301

VOLUME ___OF___OF SUBMISSION
CGA 329351

STUDY TITLE

AN ACUTE ORAL TOXICITY STUDY WITH THE NORTHERN BOBWHITE

DATA REQUIREMENT

US EPA FIFRA GUIDELINE 71-1(a)

AUTHORS:

STUDY COMPLETION DATE

AUGUST 21, 1995

PERFORMING LABORATORY

WILDLIFE INTERNATIONAL LTD.
8598 COMMERCE DRIVE
EASTON, MARYLAND 21601

LABORATORY STUDY IDENTIFICATION NUMBER

108-375

SPONSOR

CIBA CROP PROTECTION
CIBA-GEIGY CORPORATION
BOX 18300
GREENSBORO, NC 27419-8300

STATEMENT OF <u>NO</u> DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of FIFRA Section 10(d) (1) (A), (B), or (C).

Company: Ciba-Geigy Corporation

Company Agent: [redacted] Ph.D.

Title: [redacted]

Signature:

Date: 10/18/95

These data are the property of Ciba-Geigy Corporation, and as such, are considered to be confidential for all purposes other than compliance with FIFRA Section 10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality which may exist under any other statute or in any other country.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The Good Laboratory Practice Compliance Statement found on Page 4, and signed by the Study Director, is truthful and accurate.

Submitter:

Title:

Signature:

Date: 17 OCT 95

Submitter/Sponsor: Ciba-Geigy Corporation
Crop Protection Division
Post Office Box 18300
Greensboro, NC 27419

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

SPONSOR: Ciba-Geigy Corporation

TITLE: CGA 329,351: An Acute Oral Toxicity Study with the Northern Bobwhite

WILDLIFE INTERNATIONAL LTD. PROJECT NO.: 108-375

STUDY COMPLETION: August 21, 1995

This study was conducted to conform with Good Laboratory Practice Standards as published by the U. S. Environmental Protection Agency, Office of Pesticide Programs in 40 CFR Part 160, 17 August 1989; OECD, ISBN 92-84-12367-9, Paris 1982, and Japan MAFF, 59 NohSan, Notification No. 3850, Agricultural Production Bureau, 10 August 1984 with the following exception:

Analytical methods were not performed as part of this study to determine the concentration, uniformity, and stability of the test substance in the carrier.

STUDY DIRECTOR: _____ DATE 8-21-95

MANAGEMENT:

_____ DATE 8/21/95

Manager, Avian Non-Target/Insect Toxicology

QUALITY ASSURANCE STATEMENT

WILDLIFE INTERNATIONAL LTD. PROJECT NO: 108-375

This study was examined for conformance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency, Office of Pesticide Programs in 40 CFR Part 160, 17 August 1989; OECD, ISBN 92-84-12367-9, Paris 1982; and Japan MAFF, 59 NohSan, Notification No. 3850, Agricultural Production Bureau, 10 August 1984. The dates of all audits and inspections and the dates any findings were reported to the Study Director/Laboratory Management were as follows:

ACTIVITY	DATE CONDUCTED	DATE REPORTED TO: STUDY DIRECTOR	MANAGEMENT
Test Substance preparation, body weights, and dosing	April 28, 1995	April 28, 1995	May 1, 1995
Data and Draft	May 18-19, 1995	May 22, 1995	May 23, 1995
Final Report	August 21, 1995	August 21, 1995	August 21, 1995

5.1.2.e Woo DATE 8-21-95

Quality Assurance Representative

REPORT APPROVAL

SPONSOR: Ciba-Geigy Corporation

TITLE: CGA 329,351: An Acute Oral Toxicity Study with the Northern Bobwhite

WILDLIFE INTERNATIONAL LTD. PROJECT NO.: 108-375

STUDY DIRECTOR:

5.1.2.e Woo _____ 8-21-95
Date

MANAGEMENT:

5.1.2.e Woo _____ 8/24/95
Date

Manager, Avian/Non-Target Insect Toxicology

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SUMMARY

SPONSOR:Ciba-Geigy Corporation

TEST SUBSTANCE:CGA 329,351

WILDLIFE INTERNATIONAL LTD. PROJECT NO: 108-375

STUDY:CGA 329,351: An Acute Oral Toxicity Study with the Northern Bobwhite.

