(9-15-92)

MRID No. 418695-05

DATA EVALUATION RECORD

1. **CHEMICAL:** Cimectacarb.
Shaughnessey Number: 112602.

2. **TEST MATERIAL:** CGA 163935; Batch No. P705002; 96.6% purity; a brown solid/liquid.

3. **STUDY TYPE:** Avian Reproduction Study.
Species Tested: Bobwhite quail (*Colinus virginianus*).

4. **CITATION:** Hakin, B. 1991. The effects of dietary inclusion of CGA 163935 on reproduction in the bobwhite quail. Study performed by Huntingdon Research Centre, Ltd., Huntingdon, Cambridgeshire, UK. HRC report No. CBG 475/9085. Submitted by Ciba-Geigy Corporation, Greensboro, NC. EPA MRID No. 418695-05.

5. **REVIEWED BY:**

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Signature: P. Kosalwat for CFP
Date: 9/1/92

6. **APPROVED BY:**

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Signature: P. Kosalwat
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Supervisor, EEB/EFED
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Date:

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an avian reproduction study. Cimectacarb nominal dietary concentrations of 65 ppm, 200 ppm, and 600 ppm had no adverse effects upon behavior, food consumption, ~~or reproduction~~ of bobwhite quail during the 22-week exposure period. The NOEC was ~~600~~ 200 ppm based on effects to number of eggs

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Bobwhite quail (*Colinus virginianus*) were purchased from a supplier in Cambridgeshire, England. The birds were acclimated to the facilities for 7 days prior to initiation of the test. The birds were approximately 8 months of age at test initiation, and were identified by individual wing tags.

B. **Dose/Diet Preparation/Food Consumption:** Test diets were prepared by mixing Cimectacarb directly into the feed without the use of a vehicle. The control diet consisted of basal feed only. The control diet and three test concentrations [65, 200, and 600 parts per million (ppm)] were prepared weekly. After preparation, the diets were stored in closed paper sacks at room temperature until fed to the birds. Birds were given untreated diet during the one-week pre-treatment period. Each of the four groups of adult birds was then fed the appropriate diet for 22 weeks. Dietary concentrations were not adjusted for purity of the test substance.

Basal diet for adult birds was quail layer diet manufactured by Special Diets Services, Witham, Essex. The composition of the diet was presented in the report. Food and water were supplied *ad libitum* during acclimation and during the test. Homogeneity and stability samples were taken from a trial mix of treatment diets (50 ppm and 1000 ppm). Stability of the test chemical was determined in the trial mix by analyzing subsamples stored for 0, 4, 9, and 14 days at room temperature in the animal room. Samples were taken from the test diets during weeks 1, 12, and 21 for confirmation of dietary concentrations of Cimectacarb. Analyses were performed by Huntingdon Research Centre (HRC) Department of Analytical Chemistry using high performance liquid chromatography. Group food consumption was determined weekly throughout the study.

C. **Design:** The birds were distributed into four groups using a randomized block design as follows:

Cimectacarb Nominal Concentration	Number of Pens	Birds Per Pen	
		Males	Females
Control (0 ppm)	20	1	1
65 ppm	20	1	1
200 ppm	20	1	1
600 ppm	20	1	1

In addition, 4 replicates per treatment were maintained as replacements if needed prior to egg production.

D. **Pen Facilities:** Adult birds were housed indoors in pens constructed of polythene-coated steel wire. Pens measured approximately 30 cm x 40 cm x 25 cm. The mean daily maximum and minimum temperatures in the adult study rooms were 24°C and 20°C, respectively. The mean relative humidity was 78%.

The photoperiod during acclimation and during the first 6 weeks of the study was 7 hours of light per day. At the beginning of week 7, the lighting was increased to 16 hours per day, and was maintained at that level throughout the remainder of the study.

E. **Adult Observations/Gross Pathology:** Observations were made daily throughout the study for signs of toxicity or abnormal behavior. Gross pathological examinations were conducted on all birds that died during the study, as well as on selected birds that survived until study termination. Adult birds were individually weighed on the following days: -7, 1, 15, 29, 43, 57, and 155.

