to adult mallard ducks and bobwhite quail by oral gavage. Following a single oral dose no LD50 could be determined in the maximum dosing group of 2000 $mg.kg^{-1}$ body weight.

Statistical analysis indicated that single administration of NC 302 has lowered the body weights of both types of birds. In addition, there was some evidence of reduced food consumption in both species, on the day following dosing. This was more obvious in the bobwhite quail where reductions persisted for 2 days at dose levels of 1500 and 2000 $mg.kg^{-1}$. These effects were transient, however, in that on subsequent days the food consumption returned to normal.

No significant lesions were found in any of the birds as a result of NC 302 administration.

REVIEWER'S EVALUATION

Test Procedure

The following item was not reported:

Percent of active ingredient

The following items did not meet the guidelines requirements:

1. Mallards were twelve weeks rather than the minimum of 16 weeks.

2. Bobwhite quail were not fasted.

3. Mallards were fasted overnight (whether this was 15 hours is unknown).

Statistical Analysis

The statistical analysis for this study was confined to non-parametric analysis of variance for both body weight and food consumption. No LD_{50} method was needed since only one mortality occurred. This death did not appear to be due to the toxicity of the chemical.

The use of a non-parametric method to analyze body weight is not correct. Non-parametric assumes the population tested is not normally distributed, which would not be the case for body weight. Hence, EEB used a parametric anova for analysis (see attached printouts). Of the two birds, the body weight of the Mallard appeared to be dose related. The Bobwhite data may have been influenced by the lack of a prefasting period prior to the study.

Discussion and Result

The Mallard portion of the study is repairable for registration purposes. The Bobwhite Quail portion is not. Provided the percent active ingredient is reported the Mallard study would be acceptable, although the Mallards were below the minimal age of 16 weeks. The low sensitivity of Mallards appears to allow for this error. On the other hand, by not fasting the Bobwhite Quail, the effect of food and the chemical interaction bias the results. Hence, interpretation and comparison of this data to similar data is difficult because of this dietary factor. Therefore, Bobwhite Quail portion of the study is not acceptable for registration.

Conclusion

Category - Supplemental

Rational - The chemical was not sufficiently identified as to the percent of active ingredient. The Bobwhite quail was not pre-fasted prior to the study.

Repairability - The Mallard portion can be repaired if the percent active ingredient is reported. The Bobwhite Quail portion cannot be repaired because the effect of the lack of pre-fasting period is unknown.

1 SAS 13:36 THURSDAY, MAY 26, 1983 1

GENERAL LINEAR MODELS PROCEDURE

CLASS LEVEL INFORMATION

Mallard Duck

CLASS	LEVELS	VALUES
[redacted]	6	1 2 3 4 5 6
FB	7	1 2 3 4 5 6 7

NUMBER OF OBSERVATIONS IN DATA SET = 42

1 SAS 13:36 THURSDAY, MAY 26, 1983 2

GENERAL LINEAR MODELS PROCEDURE

DEPENDENT VARIABLE: VAR

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE
MODEL	11	92481.34904762	8407.39536797	54.25
ERROR	30	4649.08714284	154.96957143	PR > F
CORRECTED TOTAL	41	97130.43619046		0.0001

R-SQUARE	C.V.	ROOT MSE	VAR MEAN
0.952136	1.2148	12.44867750	1024.79047619

SOURCE	DF	TYPE I SS	F VALUE	PR > F
FA	5	54282.39619048	70.06	0.0001
FB	6	38198.95285714	41.08	0.0001

SOURCE	DF	TYPE III SS	F VALUE	PR > F
FA	5	54282.39619048	70.06	0.0001
FB	6	38198.95285714	41.08	0.0001

1 SAS 13:36 THURSDAY, MAY 26, 1983 3

GENERAL LINEAR MODELS PROCEDURE

DUNCAN'S MULTIPLE RANGE TEST FOR VARIABLE: VAR
NOTE: THIS TEST CONTROLS THE TYPE I COMPARISONWISE ERROR RATE,
NOT THE EXPERIMENTWISE ERROR RATE.
ALPHA=0.05 DF=30 MSE=154.97
MEANS WITH THE SAME LETTER ARE NOT SIGNIFICANTLY DIFFERENT.

DUNCAN GROUPING	MEAN	N	[redacted]
A	1088.9	7	1 — 0
B	1039.1	7	4 — 1000
C	1023.5	7	3 — 750
C			
C	1018.0	7	2 — 500
C			
C	1011.1	7	5 — 1500
D	968.1	7	6 — 2000

1 SAS 13:36 THURSDAY, MAY 26, 1983 4

GENERAL LINEAR MODELS PROCEDURE

DUNCAN'S MULTIPLE RANGE TEST FOR VARIABLE: VAR
NOTE: THIS TEST CONTROLS THE TYPE I COMPARISONWISE ERROR RATE,
NOT THE EXPERIMENTWISE ERROR RATE.
ALPHA=0.05 DF=30 MSE=154.97
MEANS WITH THE SAME LETTER ARE NOT SIGNIFICANTLY DIFFERENT.