RESULTS: The acute oral LD50 value for northern bobwhite exposed to CGA 329,351 as a single oral dosage was determined to be approximately 981 mg a.i./kg with 95% confidence limits of 720 and 1200 mg a.i./kg. The no mortality dosage was 720 mg a.i./kg. The no observed effect dosage was determined to be 259 mg a.i./kg, based upon the signs of toxicity noted at the 432 mg a.i./kg and higher test dosages.

TEST DATES:Hatch - October 4, 1994
Acclimation - January 12, 1995
Experimental Start - April 28, 1995
Experimental Termination - May 12, 1995

TEST LEVELS:0, 93, 156, 259, 432, 720, 1200 & 2000 mg a.i./kg

TEST ANIMALS:Northern bobwhite (*Colinus virginianus*)

AGE TEST ANIMALS:29 weeks of age at test initiation.

SOURCE TEST ANIMALS: Top Flight Quail Farm
P.O. Box 262
Belvidere, New Jersey 07823

STUDY COMPLETION: August 21, 1995

INTRODUCTION

This study was conducted by Wildlife International Ltd. under contract to Ciba-Geigy Corporation. The test was conducted at the Wildlife International Ltd. avian toxicology facility in Easton, Maryland from April 28, 1995 to May 12, 1995. Raw data and a copy of the final report are filed under Project Number 108-375 in the archives located at Wildlife International Ltd.

OBJECTIVE

The objective of this study was to evaluate the acute toxicity of CGA 329,351 administered to the northern bobwhite as a single oral dose.

MATERIALS AND METHODS

The methods used in conducting this study are based upon procedures specified in Section 71-1 of the Environmental Protection Agency Registration Guidelines Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms (1).

Test Substance

The test substance was received from Ciba-Geigy Corporation on April 11, 1995 and was assigned Wildlife International Ltd. Identification Number WIL-3193 upon receipt. The test substance was a dark brown, viscous liquid, identified on the label as: GLP Test Substance; Product: CGA-329351 Technical; ID No.: FL-950307; ARS-31012; AMT: 500 gram(s); Purity: 96.6%; Batch Code: 501004; Storage Conditions: RT; Expiration: 16-Mar-97. The reported purity of the test substance was 96.6%. The test substance was stored at ambient room temperature.

Treatment Groups

Ten northern bobwhite, five males and five females, were assigned to each of the treatment groups and the control group by indiscriminate draw. The test consisted of a geometric series of seven dosage groups and two control groups. Nominal dosages used in this study were 0, 93, 156, 259, 432, 720, 1200 and 2000 milligrams active ingredient (a.i.) of CGA 329,351 per kilogram of body weight. The dosages were established based upon known

toxicity data. The control group was dosed with diluent only.

Birds were acclimated for 15 weeks prior to test initiation. The birds were fasted for at least 15 hours prior to dosing. At initiation of the test, a single dose of the test substance in diluent was orally intubated directly into the crop or proventriculus of each bird using a stainless steel cannula. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight (Appendix I). The control birds received a corresponding volume of diluent only. All treatment and control birds received a constant dosage volume of 4 milliliters per kilogram of body weight.

Duration of the Study

The primary phases of this study and their durations were:

1. Acclimation - 15 weeks
2. Fasting - At least 15 hours prior to dosing.
3. Dosing - Experimental Start Date - April 28, 1995
4. Post-dosing observation - 14 days

Test Birds

All northern bobwhite (*Colinus virginianus*) were 29 weeks of age and appeared to be in good health at initiation of the test. Bobwhite ranged in weight from 169 to 227 grams at test initiation. The birds were obtained from Top Flight Quail Farm, Belvidere, New Jersey 07823. Test birds were purchased reproductively immature and maintained separately by sex at Wildlife International Ltd. under conditions that would not facilitate reproduction. All birds were from the same hatch, pen-reared and phenotypically indistinguishable from wild birds. Birds were assigned to seven test groups and one control group. Each treatment or control group contained five males and five females. Individual birds within each pen were identified by colored leg bands. All test birds were acclimated to the caging and facilities for 15 weeks prior to the initiation of the test.