F. **Eggs/Eggshell Thickness:** Eggs were collected daily during the 12-week production period, and stored at 16°C. Following each 7-day collection period, the eggs were candled and any cracked eggs were recorded and discarded. All normal eggs (except those used for eggshell thickness measurements) were placed in an incubator set to operate at 37.7°C and 55% relative humidity. Eggs were turned automatically every hour while in the incubator. Eggs were candled on day 11 to determine early embryonic death and on day 18 to determine late embryonic death. After 21 days of incubation, the eggs were placed in a hatcher maintained at 37.5°C. All eggs collected the first day of even-numbered weeks were used for egg shell thickness measurements. The thickness of the shells was measured at 4 points around the circumference using a micrometer calibrated to 0.01 mm.

G. **Hatchlings:** Upon removal from the hatcher, chicks were individually weighed and identified by leg bands. The hatchlings were housed in wooden pens with concrete floors. The mean daily minimum and maximum temperatures were 25°C and 29°C, respectively. The mean relative humidity was 60%. Hatchlings were fed untreated diet (HRC chick meal), and were observed daily. Food and water were available *ad libitum*. At 14 days of age, individual body weights were measured. Gross pathological examinations were conducted on chicks that died during the 14-day observation period.

H. **Statistics:** Analysis of variance was used to analyze adult food consumption, adult body weight, number of eggs laid, egg weight, % eggs damaged, egg shell thickness, infertile eggs/eggs set, early embryonic deaths/fertile eggs, late embryonic deaths/fertile eggs, eggs hatched/day 18 viable eggs, eggs hatched/fertile eggs, 14-day survivors/eggs hatched, offspring body weight at hatching and 14 days later, number of live 3-week embryos/fertile eggs, and number of 14-day survivors/adult female. Williams' test was used to compare individual treatment groups with the control.

12. **REPORTED RESULTS:**

A. **Diet Analysis:** All mean measured concentrations of Cimectacarb taken from dietary samples were within 5% of nominal values (Addendum, Table 1, attached). Analyses of samples taken from the trial mix showed that Cimectacarb was homogeneously blended and was stable throughout the 14-day storage period (Addendum, Tables 3 and 4, attached).

B. **Adult Mortality and Behavioral Reactions:** Adult mortality during the study was as follows: 3 control birds, 5 at 65 ppm, 3 at 200 ppm, and 2 at 600 ppm. All but one of the above mortalities occurred after the first day of week 11 (the beginning of the egg production period); those birds were not replaced. Nine birds were observed limping during the study (three in control group, and two birds from each of the treatment groups). In the 65 ppm treatment group, one bird was thin, subdued and unsteady, and another bird was unsteady. At 200 ppm, one bird had a cut wing tip, and another bird had cut feet. At the highest treatment level (600 ppm), one bird had a closed eye and another was subdued. Individual adult bird health observations are given in Appendix 5 (attached).

The only abnormalities observed during gross pathological examinations were in 11 of the birds that died during the study. Other birds which died or were sacrificed during the study showed no abnormalities. In the control group, one bird had swollen and cut feet, and another was very thin. In the 65 ppm treatment group, four birds were reported to be thin. One of these birds also had a liver coated with white gelatinous material. Another bird in this group had cuts on both feet. Abnormalities reported in the 200 ppm group were two thin birds, and one bird with blood around the vent. In the 600 ppm group, the only observed abnormality was one thin bird with cut feet.

C. **Adult Body Weight and Food Consumption:** There was no evidence of any treatment-related effect on body weight. When compared to the control group, there were no significant differences in body weight at any concentration tested (Table 4, attached). Food consumption was similar in all groups, with no evidence of treatment-related effects (Tables 5 and 6, attached).

D. **Reproduction:** When compared to the control group, the test material did not exert significant adverse effects on any reproductive parameters measured (Tables 1a, 1b, 10, 11, and 13, attached) except eggs ~~laid~~ set at which the 600 ppm dose showed significantly less eggs set than controls. There were significantly fewer late embryonic deaths in the highest treatment group (600 ppm) than in controls. The incidence of late embryonic death at Day 18 was generally low (Table 12, attached). A greater number of chicks hatched in the 200 and 600 ppm groups than in controls, when considered as a proportion of eggs set on Day 18 or as a proportion of fertile eggs (Table 14, attached).

