

US EPA ARCHIVE DOCUMENT

DATA EVALUATION RECORD

EEB
09 NOV 1993
H. Rose

1. **CHEMICAL:** Hexaflumuron.
Shaughnessey No. 118202.
2. **TEST MATERIAL:** Hexaflumuron; 1-(3,5-dichloro-4-(1,1,2,2,-tetrafluoroethoxy)phenyl-3-(2,6-difluorobenzoyl) urea; CAS No. 86479-06-3; Batch No. 473T-0886-30; Lot No. 269631; 98.1% purity; a white powder.
3. **STUDY TYPE:** 71-2. Avian Dietary LC₅₀ Test. Species Tested: Mallard duck (*Anas platyrhynchos*).
4. **CITATION:** Mayes, M.A. 1992. The Dietary Toxicity of XRD 473 to the Mallard Duck: Summary Evaluation and Original Study (Attached in Appendix A). Study ID No. DWC 512-871194. Performed by Huntingdon Research Centre Ltd., Huntingdon, England (1987). Submitted by DowElanco. EPA MRID No. 426485-10.

5. **REVIEWED BY:**

Mark A. Mossler, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: *Mark A. Mossler*

Date: 6/21/93

6. **APPROVED BY:**

Michael Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
Applied Sciences, Inc.

Signature: *Michael L. Whitten*

Date: 6-21-93

Henry T. Craven, M.S.
Supervisor, EEB/EFED
USEPA

Signature: *Henry T. Craven*

Date: 11/23/93

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an acute dietary avian study. The 8-day LC₅₀ value of >5200 ppm classifies hexaflumuron as practically non-toxic to the mallard duck. The NOEC was 2600 ppm.
8. **RECOMMENDATIONS:** N/A.
9. **BACKGROUND:**

5.5

10. DISCUSSION OF INDIVIDUAL TESTS: N/A.

11. MATERIALS AND METHODS:

A. Test Animals: Mallard ducks (*Anas platyrhynchos*) were obtained from a supplier in Kent, UK. All birds were in apparent good health at the beginning of the pre-treatment period (day -3) and group mean bodyweights ranged from 51 to 52 g. The birds were 8 days of age at test initiation.

B. Test System: The birds were housed indoors in steel brooders (80 x 36 x 30 cm). Floors were constructed of wire mesh and each brooder contained a drinker and feeding tray. During the test, the mean minimum and maximum daily temperatures in the building were 29 and 33°C, respectively. The mean relative humidity was 59%. A continuous photoperiod was used throughout the study.

The birds were offered water and feed (standard chick diet) *ad libitum* throughout the study. The feed did not contain any antibiotics or growth promoters. Treatment diets were prepared by blending an appropriate amount of a pre-mix (25,000 ppm) into the diet with a blender for 7 minutes. The diets were prepared one day prior to test initiation and stored frozen until use.

C. Dosage: Eight-day dietary LC₅₀ test. Dosage levels selected for the study were 163, 325, 650, 1300, 2600, and 5200 ppm. The amount of test material added to the diet was not corrected for purity of the test substance.

D. Design: Ten ducklings per test level and in each of three controls were assigned to pens. Signs of toxicity, abnormal behavior, and mortality were assessed daily. Group mean body weights were measured at initiation and on days 5 and 8. Average feed consumption was determined by group for days 0-1, 1-2, 2-3, 3-4, 4-5, (the exposure period), days 6-8 (the observation period).

Samples of the diets were taken immediately after preparation for concentration and homogeneity analyses. Stability analyses were performed on samples collected after 7 days of storage at room temperature. Samples were analyzed for the test material using liquid chromatography.

A post-mortem examination was conducted on all ten birds from the highest concentration group.

E. Statistics: The LC₅₀ value was determined by visual inspection of the mortality data.

12. REPORTED RESULTS: Diet analyses indicated that the test material was present at the desired levels, homogeneously mixed, and stable throughout the test period (Addendum Tables 2, 3, and 4, attached).

No mortality was observed in any of the test groups. Birds at the highest concentration level appeared to be subdued on day 3 of the treatment period. The LC₅₀ was determined to be greater than 5200 ppm.

No reductions in bodyweight were noted during the exposure or observation period (Table 1, attached). There appeared to be a reduction in feed consumption in the highest concentration group during days 1 and 2 (Table 2, attached).