Animal Diet

Throughout acclimation and testing all test birds were fed a game bird ration formulated to

Wildlife International Ltd.'s specifications (Appendix II). Water, from the town of Easton public water supply, and feed were provided ad libitum during acclimation and during the test. The birds were fasted for a minimum of 15 hours prior to dosing. The birds received no form of antibiotic medication during the test.

Dosage Preparation

The test substance was dispersed in corn oil (Appendix III). The concentration of the test substance in the diluent was adjusted to provide a constant volume to body weight dosage for all treatment birds. All dosages were adjusted to 100% active ingredient. Therefore all dosages and the LD50 value are reported as milligrams of active ingredient per kilogram of body weight. Nominal dosages used in this study were 0, 93, 156, 259, 432, 720, 1200 and 2000 milligrams a.i. of CGA 329,351 per kilogram of body weight.

Housing and Environmental Conditions

Test birds were housed indoors by dosage group in batteries of pens manufactured by GQF Manufacturing Co. (Model No. 0010). Birds were assigned to pens by indiscriminate draw. Each pen had floor space that measured approximately 78 X 51 cm. Floors were sloped so that ceiling height ranged from approximately 20 to 25 cm. External walls, ceilings and floors were constructed of galvanized wire while side walls were constructed of galvanized sheeting. Each dosage group was assigned two pens. One pen contained five males and the other five females. Each group of birds was identified by pen number. Birds were maintained at ambient room temperature. Average temperature for this study was 22.1°C ±2.0°C (SD) with an average relative humidity of 40% ± 12% (SD). The photoperiod (maintained by a time clock) was 8 eight hours of light per day during acclimation and throughout the test. The light source was fluorescent lights which closely approximate noon-day sunlight (noon-day sun - 4870° Kelvin, Chroma 50 or equivalent - 5000° Kelvin). The birds were exposed to approximately 265 lux of illumination.

Housing and husbandry practices were based on guidelines established by the National Institutes of Health (2).

Observations

During acclimation all birds were observed. Birds exhibiting abnormal behavior or physical injury were not used. Following test initiation until termination all birds were observed at least twice daily. A record was maintained of all mortality, signs of toxicity, and abnormal behavior.

Animal Body Weights/Feed Consumption

Individual body weights were measured at the initiation of the test and on Days 3, 7, and 14. Average feed consumption was determined for each dosage group and the controls for Days 0-3, 4-7, and 8-14. Feed consumption was determined by measuring the change in the weight of the feed presented to the birds over a given period of time. The accuracy of feed consumption values may have been affected by the unavoidable wastage of feed by the birds.

Statistical Calculations

Mortality data were analyzed using the computer program of C.E. Stephan (3). The program was designed to calculate the LD50 value and the 95% confidence interval by probit analysis, moving average method or the binomial probability method (4,5,6). In this study the binomial probability method was used.

RESULTS

Mortalities and Clinical Observations

There were no mortalities in the control group. All birds in the control group were normal in appearance and behavior throughout the test period (Table 1). Additionally, there were no mortalities at the 93, 15, 259, 432 or 720 mg a.i./kg test dosages. There was, however 90% mortality (9 of 10) at the 1200 mg a.i./kg test dosage, and 100% mortality (10 of 10) at the 2000 mg a.i./kg test dosage.

At the 93, 156 and 259 mg a.i./kg test dosages, there were no overt signs of toxicity observed during the test period. One bird at the 259 mg a.i./kg test dosage was noted with a

neck curl on Day 0, a condition that was considered to be incidental, and not related to treatment. Otherwise, all birds at these test dosages were considered normal in appearance and behavior for the duration of the test.

Signs of toxicity at the 432 mg a.i./kg test dosage were first observed approximately two hours and twenty minutes after dosing, and continued to be exhibited through the remainder of Day 0. Signs of toxicity were exhibited by up to 6 birds in this treatment group, and included reduced reaction to external stimuli (sound and movement), loss of coordination and shallow and rapid respiration. On the morning of Day 1, all birds had recovered and were normal in appearance and behavior for the remainder of the test.

At the 720 mg a.i./kg test dosage, signs of toxicity were first noted approximately one and a quarter hours after dosing, and continued to be exhibited throughout Day 0. By the morning of Day 1, all birds had recovered and were considered normal in appearance and behavior throughout the remainder of the test.

