6-8-89

DATA EVALUATION RECORD

1. Chemical: RE-45601 (Clethodim)

2. Test Material: RE-45601 Technical (SX-1688) 82% purity.

3. Study Type: Avian Acute Oral LD_{50}
   Species Tested: Bobwhite quail (Colinus virginianus)

4. Study ID: Hinken, C. and J. Grimes. 1986. RE-45601 Technical (SX-1688): An Acute Oral Toxicity Study With The Bobwhite. Prepared by Wildlife International Ltd., Easton, MD (Project No. 162-165). Study Sponsor: Chevron Environmental Health Center, Inc., Richmond, CA. EPA Accession No. 409745-25.

   With Addendum:

   Slagowski, J.L. 1986. Addendum to Acute Oral Toxicity Study in Bobwhite Quail With RE-45601 Technical (SX-1688) Wildlife Project No. 162-165, Ortho Test No. S-2830: Dosage Formulation Analyses. Chevron Chemical Company (Laboratory Project Identification S-2830).

5. Reviewed By: David Warburton
   Wildlife Biologist
   EEB/EFED
   Signature: Dail Walton
   Date: 6/8/89

6. Approved By: Douglas J. Urban
   Supervisory Biologist
   EEB/EFED
   Signature: Douglas J Urban
   Date: 6/8/89

7. Conclusions:

   The study is scientifically sound and documents an acute oral LD_{50} >2000 mg/kg for bobwhite quail exposed to RE-45601 technical. Clethodim (RE-45601) technical may therefore be classified as practically non-toxic to bobwhite quail on an acute oral basis. The study fulfills the Guidelines requirement for avian acute oral toxicity testing.

8. Recommendations: None.

9. Background:

   The study was submitted to support, in part, a proposed Experimental Use Permit for Select 2EC herbicide to control annual and perennial grasses in cotton (EPA Record No. 238236).

10. Discussion of Individual Test: N/A.

11. Materials and Methods (Excerpted in part from submission):

a. Test Animals - All bobwhite were 18 weeks of age and appeared to be in good health at initiation of the study. Bobwhite ranged in weight from 150 grams to 208 grams at study initiation. The birds were obtained from Fritts' Quail Farm, Phillipsburg, NJ. All birds were pen-reared and phenotypically indistinguishable from wild birds. All test birds were acclimated to the caging and facilities for 22 days prior to the initiation of the study. During acclimation all birds were observed daily. Birds exhibiting abnormal behavior or physical injury were not used. The birds received no form of antibiotic medication during the study. The birds were fasted for at least 15 hours prior to dosing.

b. System - 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 random draw. Each pen measured 78 X 51 X 20-25 cm high. External walls, ceilings and sloped floors were constructed of galvanized wire while common walls were constructed of galvanized sheeting. Each dosage group was assigned two pens; one 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 was $26^{\circ} \pm 2^{\circ}C$ (SD) with a relative humidity of 75%. The photoperiod (maintained by a time clock) was eight hours of light per day during acclimation and throughout the study. The light source was Chroma 50 fluorescent lights; birds received approximately 12 footcandles of illumination. Well water and feed (a game bird ration formulated to Wildlife International Ltd.'s specifications) were provided ad libitum during acclimation and during the test. Housing and husbandry practices were based upon the "Guide for the Care and Use of Laboratory Animals", 1978 DHEW Publications No. (NIH) 78-23.

c. Dose - Two samples of the test material (SX-1688) were sent by Wildlife International for analysis. These samples were analyzed by the Research Services Laboratories of Chevron Chemical Company on July 28, 1986 and were found to contain 82.0% and 81.9% RE-45601 (active ingredient). During the actual dosing period, samples from each set of dosing formulations were sent frozen to Chevron Chemical Company for analysis.