No abnormalities were detected in any bird examined by post-mortem necropsy.

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:

The study authors made no conclusions other than those previously mentioned. The review author stated that the LC₅₀ of >5200 ppm classifies XRD 473 as practically non-toxic to the mallard.

Quality Assurance Unit and Good Laboratory Practice Statements were included in the report indicating that the study conformed with Good Laboratory Practice regulations as set forth in 40 CFR Part 160.

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

A. Test Procedure: The test procedures were in accordance with Subdivision E, ASTM, and SEP guidelines with the following exceptions:

Body weights were measured by group. Individual body weights are recommended.

The birds were not distributed randomly.

B. Statistical Analysis: The reviewer concurs that the LC₅₀ is greater than 5200 ppm.

- C. Discussion/Results: The report stated that ducklings were distributed in a manner that would equilibrate the mean weight of each test group. If the birds were weighed and put in a group on the basis of weight, they were not distributed randomly. However, the reviewer believes that the distribution was adequate for testing purposes.

This study is scientifically sound and meets the guideline requirements for an acute dietary avian study. The LC_{50} of hexaflumuron for mallard ducklings was determined to be >5200 ppm, which classifies this compound as practically non-toxic to this bird. The no-observed-effect concentration (NOEC) was 2600 ppm based on a reduction in feed consumption and signs of toxicity at the highest concentration level (5200 ppm).

D. Adequacy of the Study:

- (1) Classification: Core.
- (2) Rationale: N/A.
- (3) Repairability: N/A.

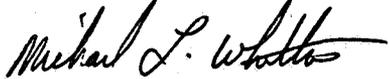
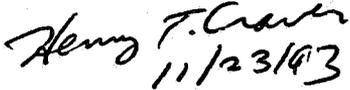
15. COMPLETION OF ONE-LINER: Yes, 6-1-93.

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1. **CHEMICAL:** Hexaflumuron.
Shaughnessey No. 118202.
2. **TEST MATERIAL:** Hexaflumuron; 1-(3,5-dichloro-4-(1,1,2,2,-tetrafluoroethoxy)phenyl-3-(2,6-difluorobenzoyl) urea; CAS No. 86479-06-3; Batch No. 473T-0886-30; Lot No. 269631; 98.1% purity; a white powder.
3. **STUDY TYPE:** 71-2. Avian Dietary LC₅₀ Test. Species Tested: Bobwhite quail (*Colinus virginianus*).
4. **CITATION:** Mayes, M.A. 1992. The Dietary Toxicity of XRD 473 to the Bobwhite Quail: Summary Evaluation and Original Study (Attached in Appendix A). Study ID No. DWC 511/871193. Performed by Huntingdon Research Centre Ltd., Huntingdon, England (1987). Submitted by DowElanco. EPA MRID No. 426485-09.
5. **REVIEWED BY:**

Mark A. Mossler, M.S. Associate Scientist KBN Engineering and Applied Sciences, Inc.	Signature:  Date: 6/21/93
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6. **APPROVED BY:**

Michael Whitten, M.S. Wildlife Toxicologist KBN Engineering and Applied Sciences, Inc.	Signature:  Date: 6-21-93
Henry T. Craven, M.S. Supervisor, EEB/EFED USEPA	Signature:  Date: 11/23/93
7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an acute dietary avian study. The 9-day LC₅₀ value of 2201 ppm classifies hexaflumuron as slightly toxic to the bobwhite quail. The NOEC was 650 ppm.
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 obtained from a supplier in Cambridgeshire, UK. All birds were in apparent good health at the beginning of the pre-treatment period (day -3) and group mean bodyweights ranged from 12.3 to 13.0 g. The birds were 11 days of age at test initiation.

B. **Test System:** The birds were housed indoors in wooden boxes (83 x 52 x 61 cm). Lids were constructed of wire mesh and each box contained a drinker and feeding tray. A 300-watt light was suspended above the pens to provide additional heat. During the test, the mean minimum and maximum daily temperatures in the building were 24 and 26°C, respectively. The mean relative humidity was 69%. A continuous photoperiod was used throughout the study.