Birds at the 1200 mg a.i./kg test dosage first exhibited signs of toxicity approximately fifteen minutes after dosing. Signs of toxicity persisted in all birds at this dosage throughout Day 0, and on the morning of Day 1, nine birds were found dead. The remaining bird at this dosage continued to exhibit signs of toxicity through the morning of Day 4. By the afternoon of Day 4, the single surviving bird had recovered and was considered normal in appearance and behavior for the remainder of the test.

At the 2000 mg a.i./kg test dosage, birds exhibited signs of toxicity immediately after dosing, and continued to do so until mortality occurred. Approximately two hours after dosing, a single mortality was noted, and by the end of Day 0, a second bird had died. On the morning of Day 1, seven birds were found dead. The remaining bird at this dosage continued to exhibit signs of toxicity until its death on Day 2.

Signs of toxicity characteristic of intoxication with CGA-329,351 were reduced reaction to

external stimuli (sound and movement), wing droop, loss of coordination, lethargy, depression, a ruffled appearance, lower limb weakness, panting, loss of righting reflex, prostrate posture, shallow and rapid respiration and coma.

Body Weight and Feed Consumption Measurements

When compared to the control group, there was no effect upon body weight among birds at the 93, 156, or 259 mg a.i./kg test dosages (Table 2). While there was no effect upon body weight among males at the 432 mg a.i./kg test dosage, there was a slight loss in body weight among females at the 432 mg a.i./kg test dosage during the period from Day 0 to Day 3. During the same time period males at the 720 mg a.i./kg test dosage showed no gain in mean body weight and females at the 720 mg a.i./kg test dosage exhibited a loss in body weight. The remaining female at the 1200 mg a.i./kg test dosage also showed a loss in body weight during the period from Day 0 to Day 3. Body weight changes and feed consumption measurements for males at the 1200 mg a.i./kg test dosage and all birds at the 2000 mg a.i./kg test dosages could not be determined due to total mortality by Day 3 of the test.

A slight reduction in feed consumption was noted for females at the 432 mg a.i./kg test dosage during the period from Day 0 to Day 3 (Table 3). A more marked reduction in feed consumption was observed for the remaining female at the 1200 mg a.i./kg test dosage during the period from Day 0 to Day 3, with a compensatory increase in feed consumption exhibited during the period from Day 4 to Day 7.

CONCLUSION

The acute oral LD50 value for northern bobwhite exposed to CGA 329,351 as a single oral dose was determined to be approximately 981 mg a.i./kg, with 95% confidence limits of 720 to 1200 mg a.i./kg. The no mortality dosage was 720 mg a.i./kg. The no observed effect dosage was determined to be 259 mg a.i./kg, based upon the clinical signs of toxicity noted at the 432 mg a.i./kg and higher test dosages.

REFERENCES

1 Environmental Protection Agency. 1982 (October). Pesticide Assessment Guidelines, FIFRA Subdivision E. Hazard Evaluation: Wildlife and Aquatic Organisms, Subsection 71-1. Office of Pesticide Programs. Washington, D.C. 86 pp.

2 National Institutes of Health. 1985. Guide for the care and use of laboratory animals. NIH Pub. No. 86-23. 83 pp.

3 Stephan, C. E. 1978. U.S. EPA, Environmental Research Laboratory, Duluth, Minnesota. Personal Communication.

4 Finney, D. J. 1971. Statistical Methods in Biological Assay, 2nd edition, Griffin Press, London.

5 Thompson, W. R. 1947. Bacteriological Reviews. Vol II, 2:115-145.

6 Stephan, C. E. 1977. Methods for Calculating an LC50. Aquatic Toxicology and Hazard Evaluations, Amer. Soc. Test Mat., Pub. No. STP 634:65-84.

TABLE 1

Cumulative Mortality from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351

Experimental Group		Number Dead/Number Exposed															
		Day of Study															
(mg a.i./kg)	Sex	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Control	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
93	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
156	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
259	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
432	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
720	M	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	
	F	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/10
1200	M	0/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	
	F	0/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	4/5	9/10
2000	M	1/5	4/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	
	F	1/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	10/10

The LD50 value was determined to be approximately 981 mg a.i./kg, with a 95% confidence interval of 720 mg a.i./kg to 1200 mg a.i./kg.

