Data Evaluation Report on the acute dietary toxicity of Pyroxsulam to avian species Bobwhite quail (*Colinus virginianus*)
PMRA Submission Number 2006-4727 EPA MRID Number 469084-19 APVMA ATS 40362

Data Requirement: : PMRA DATA CODE: 9.6.2.4
EPA DP Barcode: D332116
OECD Data Point: IIA 8.1.2
EPA Guideline: 71-2a (850.2200)

Test material: XDE-742 **Purity(%):** 98%
Common name: Pyroxsulam
Chemical name:
IUPAC: N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide
CAS name: N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide

CAS No.: 422556-08-9
Synonyms: XDE-742/BAS 770 H/X666742

Primary Reviewer: David McAdam **Date:** 28/11/2006
Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA)
R. Murphy for D. McAdam 22/02/08

Secondary Reviewer(s): Jack Holland **Date:** 22/12/2006
(DEWHA)
22/2/08

Thomas Steeger, Ph.D., Senior Biologist 4/13/08 **Date:** 09/01/2007
U.S. Environmental Protection Agency, EFED, ERB 4

Martin LeMay, M.Sc., Evaluation Officer **Date:** 15/03/2007
Environmental Assessment Division, PMRA Louise Lavoie for Martin LeMay 05/03/08

Company Code: DWE
Active Code: JUA
Use Site Category: 13, 14
EPA PC Code: 108702

CITATION: Stafford, J. M. 2005. XDE-742– Dietary toxicity test with the northern bobwhite quail *(Colinus virginianus)*. Springborn Smithers Laboratories, Wareham. Dow AgroSciences, unpublished report, study No. 040028. 14th March 2005.

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EXECUTIVE SUMMARY:

The subacute dietary toxicity of pyroxsulam to 10-d old bobwhite quail *(Colinus virginianus)* was assessed over 8 days in accordance with the US EPA Avian Dietary Toxicity Test guidelines. Pyroxsulam was administered to the birds in the diet at 0 (control) and 5000 mg/kg diet nominal. The 8-day subacute dietary LC_{50} was >5000 mg/kg diet. The 8-day NOAEC of pyroxsulam based on mortality was 5000 mg/kg diet. Analysis showed that the mean concentration was 4883 mg ac/kg diet. According to the US EPA classification, pyroxsulam would be classified as practically non-toxic to bobwhite quail on a subacute dietary exposure basis based on a nominal concentration.

There were no compound-related toxicity effects (survival or sublethal) during this 8-day study.

This toxicity study is classified as acceptable for measuring the subacute dietary toxicity of pyroxsulam in bobwhite quail.

Results Synopsis

Test Organism Size/Age:	10 days old, mean weight of 17.1 g
LC_{50}:	>5000 mg/kg diet (nominal); 4883 mg ac/kg diet (measured) 4883 95% C.I.: applicable
NOAEC:	5000 mg/kg diet (nominal); 4883 mg ac/kg diet (measured).
Probit Slope:	Not applicable

Endpoint(s) Effected: There were no compound related effects (survival or sublethal) noted during this study. The dietary exposure of 5000 mg ac/kg diet was equivalent to a daily dose of >988 mg ac/kg bw/day.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: Springborn protocol "Northern bobwhite quail *(Colinus virginianus)* dietary toxicity test (LC50) with XR-742. Following OPPTS 850.2200 and OECD 205."

Springborn Smithers Laboratories Protocol No: 022304/OPPTS/OECD/Bobwhite LC_{50}

US-EPA protocol Testing of Chemicals 205 "Avian Dietary Toxicity Test" (OECD, 1984).

US EPA. 1996. Avian Dietary Toxicity Test, OPPTS 850.2200. Ecological Effects Test Guidelines.

COMPLIANCE: This study was conducted in accordance with the OECD principles of GLP. Signed and dated GLP and Quality Assurance statements were provided.

A. MATERIALS:

1. Test Material Pyroxsulam (XDE-742)

Description:	White powder
Lot No./Batch No. :	E0952-52-01
Purity:	98%
Stability of Compound Under Test Conditions:	The analytical analyses showed that pyroxsulam was stable in the feed over 14 days.
Storage Conditions of Test Chemicals:	Stored at room temperature

Physicochemical properties of XDE-742 *(from company's Study Profile Template report for this study of the dietary toxicity of pyroxsulam to the northern bobwhite quail)*