The percentage of fertile eggs which were classified as dead in the shell was lower in all treatment groups than in the controls (Table 14, attached).

E. **Egg Shell Thickness:** Mean egg shell thickness was similar in all groups, with no evidence of any difference between treatment groups (Table 11, attached).

F. **Offspring:** Chick bodyweights at hatch and at 14 days of age were similar in all groups, with no statistically significant differences (Table 15, attached).

The percentage of chicks surviving to 14 days was similar in all groups with no significant treatment-related effects detected (Table 1b, attached). The percentage of 14-day survivors per number of eggs set and number of 14-day survivors per female bird was also similar in all groups. There were no statistically significant differences in treatment groups compared with controls.

Gross pathological examinations of chicks found dead or sacrificed at 14 days of age during the test period revealed no abnormal findings.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** "Under the conditions of this test, there was no evidence that dietary administration of CGA 163935 to the Bobwhite quail at dose levels of 65, 200, and 600 ppm produced any significant adverse effects on the reproductive capacity of the birds. There was a significantly lower proportion of late embryonic deaths in Group D (CGA 163935 at 600 ppm) and the proportion of chicks hatching was also significantly higher in Group D and Group C (CGA 163935 at 200 ppm) than in the controls. No other significant effects were observed."

The report stated that study was conducted in conformance with Good Laboratory Practice regulations. The GLP statement was signed by the HRC Study Director and the Laboratory Manager. Quality assurance audits were conducted during the study and the final report was signed by the Systems Compliance Auditor of Huntingdon Research Centre Ltd.

14. **Reviewer's Discussion and Interpretation of the Study:**

A. **Test Procedure:** The test procedures were in accordance with Subdivision E - Hazard Evaluation: Wildlife and Aquatic Organisms, ASTM, and SEP guidelines except for the following deviations:

The acclimation period was one week; a two- to six-week period is recommended.

A solvent (test vehicle) was not used in the preparation of the test diets. However, analysis of the trial mix of treatment diets showed that the test material was homogeneously blended in the test diets.

The mean relative humidity in the adult study rooms was 78%; the recommended relative humidity is 55%.

B. **Statistical Analysis:** Statistical analyses of reproductive parameters were performed by the reviewer (attached) using analysis of variance (ANOVA) following square-root transformation of the count data and arcsine square-root transformation of the ratio data. The comparisons between the control and each treatment group were made using multiple comparison tests. The computer program used is based on the EEB Birdall program, with an exception that the count data were square-root transformed before the ANOVA.

Analyses of reproductive parameters confirmed the results reported by the authors.

C. **Discussion/Results:** Chemical analyses of food samples taken during weeks 1, 12, and 21 show that measured concentrations of Cimectacarb were very similar to nominal concentrations; all measured values were within 5% of nominal values. Homogeneity and stability of the test material in the diet were evaluated in a trial mix, rather than in the actual treatment diets. However, judging from the data using the trial mix, Cimectacarb was stable in the diet, and the method of preparation achieved a homogeneous mix.

The percentage of cracked eggs in the control group (10%) is unusually high (Table 9, attached). Typically, 0.5% to 2.0% cracked eggs may be expected for the bobwhite quail (Technical Support Document to Subdivision E - Hazard Evaluation: Wildlife and Aquatic Organisms). The authors provided no explanation for this high value. Statistical analysis of this parameter showed no significant differences between groups. However, the high value in the control group may have confounded the analysis. Only one treatment group (600 ppm) had a higher proportion of cracked eggs (12%) than the control. However, since no other adverse effects were observed, this 2% increase was probably not due to treatment effects. Therefore, the NOEC for this study is determined to be 600 ppm, the highest concentration tested.

The study is scientifically sound and fulfills the guideline requirements for an avian reproduction study.

D. **Adequacy of the Study:**

(1) **Classification:** Core.

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

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

15. **COMPLETION OF ONE-LINER:** Yes; July 16, 1992.

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