TABLE 2

Mean Body Weight from a Northern Bobwhite Acute Oral
Toxicity Study with CGA 329,351

Experimental Group		Mean Body Weights in Grams ± standard deviation*							
(mg a.i./kg)	Sex	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Control	M	198±18	2±4	200±17	-2±2	198±17	-2±2	196±17	-2±3
	F	187±13	8±2	195±12	-4±2	191±12	-2±2	191±10	4±5
93	M	196±14	3±4	199±11	-4±1	195±11	-1±2	194±13	-3±3
	F	192±18	4±2	196±17	-2±3	194±16	0±2	193±16	1±6
156	M	195±13	4±3	199±12	-3±3	196±13	-1±3	195±12	0±2
	F	204±13	4±3	207±12	-3±3	205±11	0±1	205±10	1±3
259	M	193±17	5±1	197±17	-3±1	195±18	0±1	195±17	2±2
	F	194±13	3±4	197±12	-5±2	192±14	1±3	193±13	-1±5
432	M	199± 9	3±4	201±11	-6±1	196±12	2±4	198±14	-1±6
	F	198±16	-1±6	196±14	-1±5	196±14	0±3	196±15	-2±2
720	M	205± 9	0±6	206±10	0±2	206±10	3±3	209± 9	4±7
	F	196±17	-1±2	195±17	-2±2	193±16	0±2	193±15	-3±3
1200	M	195±16	-	-	-	-	-	-	-
	F	203±11	-1	188	-3	185	8	193	4
2000	M	188±10	-	-	-	-	-	-	-
	F	196± 8	-	-	-	-	-	-	-

* The means for body weights and body weight changes are calculated and rounded separately.
(-) = Total mortality.

TABLE 3

Feed Consumption from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351

Experimental Group (mg a.i./kg)	Sex	Estimated Mean Feed Consumption Grams/Bird/Day		
		Days 0-3	Days 4-7	Days 8-14
Control	M	12	14	13
	F	23	24	16
93	M	22	20	18
	F	13	15	14
156	M	14	15	15
	F	21	19	17
259	M	21	24	16
	F	27	27	20
432	M	18	23	17
	F	11	21	18
720	M	19	26	17
	F	23	28	18
1200	M	-	-	-
	F	8	61	19
2000	M	-	-	-
	F	-	-	-

(-) = Total mortality.

APPENDIX I
Dosing Regime from a Northern Bobwhite Acute Oral
Toxicity Study with CGA 329,351

The following stock solutions were prepared:
Stock solution #1 1.2034 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #2 2.0184 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #3 3.3514 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #4 5.5902 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #5 9.3169 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #6 15.5280 g CGA 329,351 + sufficient diluent to obtain 50 ml.
Stock solution #7 25.8799 g CGA 329,351 + sufficient diluent to obtain 50 ml.
The birds were individually weighed. Calculated dosages were as follows*:

Experimental Group (mg a.i./kg)		Males					Females				
		1	2	3	4	5	6	7	8	9	10
0	Weight of Bird (g)	186	184	227	203	190	194	178	200	169	194
	Volume of Diluent (ml)	0.744	0.736	0.908	0.812	0.760	0.776	0.712	0.800	0.676	0.776
93	Weight of Bird (g)	220	189	194	194	185	197	216	198	176	173
	Volume of Stock Solution #1 (ml)	0.880	0.756	0.776	0.776	0.740	0.788	0.864	0.792	0.704	0.692
	Amount of Test Substance (g)	0.0212	0.0182	0.0187	0.0187	0.0178	0.0190	0.0208	0.0191	0.0169	0.0167
156	Weight of Bird	201	178	192	191	214	185	209	197	214	214
	Volume of Stock Solution #2 (ml)	0.804	0.712	0.768	0.764	0.856	0.740	0.836	0.788	0.856	0.856
	Amount of Test Substance (g)	0.0325	0.0287	0.0310	0.0308	0.0346	0.0299	0.0337	0.0318	0.0346	0.0346

* The actual dose administered was accurate to the nearest 0.01 ml.