DUNCAN GROUPING	MEAN	N	[redacted]
A	1054.3	6	7
A			
A	1053.7	6	6
B	1035.9	6	5
B			
B	1029.4	6	4
B			
B	1021.6	6	2
B			
B	1020.9	6	3
C	957.8	6	1

? logoff

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Bobwhite Quail

```
VAR DOSE N RES;
? fetch 2251 clr
? l'n.c.'
        CARY, N.C. 27511-8000
? l 193/1
        CARY, N.C. 27511-8000
1                                   SAS       11:36 THURSDAY, MAY 26, 1983    1

                         GENERAL LINEAR MODELS PROCEDURE

                            CLASS LEVEL INFORMATION

                       CLASS     LEVELS     VALUES

                                  6         1 2 3 4 5 6

                       FB         7         1 2 3 4 5 6 7


                    NUMBER OF OBSERVATIONS IN DATA SET = 42
1                                   SAS       11:36 THURSDAY, MAY 26, 1983    2

                         GENERAL LINEAR MODELS PROCEDURE

 DEPENDENT VARIABLE: VAR

 SOURCE                  DF       SUM OF SQUARES        MEAN SQUARE       F VALUE

 MODEL                   11       1250.15472340       113.65042940         14.67

 ERROR                   30        232.47003850         7.74900128        PR > F

 CORRECTED TOTAL         41       1482.62476191                           0.0001


 R-SQUARE              C.V.            ROOT MSE           VAR MEAN

 0.843204            1.5098          2.78370280       184.38095238


 SOURCE                  DF          TYPE I SS    F VALUE    PR > F

 FA                       5       627.64761905      16.20    0.0001
 FB                       6       622.50710436      13.39    0.0001


 SOURCE                  DF        TYPE III SS    F VALUE    PR > F

 FA                       5       646.39696150      16.68    0.0001
 FB                       6       622.50710436      13.39    0.0001
1                                   SAS       11:36 THURSDAY, MAY 26, 1983    3

                         GENERAL LINEAR MODELS PROCEDURE

 DUNCAN'S MULTIPLE RANGE TEST FOR VARIABLE: VAR
 NOTE: THIS TEST CONTROLS THE TYPE I COMPARISONWISE ERROR RATE,
       NOT THE EXPERIMENTWISE ERROR RATE.
OALPHA=0.05  DF=30  MSE=7.749
OMEANS WITH THE SAME LETTER ARE NOT SIGNIFICANTLY DIFFERENT.

 DUNCAN   GROUPING            MEAN      N   Bodyweight Dose

                   A        190.40      7   1  — 0
                   A
         B         A        187.56      7   2  — 500
         B
         B         C        184.87      7   6  — 2000
                   C
                   C        183.01      7   5  — 1500
                   C
                   C        182.04      7   4  — 1000

                   D        178.40      7   3  — 750
1                                   SAS       11:36 THURSDAY, MAY 26, 1983    4

                         GENERAL LINEAR MODELS PROCEDURE

 DUNCAN'S MULTIPLE RANGE TEST FOR VARIABLE: VAR
 NOTE: THIS TEST CONTROLS THE TYPE I COMPARISONWISE ERROR RATE,
       NOT THE EXPERIMENTWISE ERROR RATE.
OALPHA=0.05  DF=30  MSE=7.749
OWARNING: CELL SIZES ARE NOT EQUAL.
 HARMONIC MEAN OF CELL SIZES=5.95142
OMEANS WITH THE SAME LETTER ARE NOT SIGNIFICANTLY DIFFERENT.

 DUNCAN   GROUPING            MEAN      N

                   A        190.00      6   7
                   A
         B         A        188.60      6   6
         B
         B         C        185.67      6   5
                   C
                   C        184.33      6   4
                   C
                   C        183.08      6   2

                   D        179.76      5   3
                   D
```

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TABLE 1

Determination of Acute Toxicity of NC 302 to Birds: Mallard Ducks
Body Weight: Group Mean Values (g)

Day	Dose Group/Dose Level ($mg.kg^{-1}$ body weight)					
	1	2	3	4	5	6
	0	500	750	1000	1500	2000
24 August	1017.7	938.2	959.4	942.9	974.3	914.2
31 August	1087.1	1020.2	1012.3	1023.1	1024.2	962.6
4 September	1081.9	1022.4	1027.8	1037.1	994.1	961.9
7 September	1082.6	1018.3	1032.9	1050.6	1012.8	979.4
10 September	1096.0	1026.5	1031.5	1062.8	1011.7	986.7
13 September	1122.3	1052.2	1047.4	1082.9	1028.9	988.3
15 September	1134.5	1047.9	1053.5	1074.3	1032.0	983.9