Parameter	Values	Comments
Water solubility at 20°C	pH 4 0.0164 g/L pH 6 0.0626 g/L pH 7 3.2 g/L pH 9 13.7 g/L	Turner (2004a) Turner (2004a) Turner (2004a) Turner (2004a)
Vapor pressure	$<1 \times 10^{-7}$ Pa at 20 °C	Madsen (2003)
UV absorption	NA	
pKa	4.670	Cathie (2004)
Kow	pH 4 0.097 pH 7 0.024 pH 9 12.1	Turner (2004b) Turner (2004b) Turner (2004b)

2. **Test organism**:

Species: Bobwhite Quail *(Colinus virginianus)*
Age at study initiation: 10 days
Weight at study initiation: mean weight of 17.1 g (12.8-21.8 g)
Source: Stevensons Quail Farm, Riverside, Texas

B. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding Study: The results of an acute oral study gave an LD_{50} >2000 mg/kg bw and, consequently, a limit test was selected for the definitive subacute dietary study with two groups; control and 5000 mg/kg feed.

b) Definitive Study

Table 1: Experimental Parameters

Parameter	Details	Remarks *Criteria*
Acclimation Period: Conditions (same as test or not): Feeding: Health (any mortality observed):	10 days before test Same as test Daily basal diet (Purina® Game Bird Stratena® Lot No. 063APR2804) Good health, mortality was zero.	Guideline conditions met. *US EPA and OECD requires at least 7 days of acclimation*
Pen size and construction materials	81 X 41 X 25 cm, polycarbonate-coated wire mesh.	Floor area 3320 cm^2 and gives 275 cm^2 per bird. Does not meet Guideline requirements. *EPA requires: about 35 x 100 x 24 cm; OECD requires: 300 cm^2 for bobwhite and 600 cm^2 for mallard*
Test duration	8 days test in total. 5 days of treated feed and 3 days of clean feed.	Guideline conditions met. *EPA/OECD requires: 5 days with treated feed and at least 3 days observation with "clean" feed.*
Test concentrations Nominal: Measured:	0 (control) and 5000 mg/kg feed 0 (control) and 4883 mg ac/kg feed	Acceptable for a limit test *Four minimum, 5 or 6 strongly recommended, in a geometric scale, unless LC_{50} > 5000 mg ai/kg diet.* Measured conc. should be 80% of the nominal
Solvent/vehicle, if used Type: Amount:	Acetone; 70 mL; 1.12% v/wt Corn oil, 98 mL; 1.6% v/wt (1.5% w/w)	Includes 20 mL of acetone as rinsate. Guideline conditions met. *EPA requires: Distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic. Solvent not more than 2%.*
Diet preparation and feeding	*Control diet:*	The study states that the acetone evaporated during mixing.

Parameter	Details	Remarks *Criteria*
	50 mL acetone; 98 mL corn oil; 20 mL rinsate; Basal diet (6 kg) *Treated diet:* As above + Test substance (30 g in 6 kg, 5000 mg/kg)	*EPA requires: Control group tested with diet containing the maximum amount of vehicle used in treated diets*
Was detailed description and nutrient analysis of the basal diet provided (Yes/No)	Yes	
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	Meets Guideline requirements
Feed withholding period	Not reported	Not a requirement of the US or OECD Guidelines
Number of birds per replicate/groups For vehicle control: For treated:	12 birds per replicate	*EPA requires: 10 birds each (strongly recommended)*
Number of replicates/group (if used) For negative control: For vehicle control: For treated:	2 replicates for control (24 birds) 1 replicate in treatment (12 birds)	
Test conditions Temperature: Relative humidity (%): Photoperiod:	25-32°C under brooder heaters 23-29°C within test room Humidity 31-63% 14 hours light and 10 hours darkness	Temperature acceptable according to US EPA 850.2200 and OECD Guidelines. Humidity below US and OECD Guideline requirements. *Brooder temperature:* *EPA: about 35°C (95°F)* *Room temperature:* *EPA: 22-27°C (71-81°F);* *OECD: range of 22-38 °C based on bird age and species (see OECD 205)* *Relative humidity:* *EPA: 30-80%* *OECD: 50-85% based on bird species (see OECD 205)* *Photoperiod:* *EPA: Minimum of 14 h of light* *OECD: 12-16 h of light*

Parameter	Details	Remarks *Criteria*
Reference chemical, if used Name: Concentration tested:	Not applicable	