APPENDIX I
Dosing Regime from a Northern Bobwhite Acute Oral
Toxicity Study with CGA 329,351
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Experimental Group (mg a.i./kg)		Males					Females				
		1	2	3	4	5	6	7	8	9	10
259	Weight of Bird (g)	177	197	176	218	195	215	183	195	193	186
	Volume of Stock Solution #3 (g)	0.708	0.788	0.704	0.872	0.780	0.860	0.732	0.780	0.772	0.744
	Amount of Test Substance (g)	0.0475	0.0528	0.0472	0.0584	0.0523	0.0576	0.0491	0.0523	0.0517	0.0499
432	Weight of Bird (g)	203	212	196	187	195	217	188	177	209	198
	Volume of Stock Solution #4 (ml)	0.812	0.848	0.784	0.748	0.780	0.868	0.752	0.708	0.836	0.792
	Amount of Test Substance (g)	0.0908	0.0948	0.0877	0.0836	0.0872	0.0970	0.0841	0.0792	0.0935	0.0885
720	Weight of Bird	193	210	203	217	204	200	192	222	192	174
	Volume of Stock Solution #5 (ml)	0.772	0.840	0.812	0.868	0.816	0.800	0.768	0.888	0.768	0.696
	Amount of Test Substance (g)	0.1439	0.1565	0.1513	0.1617	0.1521	0.1491	0.1431	0.1655	0.1431	0.1297

APPENDIX I
Dosing Regime from a Northern Bobwhite Acute Oral
Toxicity Study with CGA 329,351
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Experimental Group (mg a.i./kg)		Males 1	Males 2	Males 3	Males 4	Males 5	Females 6	Females 7	Females 8	Females 9	Females 10
1200	Weight of Bird (g)	216	180	192	182	207	212	213	196	207	189
	Volume of Stock Solution # 6 (g)	0.864	0.720	0.768	0.728	0.828	0.848	0.852	0.784	0.828	0.756
	Amount of Test Substance (g)	0.2683	0.2236	0.2385	0.2261	0.2571	0.2634	0.2646	0.2435	0.2571	0.2348
2000	Weight of Bird (g)	183	173	192	199	192	201	206	195	193	185
	Volume of Stock Solution #7 (ml)	0.732	0.692	0.768	0.796	0.768	0.804	0.824	0.780	0.772	0.740
	Amount of Test Substance (g)	0.3789	0.3582	0.3975	0.4120	0.3975	0.4161	0.4265	0.4037	0.3996	0.3830

APPENDIX II

DIET FORMULATION

WILDLIFE INTERNATIONAL LTD. GAME BIRD RATION[1]

INGREDIENTS	PERCENT (%)
Fine Corn Meal	37.45
Ground Oats	5.00
Alfalfa Meal Dehydrated, 17% Protein	3.00
CDP (Phosphate Source)	0.70
Dried Whey	2.50
Fish Meal, 60% Protein	6.00
Meat Poultry Blend, 58% Protein	4.00
Wheat Midds	5.00
Soy Bean Meal, 48% Protein	34.80
Salt Iodized	0.10
Ground Limestone	0.60
GL Ferm (Fermatco)[2]	0.25
Methionine Premix	0.20
Vitamin and Mineral Premix (see below)	0.40
Total	100.00

VITAMIN AND MINERAL PREMIX	AMOUNT ADDED PER TON
Vitamin D_3	2,000,000 I.C.U.
Vitamin A	7,000,000 I.U.
Riboflavin	6 grams
Niacin	40 grams
Pantothenic Acid	10 grams
Vitamin B_{12}	8 mgs
Folic Acid	600 mgs
Biotin	64 mgs
Pyridoxine	1.2 grams
Thiamine	1.2 grams
Vitamin E	20,000 I.U.
Vitamin K (Menadione Dimethylpyrimidinol Bisulfite)	5.8 grams
Manganese	102 grams
Zinc	47 grams
Copper	6.8 grams
Iodine	1.5 grams
Iron	51 grams
Selenium	182 mgs

[1] The guaranteed analysis is a minimum of 27% protein, a minimum of 2.5% crude fat and a maximum of 5% crude fiber.

[2] Fermentation By-Products (Source of Unidentified Growth Factors).