The birds were offered water and feed (standard chick diet) *ad libitum* throughout the study. The feed did not contain any antibiotics or growth promoters. Treatment diets were prepared by blending an appropriate amount of a pre-mix (25,000 ppm) into the diet with a blender for 7 minutes. The diets were prepared one day prior to test initiation and stored frozen until use.

C. **Dosage:** Nine-day dietary LC₅₀ test. Dosage levels selected for the study were 163, 325, 650, 1300, 2600, and 5200 ppm. The amount of test material added to the diet was not corrected for purity of the test substance.

D. **Design:** Ten quail per test level and in each of three controls were assigned to pens. Signs of toxicity, abnormal behavior, and mortality were assessed daily. Group mean body weights were measured at initiation and on days 5, 8, and 9. Average feed consumption was determined by group for days 0-1, 1-2, 2-3, 3-4, 4-5, (the exposure period), days 6-8 (the observation period), and day 9 (an extra day of observation to provide a 72-hour mortality-free period).

Samples of the diets were taken immediately after preparation for concentration and homogeneity analyses. Stability analyses were performed on samples collected after 7 days of storage at room temperature. Samples were analyzed for the test material using liquid chromatography.

A post-mortem examination was conducted on the birds which died during the study and on the ten birds which survived in the two highest concentration treatment groups.

E. Statistics: The LC₅₀ value was determined using probit analysis.

- 12. REPORTED RESULTS:** Diet analyses indicated that the test material was present at the desired levels, homogeneously mixed, and stable throughout the test period (Addendum Tables 2, 3, and 4, attached).

Mortality data are presented in Table 1 (attached). Twenty, sixty, and thirty percent mortality was observed at the three highest treatment levels, respectively. Two birds (one from the 1300 ppm group and one from the 2600 ppm group) died on day 6 of the study, and therefore, the observation period was extended from three to four days. There were no overt signs of toxicity. The LC₅₀ was determined to be 4786 ppm (95% confidence interval of 2690-28,381 ppm), which is equivalent to a daily intake of approximately 900 mg/kg/day over a 5-day period.

A reduction in bodyweight was noted for the 2600 ppm group for days 0-5 and the amount of bodyweight increase in the 5200 ppm group was smaller than the controls for this same time period (Table 2, attached). All groups showed bodyweight increases during the observation period.

There appeared to be a reduction in feed consumption in the two highest concentration groups during the exposure period. Food consumption increased during the observation period (Table 3, attached).

No abnormalities were detected in any bird examined by post-mortem necropsy.

- 13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:**
The study authors made no conclusions other than those previously mentioned. The review author stated that the LC₅₀ of 4786 ppm classifies XRD 473 as slightly toxic to the bobwhite quail and that the no observed effect level was 650 ppm.

Quality Assurance Unit and Good Laboratory Practice Statements were included in the report indicating that the study conformed with Good Laboratory Practice regulations as set forth in 40 CFR Part 160.

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

- A. Test Procedure:** The test procedures were in accordance with Subdivision E, ASTM, and SEP guidelines with the following exceptions:

Body weights were measured by group. Individual body weights are recommended.

The birds were not distributed randomly.

- B. Statistical Analysis:** Using EPA's Toxanal program, the reviewer obtained a more conservative estimate of the LC₅₀ using moving average angle analysis (2201 ppm). Although the 95% confidence interval extends infinitely, the reviewer believes that this value is a more conservative estimate of the LC₅₀ than that of the authors (see attached printout).

- C. Discussion/Results:** The report stated that chicks were distributed in a manner that would equilibrate the mean weight of each test group. If the chicks were weighed and put in a group on the basis of weight, they were not distributed randomly. However, the reviewer believes that the distribution was adequate for testing purposes.

Upon review of the bodyweight and feed consumption data, the reviewer concurs with the review author that the no-observed-effect concentration (NOEC) is 650 ppm.

This study is scientifically sound and meets the guideline requirements for an acute dietary avian study. The LC₅₀ of hexaflumuron for bobwhite quail was determined to be 2201 ppm, which classifies this compound as slightly toxic to this bird. The NOEC was 650 ppm based on mortality and a reduction in bodyweight gain (or bodyweight loss) at higher concentration levels.

- D. Adequacy of the Study:**

- (1) **Classification:** Core.
- (2) **Rationale:** N/A.
- (3) **Repairability:** N/A.

- 15. COMPLETION OF ONE-LINER:** Yes, 6-1-93.