Data Evaluation Report on the Acute Oral Toxicity of GF-443 on Avian Species *Colinus virginianus*

PMRA Submission Number EPA MRID Number 45831001

Data Requirement:	PMRA DATA CODE	
	EPA DP Barcode	D288160
	OECD Data Point	
	EPA MRID	45831001
	EPA Guideline	§71-1

Test material: GF-443 **Purity:** Not reported

Common name: Submitted to support registration for penoxsulam (not otherwise specified)

Chemical name: IUPAC: Not reported
CAS name: Not reported
CAS No.: Not reported
Synonyms: Not reported

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Date: 10/17/03

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Reference/Submission No.:

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

Date Evaluation Completed:

CITATION: Mach, J.J. 2002. Avian Single-Dose Oral LD_{50} Test with GF-443 in Northern Bobwhite (*Colinus virginianus*). Unpublished study performed by Genesis Laboratories, Inc., Wellington, CO. Laboratory Study No. 02004. Study sponsored by The Dow Chemical Company for Dow AgroSciences LLC, Indianapolis, IN. Study initiated April 5, 2002 and completed May 30, 2002.

EXECUTIVE SUMMARY:

The acute oral toxicity of GF-443 (21.9% EUP of penoxsulam) to 21-week-old Northern Bobwhite quail (*Colinus virginianus*) was assessed over 14 days. GF-443 was administered to the birds via gavage at nominal concentrations of 0, 778, 1296, 2160, 3600, 6000, and 10,000 mg/kg bw of the EUP. The nominal concentrations of the active ingredient were 170, 283,473, 778, 1314, 2190 mg ai/kg.

No mortalities or treatment-related sub-lethal effects were observed during the study. In addition, no significant differences in body weights were observed. A statistically-significant reduction in feed consumption was observed on Days 0-3 at the 2190 mg ai/kg bw dose group compared to the control (15 versus 19 g/bird/day). Feed consumption recovered for the remainder of the study. No treatment-related abnormalities were observed at terminal necropsy. The 14-day acute oral LD_{50} is >2190 mg ai/kg bw, which categorizes GF-443 as practically nontoxic to Northern Bobwhite quail on an acute oral basis.

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Northern Bobwhite quail (§71-1). This study is classified as CORE.

Results Synopsis

Test Organism Size/Age: 21-weeks old, 167-214 g (combined sexes)

LD_{50}: >2,190 mg/kg bw
NOAEL: 1,302 mg/kg bw
LOAEL: 2,190 mg/kg bw
Endpoint(s) Affected: Transient effects on feed consumption

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study protocol was based on procedures outlined in the U.S. EPA Pesticide Assessment Guidelines, Series §71-1. The following deviation from guideline §71.1 were observed:

The identity and purity of the test substance were not reported. Although this study was submitted to support the registration of penoxsulam, it was unclear if GF-443 was a synonym for penoxsulam, a metabolite, or some other ingredient of a formulated or end-use product. Eventually it was determined that it is an EUP with 21.9% ai.

This deviation is considered significant, and as a result, this study does not fulfill guideline requirements.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

A. MATERIALS:

1. Test Material GF-443 (21.9% ai)

Description: Cream to light tan liquid

Lot No./Batch No.: E-828-59

Purity: Not specified

Stability of Compound Under Test Conditions: N/A

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: 21 weeks old

Weight at study initiation: 167-214 g

Source: Dyes Quail Farm/Colorado Game Bird Ranch, Yuma, CO.

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:	17 days.	
Conditions (same as test or not):	Same as test.	*EPA recommends that birds be pre-conditioned to the test facilities for at least 15 days.* *OECD recommends that birds be pre-conditioned to the test facilities for at least 7 days.*
Feeding:	Dry, non-medicated Turkey and Gamebird Grower (Ranch-Way, Inc.) and tap water were provided, *ad libitum*, during acclimation and testing.	
Health (any mortality observed):	General physical condition and suitability for testing were determined by a veterinarian prior to testing.	
Pen size and construction materials	Steel wire pens; 51 x 25 x 25.5 cm (floor surface area of 1275 cm^2).	
		EPA requires: pens must conform to good husbandry practices and should not create crowding stress. *OECD lists no criteria for pen construction other than stating that pens should be suitable for the captive rearing of that species.*
Test duration	14 Days	
		EPA requires a day for dosing and at least 14 days observation.
Dose preparation	A single dosing solution was prepared using GF-445 and HPLC-grade water.	
Indicate method of confirmation of dose	The actual amount (mL) of test substance administered was determined (Appendix A1, pp. 22-24).	
Mode of dose administration	Oral, via gavage.	
		Gavage or gelatin capsule.

Parameter	Details	Remarks *Criteria*
Dose levels nominal: measured:	0 (vehicle control), 778, 1296, 2160, 3600, 6000, and 10,000 mg/kg bw EUP (21.9% ai). Not reported	*EPA requires a minimum of 5 treatment levels unless LD_{50} is demonstrated to be greater than 2000 mg ai/kg*
Solvent/vehicle, if used type: amount/bw:	HPLC-grade water Approximately 1.0% bw	*EPA recommends that the test material be administered without a vehicle if possible. Maximum vehicle should not exceed 0.1 to 1.0% of body weight.*
Number of birds per groups/treatment for negative control: for solvent/vehicle control: for treated:	N/A 10 10	5 males and 5 females/group *EPA recommends 10 birds per treatment group and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	Birds were fasted for approximately 20-21 hours prior to dosing.	*EPA recommends that food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photo-period:	19-26°C (mean min. = 20°C; mean max. = 25°C) 21-34% (mean min. = 23%; mean max. = 28%) 10-hours light/14-hours dark.	Average light intensity was 2.8 foot-candles. Air exchange rate was 10-15 per hour. *EPA recommends that a 10 hr light/14 hr dark photo-period.*
Reference chemical, if used name: concentrations tested:	None used.	