The test material was dispersed in carboxymethyl cellulose, Tween 80 and distilled water. The dosages and LD_{50} value reported were not corrected for purity of the test substance. Nominal dosages used in this study were 500, 875, 1250, 1650, and 2000 milligrams of RE-45601 technical per kilogram of body weight. At initiation of the test, a single dose of the test material in diluent was orally intubated directly into the crop or proventriculus of each bird using a stainless steel catheter. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight (see attached

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Addendum I). The control birds received a corresponding volume of diluent only. All treatment and control birds received a constant dosage volume of 5 ml per kilogram of body weight.

d. Design - Groups of 10 bobwhite, five males and five females, were assigned to each of the treatment groups and the control group by random draw. The test consisted of a geometric series of five dosage groups (discussed above) and a control group. Following test initiation until termination all birds were observed at least twice daily. A record was maintained of all mortality, signs of toxicity, or abnormal behavior. Individual body weights were measured at initiation of the test and by group on Days 3, 7 and 14 of the test. Average estimated feed consumption was determined for each dosage group and the control for Days 0-3, 4-7 and 8-14. Feed consumption was measured accurately, but is presented as an estimate due to the unavoidable wastage by the birds.

e. Statistics - Mortality pattern was not conducive to calculating the LD_{50} value. Therefore, an estimation of the LD_{50} value was made by a visual inspection of the mortality data.

12. Reported Results (Excerpted in part from submission):

There were no mortalities in the control group. All birds were normal in appearance and behavior throughout the test period.

There were no mortalities at any dosage tested. There were no overt signs of toxicity at the 500 mg/kg, 875 mg/kg and 1250 mg/kg dosages. All birds were normal in appearance and behavior throughout the test period. At the 1650 mg/kg dosage, signs of toxicity were first noted in the morning observation of Day 1. In addition, one female was noted as having a torn toenail on its left foot in the morning observation on Day 12. This condition was not considered to be treatment-related. By the morning observation of Day 6, all birds were normal in appearance and behavior and remained so until study termination. At the 2000 mg/kg dosage, signs of toxicity were first noted on the morning observation of Day 1. One male developed conjunctivitus in its left eye on Day 3, which had cleared by Day 13. All other birds were normal in appearance and behavior by the morning observation of Day 6 and remained so until study termination. Typical signs of toxicity displayed by the birds dosed with RE-45601 technical were lethargy, wing droop and a ruffled appearance.

When compared to the control, there was no apparent effect upon body weight gain at the 500 mg/kg, 875 mg/kg and 1250 mg/kg dosages (see attached Table 2). During the first three days of the study, there was a reduction in body weight gain at the 1650 mg/kg dosage and a loss in body weight at the 2000 mg/kg dosage. In addition, during this same time period, there was a corresponding reduction in feed consumption at both 1650 and 2000 mg/kg when compared to the control group.

3

The data from the results of the dosage formulation analysis (attached) show that the formulations were within acceptable limits.

13. Study Author's Conclusions/QA Measures:

The bobwhite acute oral LD_{50} value for RE-45601 technical was determined to be greater than ~~2000 mg~~/kg, the highest dosage tested. The no-observed-effect dosage was determined to be 1250 mg/kg, based upon overt signs of toxicity and a reduction in weight gain at 1650 mg/kg.

The study was examined for conformance with Good Laboratory Practices as published by the U.S. Environmental Protection Agency, Office of Pesticide Programs (Federal register, Volume 48, No. 230, November 29, 1983) by Wildlife International Ltd. Quality Assurance Officer Lee F. Doggett. The final report was determined to be an accurate reflection of the data obtained.

14. Reviewer's Discussion and Interpretation of Study:

a. Test Procedures - The study was conducted according to Agency recommended procedures, with the exception that feed consumption data was grouped into 3 periods instead of being reported as average daily consumption.

b. Statistical Analysis - Not required due to mortality pattern.

c. Discussion/Results - Reviewer noted that when compared to the control, there was a reduction in body weight gain at all treatment levels during the first three days, not just the higher two levels as reported. Decreased total weight chain was also noted at all levels. Provided that the amount of test material administered to the birds was as reported in Addendum I, and given an 82% average purity of the material, reviewer calculates that actual dosage levels were 478, 888, 1398, 2072, and 2813 mg/kg. Regardless, EEB concurs with the study author's conclusion of an acute oral LD_{50} value of greater than 2000 mg/kg for bobwhite quail administered RE-45601 technical. Clethodim (RE-45601) technical may therefore be classified as practically non-toxic to bobwhite quail on an acute oral basis.

d. Adequacy of Study -

1) Classification - Core for RE-45601 technical.
2) Rationale - Conducted according to Agency protocol with minor exceptions.
3) Reparability - N/A.

CLETHODIM

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