2. Observations:

Table 2: Observations

Parameters	Details	Remarks *Criteria*
Parameters measured (mortality/body weight/ mean feed consumption/ others)	Mortality, body weight, feed consumption; morbidity/intoxication	*OECD : the mortality in the controls should not be exceed 10% at the end of the test.*
Indicate the stability and homogeneity of test chemical in the diet	Homogeneity: mean 99.4%; range 83.9-113% Stability: Day 5 = 100% Day 14: 101%	The test substance was well mixed in the diet and stable in the diet.
Indicate if the test material was regurgitated	Not reported	Study indicates no abnormal behavioral observations.
Treatments on which necropsies were performed	Postmortem examinations were conducted on 8 surviving birds from the control group and 4 from the treatment group.	Meets Guidelines requirements
Observation intervals	3 times on day 1 and twice daily thereafter	Meets Guidelines requirements
Were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. MORTALITY: No mortality occurred during the study. Therefore, the LC_{50} was empirically determined to be >5000 mg/kg feed. Based on mean feed consumption, concentration in diet and average body weights for day 0 and day 5, the study report indicates that 5000 mg/kg feed corresponds to 988 mg ac/kg bw/day (not required by Guideline).

Table 3: Effect of pyroxsulam (XDE-742) on mortality of Bobwhite quail.

Treatment Nominal 5000 mg/kg diet mean measured 4883 mg ac/kg diet	**No. of birds per treatment**	**Cumulative mortality**	
		day 5	**day 8**
Solvent/vehicle control	24	0	0
Test concentration	12	0	0
LC_{50}	>5000 mg/kg feed (nominal); >4883 mg/kg feed (mean measured)		
NOAEC	5000 mg/kg feed (nominal); 4883 mg/kg feed (mean measured)		
Reference chemical	Not applicable		

B. SUB-LETHAL TOXICITY ENDPOINTS:

No abnormal behavioral observations occurred during the study and no abnormal findings were noted during the post-mortem examinations. Mean changes in body weight were not significantly different among groups at any time during the study. There was no compound related toxicity effects (survival or sub-lethal), including feed consumption, during this 8 day study.

Table 4: Sublethal effects of pyroxsulam (XDE-742) on Bobwhite Quail.

Treatment Nominal 5000 mg/kg diet mean measured 4883 mg ac/kg diet	Observation							
	Body weight, g			Food consumption, g/day			Other endpoint	
	Day 0	Day 5	Day 8	Day 0	Day 5	Day 8	Day 0	Day 8
Control 1	17.5	30.2	39.6	4.2	5.8	7.2	NA	NA
Control 2	16.1	28.7	37.9	4.0	5.3	6.7	NA	NA
Test concentration 5000 mg ac/kg	17.8	31.8	40.0	4.5	5.7	7.6	NA	NA
EC_{50}	Not applicable (no adverse effects)							
NOAEC	5000 mg/kg feed (nominal); 4883 mg/kg feed (mean measured)							
Reference chemical	Not applicable							

C. REPORTED STATISTICS: Body weight data taken prior to start of treated feed was analyzed using Levene's Test for homogeneity of variance among cages. Statistical analyses were conducted to determine whether significant differences in change in body weight existed between the control and the treatment group. Body weight data sets were first checked for normality using Chi-square test and for homogeneity of variance using Bartlett's test. Dunnett's test was used for mean differences between the treatment group and the control group.

D. VERIFICATION OF STATISTICAL RESULTS BY THE REVIEWER: Statistics not analyzed. It could be determined visually that there were no adverse effects on body weight or food consumption.

Statistical Method:
LC_{50}: Not applicable
NOAEC: 5000 mg/kg feed (nominal); 4883 mg/kg feed (measured).
Probit Slope: Not applicable

E. STUDY DEFICIENCIES: No significant deficiencies noted. Minor deficiencies were:

- Study was conducted as a limit test but this is not included in the Guideline (see reviewer's comments).
- Floor space less than US EPA Guideline.

- Relative humidity less than in Guidelines (US EPA and OECD) requirements

These minor deficiencies did not affect the acceptability of the study.

F. REVIEWER'S COMMENTS: The study is a limit test but the test guideline used (US EPA OPPTS 850.2200) does not include reference to a limit test. Although not entirely consistent with US EPA Guideline requirements for testing multiple treatment concentrations, this limit test is a scientifically sound method for compounds with no toxicity to the test organisms and is consistent with OECD testing guidelines and as such is considered by the reviewer to be acceptable.

G. CONCLUSIONS: The study is classified as acceptable. The LD_{50} was >5000 mg/kg diet (nominal); 4883 mg ac/kg feed (measured) and the NOAEC was 5000 mg/kg (nominal); 4883 mg ac/kg feed (measured). Pyroxsulam is practically non-toxic to Bobwhite quail in this subacute dietary toxicity study based on the nominal concentration and, based on the mean measured NOAEC, at worst, slightly toxic.

III. REFERENCES:

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