Data Evaluation Report on the Acute Dietary Toxicity of XDE-638 to Bobwhite Quail (*Colinus Virginianus*)
PMRA Submission Number EPA MRID Number 45831002

Data Requirement:	PMRA DATA CODE	
	EPA DP Barcode	D288160
	OECD Data Point	
	EPA MRID	45831002
	EPA Guideline	§71-2a

Test material: XDE-638 **Purity:** 97.5%
Common name: Penoxsulam
Chemical name: IUPAC: Not reported
CAS name: 2-(2,2-Difluoroethoxy)-N-(5,8-dimethoxy[1,2,4]triazolo[1,5-C]pyrimidin-2-yl)-6-(trifluoromethyl)benzenesulfonamide
CAS No.: Not reported
Synonyms: Not reported

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Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: ~~199031~~ 119031

Date Evaluation Completed:

CITATION: Troup, R. and B.A. Medlicott. 2002. XDE-638: Avian Acute Dietary Toxicity Test with Northern Bobwhite (*Colinus virginianus*). Unpublished study performed by Genesis Laboratories, Inc., Wellington, CO. Laboratory Study No. 99025. Study sponsored by Dow AgroSciences LLC, Indianapolis, IN. Study initiated September 27, 1999 and completed March 23, 2002.

EXECUTIVE SUMMARY:

The acute dietary toxicity of XDE-638 (penoxsulam) to 14-day old Northern Bobwhite quail (*Colinus virginianus*) was assessed over 8 days. XDE-638 was administered to the birds in the diet at nominal concentrations of 0 (vehicle control), 1000, 1500, 2250, 3375, and 5063 ppm. Mean-measured concentrations were <LOD (control), 877, 1456, 2091, 3110, and 4411 ppm a.i., respectively.

No mortalities occurred during the 8-day study. In addition, there were no sub-lethal signs of toxicity, or treatment-related effects on body weights or feed consumption. No significant gross pathological findings were observed. The 8-day acute dietary LC_{50} was >4411 ppm a.i., the highest concentration tested, which categorizes XDE-638 (penoxsulam) as slightly toxic to the Bobwhite quail on an acute dietary basis.

This toxicity study is scientifically sound. However, since the concentration of acetone used in the preparation of the treated feed was not reported, this study does not fulfill the guideline requirements for an avian dietary study using the Northern Bobwhite quail (§71-2a). This study is classified as SUPPLEMENTAL, but need not be repeated.

Results Synopsis

Test Organism Size/Age : 14-days old, 19-33 g

LC_{50}: >4411 ppm a.i.
NOAEC: 4411 ppm a.i.
LOAEC: >4411 ppm a.i.
Endpoint(s) Affected: None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED:

The study protocol was based on procedures outlined in the U.S. EPA Pesticide Assessment Guidelines, Series §71-2, and OECD Guideline 205. The following deviations from guideline §71-2 were noted:

1. The concentration of acetone used in the preparation of the test feed was not reported.

2. The relative humidity was not reported.

These deviations do not affect the validity of the study; however, this study does not fulfill guideline requirements, but it need not be repeated.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance

with U.S. EPA 40 CFR Part 160 and OECD Principles of Good Laboratory Practice (1997 revision).

A. MATERIALS:

1. Test Material XDE-638

Description: White solid

Lot No./Batch No.: ND05167938 (TSN101773)

Purity: 97.5%

Stability of Compound Under Test Conditions: Stability of the test material was assessed in treated feed prepared at 1000 and 5063 ppm. Recoveries averaged 108-110% of the mean initial values after 5 days of open feeder storage, and 106-116% of the mean initial values after 10 days of open feeder storage (Appendix B, p. 32).

Storage conditions of test chemicals: Ambient

OECD requires water solubility, stability in water and light, pK_a, P_{ow}, and vapor pressure of the test compound. OECD requirements were not reported.

2. Test organism:

Species: Northern Bobwhite quail (*Colinus virginianus*)

Age at study initiation: 14 days

Weight at study initiation: 19-33 g

Source: Sand Prairie Quail Farm, Maquoketa, Iowa.

B. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding Study: No range-finding study was reported.

b) Definitive Study:

Table 1: Experimental Parameters

Parameter	Details	Remarks *Criteria*
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	7 days Same as test Dry, non-medicated Turkey and Game Bird Starter (Ranch-way, Inc.) and water were provided, *ad libitum,* during acclimation and testing. General physical condition and suitability for testing were determined. Birds were normal and active (no mortality).	
Pen size and construction materials	Galvanized steel brooders; 90 x 70 x 23 cm. The floor surface area was 6300 cm^2.	*EPA requires: about 35 x 100 x 24 cm*
Test duration	5 days with treated feed, and 3 days with"clean" feed (recovery period).	*EPA requires: 5 days with treated feed and at least 3 days observation with "clean" feed.*
Test concentrations nominal: measured:	0 (vehicle control), 1000, 1500, 2250, 3375, and 5063 ppm <LOD (control), 877, 1456, 2091, 3110, and 4411 ppm a.i.	*Four minimum, 5 or 6 strongly recommended, in a geometric scale, unless LC_{50} > 5000 ppm.*
Solvent/vehicle, if used type: amount:	Acetone Not reported	*EPA requires: Distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic. Solvent not more than 2%.*
Diet preparation and feeding	The test substance was	

Parameter	Details	Remarks
		Criteria
	mixed with acetone. The solution was then mixed with feed for a total of 25 minutes.	*EPA requires: Control group tested with diet containing the maximum amount of vehicle used in treated diets?*
Feed withholding period	None	
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	
Number of birds per replicate/group for negative control: for vehicle control: for treated:	 N/A 10 10	 *EPA requires: 10 (strongly recommended)*
Number of replicates/group (if used) for negative control: for vehicle control: for treated:	 N/A 3 1	
Test conditions temperature: relative humidity(%): photoperiod:	 Brooder: 37-40°C Not reported 16 hours light/8 hours dark	The relative humidity was not reported. ***Brooder temperature:*** *about 35 °C (95 °F)* ***Room temperature:*** *22-27 °C (71-81 °F)* ***Relative humidity:*** *30-80%* ***Photoperiod:*** *Minimum of 14 h of light.*
Reference chemical, if used	None used.	

2. Observations:

Table 2: Observations

Criteria	Details	Remarks *Criteria*
Parameters measured (mortality/body weight/ mean feed consumption/ others)	- Mortality - Clinical signs of toxicity - Mean feed consumption (g/bird/day) - Mean body weight	
Indicate the stability and homogeneity of test chemical in the diet	Stability: Verified. Stability of the test material in avian diet was assessed in treated feed prepared at 1000 (lowest) and 5063 (highest) ppm and stored in metal quail feeders. Recoveries averaged 108-110% of the mean initial value after 5 days and 106-116% of the mean initial value after 10 days (Appendix B, p. 32). Homogeneity: Homogeneity (top, middle and bottom) was tested for samples taken from the 1000 (lowest) and 5063 (highest) ppm groups. Coefficients of variation (RSD) were 7.89% for the low dose group and 4.82% for the high dose group (Appendix B, pp. 29-30).	Stability and homogeneity of the test material was not tested in treated feed at 1500, 2250, 3375 ppm. A freezer stability study was also conducted. Samples were stored for 22 days under frozen storage at Genesis Laboratory, and another 31 days (total of 53 days) under frozen storage at the analytical laboratory. Recoveries averaged 86.6-92% of the mean initial value (Appendix B, p. 31).
Indicate if the test material was regurgitated	Regurgitation was not reported.	
Treatments on which necropsies were performed	Necropsies were performed on four birds from each treatment	

	group.	
Observation intervals	Mortality and signs of toxicity were measured twice daily. Food consumption was recorded daily. Body weights were determined on Days 0, 5, and 8.	
Were raw data included?	Raw data were included.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortalities occurred after 5 days on treated diets or during the 3 day recovery period (Table I, p. 16).

Table 3: Effect of XDE-638 on mortality of Northern Bobwhite quail.

