DATA EVALUATION RECORD
AVIAN SINGLE-DOSE LD_{50} TEST
GUIDELINE 71-1

1. CHEMICAL: Spinosed (also known as Factor A and Factor D)

   Shaughnessey #: 110003

2. TEST MATERIAL: XDE-105; Lot ACD13651; 88% potency as combined compounds; light grey to white solid

3. CITATION A. G. Murray, J. L. Seacat, and D. W. Grothe 1992. The Toxicity of XDE-105 to Bobwhite in a 14-Day Acute Oral Study; Laboratory Project ID A01091; Lilly Research Laboratories, Greenfield, IN 46140; Submitted by DowElanco, Indianapolis, IN 46258-1189; MRID 43414529

4. REVIEWED BY:

   Joanne S. Edwards
   Entomologist
   Ecological Effects Branch
   Environmental Fate and
   Effects Division (7507C)

   Signature: Joanne S Edwards
   Date: 3/14/95

5. APPROVED BY:

   Leslie W. Touart
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   Signature: L. W. T.
   Date: 3/24/95

6. CONCLUSIONS: This study is scientifically sound, but classified supplemental. For purposes of risk assessment, the single oral LD_{50} for bobwhite quail exposed to XDE-105 is considered to be >1333 mg/kg, which classifies the test material as slightly toxic to birds.

7. ADEQUACY OF THE STUDY: Supplemental

8. RATIONAL FOR CLASSIFICATION: Birds were triple dosed over a 5.5 hour (pg 13 of report, attached). No explanation provided as to why administration wasn't through gelatin capsules or why dosing took place over 5.5 hrs. Since the authors indicated the second dose immediately followed the first, the EEB will consider for risk assessment purposes the highest nominal to be 1333 mg/kg (= 2/3 of the nominal 2000 mg/kg). The registrant has the option of repeating the study or accepting this approach.

9. BACKGROUND: New chemical EUP.

10. MATERIALS AND METHODS:

A. Test Organisms:

Guideline Criteria	Reported Information
Species: A wild waterfowl species, preferably the mallard (*Anas platyrhynchos*), or an upland game bird species, preferably the bobwhite (*Colinus virginianus*).	Northern Bobwhite (Colinus virginianus)
Age at beginning of test: At least 16 weeks old.	16 wks; initial body weights were 222 ± 17 g (males) and 214 ± 15 g (females)
Supplier	Barrett Quail Farm, Houston, TX
Acclimation period: At least 15 days.	approx. 21 days

B. Test System:

Guideline Criteria	Reported Information
Pen facilities adequate?	yes; temperature in test room averaged 24 to 26 °C; relative humidity was maintained between 43% and 56%; stainless steel pens measured 25 X 45 cm (W X L); two birds (same sex) per pen were housed
Photoperiod: 10-hr light : 14-hr dark is recommended.	8-hr light regime
Diet was nutritious and appropriate for species?	yes; analysis of diet formulation included in report
Feed withheld at least 15 hours prior to dosing?	yes (withheld approx. 16 hours)

C. Test Design:

Guideline Criteria	Reported Information
Range finding test?	yes
Definitive Test **Nominal concentrations:** At least five, in a geometric scale, unless LD_{50} > 2000 mg AI / kg.	50, 200, 500, 100, and 2,000 mg/kg a.i. (dosages were corrected for purity of test substance)
Controls: water control or vehicle control (if vehicle is used)	control group dosed with 10% aqueous acacia solution
Number of birds per group: 10 (strongly recommended)	6/sex/group; randomly assigned
Vehicle: Distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic.	10% acacia (gum arabic)
Amount of vehicle per body weight: Constant volume/weight % of body weight, not to exceed 1% (1ml/100g).	dosages were adjusted to purity of test substance; see comment below.
Observations period: At least 14 days.	14 days

Comment: The authors stated that corn oil and water were determined to be unacceptable carriers, and that aqueous acacia was determined acceptable at concentrations of XDE-105 $\leq$ 80 mg/ml. The study authors administered the test material in three separate doses because of maximum dose volume requirements and the difficulties in maintaining suspensions of test material in the aqueous acacia solution. The total dose volume was 25 ml/kg of body weight, given as three 8.3 ml/kg doses. After the first dose was given a second was given immediately. The authors stated that the dosing time for the entire study was aprox. 5.5 hours.

