(9-15-92)

MRID No. 418695-04

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: Mallard duck (*Anas platyrhynchos*).

4. **CITATION:** Hakin, B. 1991. The effects of dietary inclusion of CGA 163935 on reproduction in the mallard duck. Study performed by Huntingdon Research Centre Ltd., Huntingdon, Cambridgeshire, UK. HRC report No. CBG 475/90108. Submitted by Ciba-Geiby Corporation. EPA MRID No. 418695-04.

5. **REVIEWED BY:**

Carolyn F. Poppell, Sc.M.
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Signature: P. Kosalwat for CFP
Date: 9/1/92

6. **APPROVED BY:**

Pim Kosalwat, Ph.D.
Senior Scientist
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Signature: P. Kosalwat
Date: 9/1/92

Henry T. Craven, M.S.
Supervisor, EEB/EFED
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Signature: Brian Montague EEB 9/9/92
Date: Henry T. Craven 9/15/9

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an avian reproduction study. Cimectacarb nominal dietary concentrations of 65, 200, and 600 ppm had no adverse effects upon behavior, body weight, food consumption, or reproduction of mallard ducks during the 23-week exposure period. The NOEC was 600 ppm.

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Mallard ducks (*Anas platyrhynchos*) used in the study were purchased from the County Game Farms, Home Farm, Hothfield, Ashford, Kent. The birds were acclimated to the facilities for 7 days prior to initiation of the test. The birds were approximately 6½ 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 ppm) were prepared weekly. After preparation, the diets were stored in closed paper sacks at room temperature until fed to the birds. The birds were given untreated diet during the one-week pre-treatment period. Each of the four groups of adult birds was fed the appropriate diet for 23 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 4, 9, and 14 days at room temperature in the animal room. Samples were taken from the test diets during weeks 2, 13, and 22 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)	6	2	5
65 ppm	6	2	5
200 ppm	6	2	5
600 ppm	6	2	5

In addition, 6 birds per group were maintained as replacements if needed prior to egg production.

D. **Pen Facilities:** Adult birds were housed indoors in pens constructed of galvanized steel. Pens measured 1.48 m x 0.73 m. The pens had solid sides and wire mesh floors. During egg production, the floors were covered with plastic "pillow" matting to minimize egg damage. The mean daily maximum and minimum temperatures in the adult study rooms were 22°C and 18-19°C, respectively. The mean relative humidity ranged from 76% to 80%.

The photoperiod during acclimation and during the first 8 weeks of the study was not specified. At the end of week 8, 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, and on selected birds that survived until study termination. Adult birds were individually weighed on the following days: -7, 1, 15, 29, 43, 57, and 162.

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 14 to determine early embryonic death and on day 21 to determine late embryonic death. After 24 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, ducklings were individually weighed and identified by leg bands. The hatchlings were housed in pens measuring 1.5 m x 1.25 m. The mean daily minimum and maximum temperatures were 25°C and 27°C, respectively. The mean relative humidity was 76%. 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 ducklings 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 21 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 each treatment group 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, 3 at 65 ppm, 3 at 200 ppm, and 4 at 600 ppm. Only two of the above mortalities occurred after week 11 (the egg production period); those birds were not replaced. Three of the other 12 mortalities were replaced by birds from the group of spare birds maintained on the same diet as the replaced birds.

Abnormal behavioral observations were noted in nine birds (Appendix 5, attached). Two birds in the control

group were bullied, and one was unable to stand on day 69. At the 65 and 200 ppm treatment levels, two birds in each group were subdued and bullied, with wounds from pecking. Three birds at the highest treatment level (600 ppm) were bullied, and two showed signs of pecking.

Gross pathological examinations of birds that died during the study revealed 11 birds with abnormalities. These included two birds with missing feathers (control and 600 ppm); five birds with signs of pecking (one at 65 ppm, two at 200 ppm, and two at 600 ppm); one bird with white spots on the liver (65 ppm); one bird with a fluid-filled body cavity and hardened liver (200 ppm); and one with intestines containing blood (600 ppm). One control bird was sacrificed during the study because of an inability to stand.

Gross pathological examinations of birds surviving to terminal sacrifice revealed abnormalities in 7 birds. These consisted of a kidney absent in one bird (control); a fluid-filled body cavity in one bird (control); a mass attached to the gizzard of one bird (65 ppm); one bird with a fluid-filled body cavity and hardened liver (200 ppm); one bird with a hardened liver (200 ppm); and two birds with fluid-filled sacs (200 and 600 ppm).

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

D. **Reproduction:** For all reproductive parameters measured, there were no significant differences between any test concentration and the control (Tables 1a, 1b, 10, and 12, attached).

E. **Egg Shell Thickness:** When compared to the control group, there were no significant differences in egg shell thickness at any concentration (Table 11, attached).

F. **Offspring:** There were neither significant differences in offspring bodyweights among groups for weight at hatch, nor for weight at 14 days (Table 15, attached). The number of ducklings surviving to 14 days was similar in all groups, with no significant treatment-

related effects detected (Table 1a, attached). Statistical analysis showed no significant differences between treatment and control groups for the percentage of 14-day survivors per number of normal hatchling and the number of 14-day survivors per female bird (Table 1b, attached).

No abnormalities were detected in post-mortem examinations of ducklings that died during the 14-day observation period.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** "Under the conditions of this test, there was no evidence that dietary administration of CGA163935 to the Mallard duck at dose levels of 65, 200, and 600 ppm produced any significant effects on the reproductive capacity of the birds."

The report stated that study was conducted in conformance with Good Laboratory Practice regulations. The GLP statement was signed by the Study Director and the HRC 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 ranged from 76% to 80%; the recommended relative humidity is 55%.

The photoperiod during the first eight weeks was not specified. The guidelines recommend a regime of seven hours of light per day during this period.

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, except for the number of eggs cracked per eggs laid. The reviewer found a significant increase in eggs cracked of eggs laid at the two highest test concentrations (3.3 and 2.8%) when compared to the control (1.8%) (see Table 1b, attached). However, this incidence might not have been treatment-related since these percentages of cracked eggs are within a typical range for mallard eggs (i.e., 0.6-6%).

C. **Discussion/Results:** Chemical analyses of food samples taken during weeks 2, 13, and 22 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 on a trial mix, rather than the actual treatment diets. However, judging from the data using the trial mix, Cimectacarb was fairly stable in the diet, and the method of preparation achieved a homogeneous mix.

The reviewer concurs with the author's conclusion that there were no treatment related effects at 65, 200, and 600 ppm. The NOEC is 600 ppm.

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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