APPENDIX III

DOSING STOCK PREPARATION

Weight and volume of constituents used to prepare dosing stocks:

Dosage (mg a.i./kg of body weight)	Test Substance (g)	Final Volume in Corn Oil (ml)
0	--	50
93	1.2034	50
156	2.0184	50
259	3.3514	50
432	5.5902	50
720	9.3169	50
1200	15.5280	50
2000	25.8799	50

The dosing stocks were prepared as follows:

- For each dosage the test substance was weighed in a tared, labeled 250 ml beaker.
- Sufficient corn oil was added to the test substance to bring the final volume to 50 ml.
- Each test mixture was blended with a glass stir rod for approximately 30 seconds, placed on a magnetic stir plate and stirred continuously during the dosing procedure.
- The negative control birds were dosed with corn oil only.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	186	0	186	-3	183	-3	180	-6
0	2	184	6	190	-4	186	-3	183	-1
	3	227	-1	226	-3	223	-1	222	-5
	4	203	6	209	-3	206	-3	203	0
	5	190	-2	188	2	190	2	192	2
	Mean	198	2	200	-2	198	-2	196	-2
	SD	± 18	± 4	± 17	± 2	± 17	± 2	± 17	± 3

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	194	8	202	-7	195	-3	192	-2
0	7	178	6	184	-3	181	-1	180	2
	8	200	8	208	-3	205	-3	202	2
	9	169	12	181	-3	178	2	180	11
	10	194	7	201	-3	198	1	199	5
	Mean	187	8	195	-4	191	-1	191	4
	SD	± 13	± 2	± 12	± 2	± 12	± 2	± 10	± 5

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351 (continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	220	-3	217	-5	212	3	215	-5
93	2	189	3	192	-5	187	-3	184	-5
	3	194	6	200	-3	197	-1	196	2
	4	194	5	199	-4	195	-3	192	-2
	5	185	4	189	-5	184	-2	182	-3
	Mean	196	3	199	-4	195	-1	194	-3
	SD	± 14	± 4	± 11	± 1	± 11	± 2	± 13	± 3
Females	6	197	5	202	-5	197	-2	195	-2
93	7	216	0	216	-1	215	-1	214	-2
	8	198	5	203	-2	201	0	201	3
	9	176	3	179	-4	175	-2	173	-3
	10	173	5	178	2	180	4	184	11
	Mean	192	4	196	-2	194	0	193	1
	SD	± 18	± 2	± 17	± 3	± 16	± 2	± 16	± 6

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351 (continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	201	1	202	0	202	1	203	2
156	2	178	8	186	-4	182	-2	180	2
	3	192	4	196	-7	189	2	191	-1
	4	191	3	194	-3	191	-2	189	-2
	5	214	4	218	-2	216	-5	211	-3
	Mean	195	4	199	-3	196	-1	195	0
	SD	± 13	± 3	± 12	± 3	± 13	± 3	± 12	± 2

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	185	3	188	-1	187	2	189	4
156	7	209	3	212	-5	207	0	207	-2
	8	197	7	204	-2	202	-2	200	3
	9	214	6	220	-6	214	-1	213	-1
	10	214	-1	213	1	214	0	214	0
	Mean	204	4	207	-3	205	0	205	1
	SD	± 13	± 3	± 12	± 3	± 11	± 1	± 10	± 3

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351
(continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	177	4	181	-3	178	1	179	2
259	2	197	6	203	-2	201	-1	200	3
	3	176	4	180	-3	177	0	177	1
	4	218	4	222	-3	219	-1	218	0
	5	195	6	201	-2	199	0	199	4
	Mean	193	5	197	-3	195	0	195	2
	SD	± 17	± 1	± 17	± 1	± 18	± 1	± 17	± 2

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	215	1	216	-3	213	-2	211	-4
259	7	183	7	190	-9	181	0	181	-2
	8	195	8	203	-4	199	2	201	6
	9	193	1	194	-6	188	-2	186	-7
	10	186	-2	184	-4	180	6	186	0
	Mean	194	3	197	-5	192	1	193	-1
	SD	± 13	± 4	± 12	± 2	± 14	± 3	± 13	± 5