Treatment, ppm a.i. mean-measured (and nominal)		No. of birds per treatment	Cumulative mortality								
			Days								
			0	1	2	3	4	5	6	7	8
Vehicle control		30	0	0	0	0	0	0	0	0	0
877 (1000)		10	0	0	0	0	0	0	0	0	0
1456 (1500)		10	0	0	0	0	0	0	0	0	0
2091 (2250)		10	0	0	0	0	0	0	0	0	0
3110 (3375)		10	0	0	0	0	0	0	0	0	0
4411 (5063)		10	0	0	0	0	0	0	0	0	0
NOAEC		4411 ppm a.i.									
LC_{50}		>4411 ppm a.i.									
Reference	mortality	N/A									

	LC_{50}	N/A
	NOAEC	N/A

B. SUB-LETHAL TOXICITY ENDPOINTS:

No sub-lethal effects were observed (Table I, p. 16). In addition, there were no significant differences in the treatment group body weights or food consumption compared to the control (Tables II and III, pp. 17-18). No significant gross pathological findings were observed (Table IV, p. 19).

Table 4: Sub-lethal effects of XDE-638 on Northern Bobwhite quail.

Treatment, ppm a.i. mean-measured (and nominal)		Observation				
		Mean body weight (g)			Food consumption (g/bird/day)	
		Day			Day	
		0	5	8	0-5	6-8
Vehicle control[1]		25	39	49	5	7
877 (1000)		26	38	47	5	7
1456 (1500)		25	38	47	5	7
2091 (2250)		24	36	46	4	6
3110 (3375)		25	37	48	5	7
4411 (5063)		25	38	48	5	7
NOAEC		4411 ppm a.i.				
EC_{50}		Not reported				
Reference chemical	NOAEC	N/A				
	EC_{50}	N/A				

[1] The vehicle control data was averaged by the reviewer.

C. REPORTED STATISTICS:

Body weight data were analyzed by a Chi-square test for normality, followed by a Bartlett's test for homogeneity of variance. If a data set passed these tests, it was analyzed by ANOVA, followed by a multiple comparison test to compare each treatment group with the control.

All analyses were conducted using TOXSTAT, v 3.4. The NOAEC and LC_{50} were visually determined based on mortalities and body weights significance data. The nominal test concentrations were used in analyses.

LC_{50}: >5063 ppm
NOAEC: 5063 ppm
Endpoint(s) Affected: None

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical analyses were not required, as there was no mortality in this study and effects on food consumption and body weight could be visually determined.

LC_{50}: >4411 ppm a.i.
NOAEC: 4411 ppm a.i.
LOAEC: >4411 ppm a.i.
Endpoint(s) Affected: None

E. STUDY DEFICIENCIES:

This study is scientifically valid; however, since the concentration of acetone used in the preparation of the test feed was not reported, this study does not fulfill the guideline requirements for an avian dietary study using the Northern Bobwhite quail (§71-2a). This study is classified as SUPPLEMENTAL, but it need not be repeated.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions were identical to the study authors'.

In the analytical laboratories report (Appendix B, pp. 28-41), two batches of treated feed were analyzed for concentration verification. Results from Batch 2 are provided on p. 33, and results from Batch 3 are provided on p. 34. The study authors reported only the results from Batch 3 as the mean-measured concentrations. It was unclear why results from Batch 2 were not included in the mean-measured values.

G. CONCLUSIONS:

This study is scientifically sound. However, since the concentration of acetone used in the treated test feed preparation was not reported, this study does not fulfill guideline requirements for an avian dietary study using the Northern Bobwhite quail (§71-2a). This study is therefore classified as SUPPLEMENTAL, but need not be repeated, because there were no treatment-related effects on mortality, sub-lethal effects, body weight, or food consumption, and necropsy after 8 days revealed no treatment-related abnormalities. The LC_{50} was >4411 ppm a.i., the highest concentration tested, which categorizes XDE-638 (penoxsulam T.G.) as slightly toxic to the Bobwhite quail on an acute dietary basis.

LC_{50}: >4411 ppm a.i.
NOAEC: 4411 ppm a.i.
LOAEC: >4411 ppm a.i.
Endpoint(s) Affected: None

III. REFERENCES:

No references were cited.