11. REPORTED RESULTS/QUALITY ASSURANCE:

Guideline Criteria	Reported Information
Individual body weights measured at beginning of test, on day 14 and at end of test if extended beyond 14 days?	individual body weights were measured at initiation and on day 14
Mean feed consumption measured at beginning of test, on day 14, and at end of test if extended beyond 14 days?	determined for each pen for days 0-7 and 7-14
Control Mortality: Not more than 10%	none
Raw data included?	no
Signs of toxicity (if any) were described?	yes

Mortality:

Nominal (mg/kg)	Control (10% acacia)	50	200	500	1000	2000
Measured (mg/kg)	-		-	-	-	
No. dead / no. exposed	0/10	0/10	0/10	0/10	2/10	2/10

Reported Statistical Results:

The LD_{50} was determined to be >2000 mg/kg. A no observed effect dosage was not reported.

Assays

Assays of freshly prepared suspensions indicated that XDE-105 assayed concentrations ranged from 96 to 100% of nominal concentrations. XDE-105 was detected in control samples (Table 1 and Appendix #, attached). The authors reported that gavage needles selected for the second and third doses may have been contaminated from a previous study with XDE-105. The authors reported that it was possible the control birds could have received small doses (1.2 to 17.7 mg/kg) of XDE-105 from this contaminant. Mean assayed concentrations of suspension samples taken throughout the dosing period represented 95% to 98% of

nominal concentrations.

Signs of Mortality/Toxicity

No mortality occurred in birds receiving ≤ 500 mg XDE-105/kg. The authors reported that observations of loose feces were strongly related to XDE-105 doses ≥ 500 mg/kg. Loose feces were observed (1 and 2 hours post-dosing) in all control birds; the affect was transient. The authors attributed this to dosing with the aqueous acacia. Ataxia was observed at dose levels ≥ 500 mg/kg.

Body Weight/Food Consumption

Food consumption:
A significant difference between the mean body weight value of female control birds and females receiving ≤500 mg XDE-105/kg; no significant difference between male control birds and males receiving ≤2000 mg XDE-105/kg.

Body Weight:
Mean body weight of females receiving ≥1000 mg/kg and mean body weight of males receiving a dose of 2000 mg XDE-105/kg compared to respective controls was significantly reduced.

A GLP Compliance Statement was included in the report indicating the study was conducted under GLP. A Quality Assurance Statement was also included.

12. REVIEWER'S DISCUSSION AND INTERPRETATION

Verification of Statistical Results: No; there was no mortality in this study.

The single oral LD_{50} for bobwhite exposed to XDE-105 is calculated to be >1333 mg/kg (see under Guideline deviations below), which classifies the test material as slightly toxic to birds.

Guideline Deviations:

The following major deviation was noted:

The authors reported that the study employed triple dosing (three equal doses) over a 5.5 hour period with the second dose given immediately (pg 13 of report, attached). No

explanation was provided as to why administration was not through a standard route (i.e. gelatine capsules), as the test material is a solid. Also, the study authors did not explain why the dosing took place over a 5.5 hour period. Since the authors did indicate that the second dose was administered immediately after the first, the EEB considers the highest nominal to be 1333 mg/kg (= 2/3 of the nominal 2000 mg/kg).

XDE-105 was detected in control samples. Since there was no mortality in the control birds, this was not found to affect the overall quality of the study.

Classification: Supplemental; does not have to be repeated if registrant is willing to accept lower LD_{50} value and toxicity classification "slightly toxic".

Rationale: Multiple dosing scheme employed in this study constitutes a major study deviation.

Repairability: No

13. COMPLETION OF ONE-LINER FOR STUDY:

DER dated 3/24/95 (MRID 43414539) Approved

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