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351
(continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	203	-2	201	-8	193	3	196	-7
432	2	212	7	219	-4	215	5	220	8
	3	196	6	202	-6	196	2	198	2
	4	187	1	188	-6	182	4	186	-1
	5	195	2	197	-5	192	-4	188	-7
	Mean	199	3	201	-6	196	2	198	-1
	SD	± 9	± 4	± 11	± 1	± 12	± 4	± 14	± 6
Females	6	217	0	217	-3	214	-2	212	-5
432	7	188	-5	183	7	190	0	190	2
	8	177	6	183	-6	177	-2	175	-2
	9	209	-9	200	2	202	5	207	-2
	10	198	1	199	-3	196	0	196	-2
	Mean	198	-1	196	-1	196	0	196	-2
	SD	± 16	± 6	± 14	± 5	± 14	± 3	± 15	± 2

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351
(continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	193	1	194	-1	193	3	196	3
720	2	210	-1	209	2	211	0	211	1
	3	203	9	212	1	213	5	218	15
	4	217	1	218	-3	215	1	216	-1
	5	204	-8	196	0	196	8	204	0
	Mean	205	0	206	0	206	3	209	4
	SD	± 9	± 6	± 10	± 2	± 10	± 3	± 9	± 7

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	200	-1	199	-2	197	2	199	-1
720	7	192	-4	188	0	188	1	189	-3
	8	222	-1	221	-4	217	-3	214	-8
	9	192	0	192	-1	191	0	191	-1
	10	174	1	175	-1	174	-2	172	-2
	Mean	196	-1	195	-2	193	0	193	-3
	SD	± 17	± 2	± 17	± 2	± 16	± 2	± 15	± 3

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite Acute Oral Toxicity Study with CGA 329,351
(continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	216	-	-	-	-	-	-	-
1200	2	180	-	-	-	-	-	-	-
	3	192	-	-	-	-	-	-	-
	4	182	-	-	-	-	-	-	-
	5	207	-	-	-	-	-	-	-
	Mean	195	-	-	-	-	-	-	-
	SD	± 16	-	-	-	-	-	-	-
Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	212	-	-	-	-	-	-	-
1200	7	213	-	-	-	-	-	-	-
	8	196	-	-	-	-	-	-	-
	9	207	-	-	-	-	-	-	-
	10	189	-1	188	-3	185	8	193	4
	Mean	203	-	188	-3	185	8	193	4
	SD	± 11	-						

(-) = Total mortality.

APPENDIX IV

Individual Body Weights (g) from a Northern Bobwhite
Acute Oral Toxicity Study with CGA 329,351
(continued)

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Males	1	183	-	-	-	-	-	-	-
2000	2	173	-	-	-	-	-	-	-
	3	192	-	-	-	-	-	-	-
	4	199	-	-	-	-	-	-	-
	5	192	-	-	-	-	-	-	-
	Mean	188	-	-	-	-	-	-	-
	SD	± 10	-	-	-	-	-	-	-

Experimental Group (mg a.i./kg)	Replicate	Day 0	Change	Day 3	Change	Day 7	Change	Day 14	Total Change
Females	6	201	-	-	-	-	-	-	-
2000	7	206	-	-	-	-	-	-	-
	8	195	-	-	-	-	-	-	-
	9	193	-	-	-	-	-	-	-
	10	185	-	-	-	-	-	-	-
	Mean	196	-	-	-	-	-	-	-
	SD	± 8	-	-	-	-	-	-	-

(-) = Total mortality.

APPENDIX V

CHANGES TO PROTOCOL

The study was conducted in accordance with the approved Protocol with the following changes:

- The experimental start date, experimental termination date, study room, test concentrations, test substance number and receipt date were amended to the protocol.
- Study Director responsibilities were reassigned.

The above changes to the approved Protocol did not adversely affect the results of this study.

APPENDIX VI

PERSONNEL INVOLVED IN STUDY

The following key personnel were involved in the conduct or management of this study:

(1) 5.1.2.e Woo, Wildlife Toxicologist
(2) 5.1.2.e Woo Avian/Non-Target Insect Toxicology
(3) 5.1.2.e Woo Biologist
(4) 5.1.2.e Woo Research Biologist
(5) 5.1.2.e Woo Biologist