2. Observations:

Table 2: Observations.

Parameter	Details	Remarks/Criteria
Parameters measured		
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/others)	- Mortality - Clinical signs of toxicity - Individual body weights - Average feed consumption	*EPA recommends:* *Body weight measured at test initiation, on Day 14 and at end of the test if the test is extended beyond 14 days.* *Calculation of mortality. Mortality must NOT be more than 10% in controls.* *Feed consumption may be measured as average daily food consumption.*
Indicate if the test material was regurgitated	Not reported.	*Regurgitation is an indication that the dose was rejected. The test may have to be repeated if the problem persists.*
Groups on which necropsies were performed	All birds that died during testing and four birds (2 males and 2 females) from the control and each treatment group were subject to a gross pathological examination.	*EPA recommends that gross necropsies be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	Mortality and Signs of Toxicity: Twice daily. Body Weight: Days 0 (before dosing), 3, 7, and 14 Feed consumption: Days 0-3, 3-7, and 7-14.	
Were raw data included?	Raw data were included.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No treatment-related mortalities occurred during the study (Table I, p. 15).

Table 3: Effect of GF-443 on mortality of *Colinus virginianus*.

Treatment (mg ai/kg bw)	No. of birds	Cumulative mortality

			day 0	day 7	day 14
Vehicle control		10	0	0	0
170		9[a]	0	0	0
283		10	0	0	0
473		10	0	0	0
778		10	0	0	0
1314		10	0	0	0
2,190		10	0	0	0
NOAEL (mortalilty)		2,190 mg ai/kg bw			
LD_{50}		>2,190 mg ai/kg bw			
Reference chemical	mortality	N/A	N/A	N/A	N/A
	LD_{50}	N/A	N/A	N/A	N/A
	NOAEL	N/A	N/A	N/A	N/A

[a] One bird was found dead caught underneath the feeder (not included in number of birds tested).

B. SUB-LETHAL TOXICITY ENDPOINTS:

No treatment-related signs of toxicity, or significant differences in body weights were observed during the study (Tables I and II, pp. 15-16). A statistically-significant reduction in feed consumption was observed on Days 0-3 at the 2,190 mg ai/kg bw dose group compared to the control (15 versus 19 g/bird/day; Table III, p. 17). Feed consumption recovered for the remainder of the study. No post-mortem abnormal findings were observed that could be attributed to treatment (Table IV, p. 18).

Table 4: Sub-lethal effects of GF-443 on *Colinus virginianus*.

Mean Body Weight, g					
Treatment, mg ai/kg bw		**Males and Females**			
		Day 0	**Day 3**	**Day 7**	**Day 14**
Vehicle Control		187	195	197	195
178		186	192	193	194
283		188	194	195	192
473		193	197	198	197
778		186	192	193	191
1314		188	191	196	194
2,190		188	190	193	193
NOAEL		2,190 mg ai/kg bw			
EC_{50}		>2,190 mg ai/kg bw			
Reference chemical	effect: NOAEL: LD_{50}:	N/A	N/A	N/A	N/A

Mean Feed Consumption, g/bird/day				
Treatment, mg/kg bw		**Days 0-3**	**Days 3-7**	**Days 7-14**
Vehicle Control		19	17	15
170		19	17	15
283		17	17	15
473		17	16	15
778		17	16	14
1314		17	17	15
2,190		15*	16	14
NOAEL		1,314 mg/kg bw		
EC_{50}		Not reported		
Reference chemical	effect NOAEL LD_{50}	N/A	N/A	N/A

*Significantly different from the control (ANOVA/Dunnett).

C. REPORTED STATISTICS:

Body weight and feed consumption data were analyzed by a Chi-square test for normality, followed by a Bartlett's test for homogeneity of variance. All data sets passed these tests, and were analyzed by ANOVA, followed by Dunnett's test to compare each treatment group with the control. All analyses were conducted using TOXSTAT, v 3.4. The LD_{50} was estimated because there were no effects on mortality.

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.

LD_{50}: >2,190 mg ai/kg bw
NOAEL: 1314 mg ai/kg bw
LOAEL: 2,190 mg ai/kg bw
Endpoint(s) Affected: Transient effects on feed consumption

E. STUDY DEFICIENCIES:

This study is scientifically sound. However, the identity and purity of the test substance were not reported. Although this study was submitted to support the registration of penoxsulam, it was unclear if GF-443 was a synonym for penoxsulam, a metabolite, or some other ingredient of a formulated or end-use product. As a

result, this study does not fulfill the guideline requirement for an avian oral LD_{50} test (§71-1) and is classified as SUPPLEMENTAL. This study may be upgraded to Core status if the appropriate identification data are provided.

F. REVIEWER'S COMMENTS:

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

G. CONCLUSIONS:

This toxicity study is scientifically sound, and fulfills the guideline requirements for an acute toxicity study for an End-Use Product (21.9%) using the Northern Bobwhite quail (§71-1). This study is classified as CORE. There were no treatment-related effects on mortality, sub-lethal effects, or body weight. A transient decrease in food consumption was observed in birds from the 2,190 mg ai/kg bw dose group between Days 0-3. Necropsy after 14 days revealed no treatment-related abnormalities. The 14-day acute oral toxicity LD_{50} was >2,190 mg ai/kg bw, which categorizes GF-443 as practically nontoxic to Northern Bobwhite quail.

LD_{50}: >2,190 mg ai/kg bw
NOAEL: 1314 mg ai/kg bw
LOAEL: 2,190 mg /kg bw
Endpoint(s) Affected: Transient effects on feed consumption

III. REFERENCES:

No references were cited.