Day of Dosing - 1 September

TABLE 2

Determination of Acute Toxicity of NC 302 to Birds: Mallard Ducks
Food Consumption: Group Mean Values (g)

Experimental Period/Day	Dose Group/Dose Level ($mg.kg^{-1}$ body weight)					
	1	2	3	4	5	6
	0	500	750	1000	1500	2000
Acclimatisation						
Day 1	112.6	134.7	129.6	109.5	120.6	118.0
2	152.1	154.2	134.8	139.1	129.3	126.7
3	172.9	170.9	175.0	144.4	146.3	138.8
4	168.5	151.8	154.1	147.6	128.8	146.8
5	189.3	177.1	187.2	186.8	163.4	162.4
6	157.8	139.9	121.6	170.4	150.2	141.9
7†	0	0	0	0	0	0
Recovery Day$^{\phi}$						
1*	230.0	199.1	207.2	216.8	190.9	176.5
2	158.8	151.4	173.2	186.3	149.4	185.8
3	149.9	134.5	147.1	159.5	153.3	155.4
4	153.9	119.0	152.0	145.3	152.4	175.1
5	156.3	125.0	171.9	151.8	174.6	174.1
6	122.8	100.0	128.4	117.4	121.5	153.6
7	132.1	128.3	143.4	152.3	180.7	132.4
8	160.3	118.5	133.5	136.7	146.7	142.8
9	149.5	140.7	173.3	148.9	159.6	167.9
10	149.2	167.6	152.6	172.5	161.8	138.1
11	151.3	178.9	164.0	184.4	196.3	189.4
12	188.8	187.7	181.4	199.3	198.0	197.8
13	130.5	120.8	134.6	150.0	156.1	124.9
14	160.1	149.9	165.3	174.8	166.0	173.6

ϕ = Maximum = 200 g except Recovery Day 1 where maximum = 230 g (Group 1) and 220 g (all other groups)

* = Inclusive of 2.5 h pretrial data (see text)

† = Food withdrawn for 15 h prior to dosing with NC 302

TABLE 3

Determination of Acute toxicity of NC 302 to Birds: Bobwhite Quail
Body Weight: Group Mean Values (g)

Day	Dose Group/Dose Level ($mg.kg^{-1}$ body weight)					
	1	2	3	4	5	6
	0	500	750	1000	1500	2000
31 August	181.8	178.9	170.0	172.3	177.8	183.6
7 September	189.7	184.0	174.9	180.0	182.1	187.8
10 September	190.7	185.6	174.4	178.9	180.0	179.9
13 September	190.6	188.8	176.7	182.9	182.6	184.4
16 September	194.2	190.4	177.6	184.2	181.9	185.7
19 September	192.6	192.7	186.3	187.5	187.2	185.3
21 September	193.2	192.5	188.9	188.5	189.5	187.4

Day of Dosing - 7 September

TABLE 4

Determination of Acute Toxicity of NC 302 to Birds: Bobwhite Quail
Food Consumption: Group Mean Values (g)

Experimental Period/Day	Dose Group/Dose Level ($mg.kg^{-1}$ body weight)					
	1	2	3	4	5	6
	0	500	750	1000	1500	2000
Acclimatisation						
Day 1	17.3	12.2	19.2	20.3	18.6	18.2
2	11.9	11.6	11.7	12.5	12.0	11.7
3	20.8	19.5	21.1	19.5	22.1	21.6
4	14.3	13.6	13.0	13.1	15.1	13.9
5	16.8	15.6	16.1	14.9	17.0	17.0
6	18.6	15.5	15.5	14.6	17.1	17.4
7	19.2	18.0	19.3	19.3	20.3	19.0
8	16.1	17.0	18.7	17.6	17.8	17.9
Recovery Day						
1	15.8	10.9	8.8	3.9	2.9	2.5
2	16.6	16.5	16.5	16.7	12.3	7.5
3	17.7	16.9	17.8	19.1	20.2	15.0
4	15.0	15.3	15.9	16.8	17.9	15.6
5	16.1	15.3	16.3	15.9	18.8	16.5
6	18.0	16.9	16.8	18.5	19.7	19.5
7	14.1	14.7	15.8	15.5	13.7	15.2
8	17.0	17.2	17.4	18.2	16.8	19.5
9	14.6	14.2	13.7	13.3	14.0	15.1
10	14.8	14.9	14.4	14.6	15.2	16.4
11	15.3	14.8	14.7+	15.4	15.3	15.7
12	11.5	13.0	14.1+	13.7	13.5	13.0
13	14.2	14.6	16.2+	15.4	15.0	15.8
14	14.3	14.6	16.9+	17.7	18.5	17.7

+ = Only 9 birds remaining in group