Data Evaluation Report on the Acute Oral Toxicity of Pyroxsulam (XDE-742) to Avian Species Bobwhite quail (*Colinus virginianus*)

PMRA Submission Number 2006-4727 EPA MRID Number 469084-16 APVMA ATS 40362

Data Requirement:	PMRA Data Code	9.6.2.1 [DM1]
	EPA DP Barcode	D332116
	OECD Data Point	IIA 8.1.1
	EPA MRID	469084-16 [DM2]
	EPA Guideline	71-1 (850.2100)

Test material:	Pyroxsulam	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	

Primary Reviewer: David McAdam: **Date:** 15/12/2006
Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA)
R. Murphy for D. McAdam 22/02/08

Secondary Reviewer: Jack Holland **Date:** 21/12/06
(DEWHA)
22/2/08

Thomas Steeger, Ph.D., Senior Biologist **Date:** 08/01/2007
U.S. Environmental Protection Agency, EFED, ERB 4
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Brigitte Lavallée (No. 1595) PMRA EAD Date: 6/03/2007
Brigitte Lavallée for Brigitte Lavallée 05/03/08

PMRA study report document # 1283218

Company Code	DWE [For PMRA]
Active Code	JUA [For PMRA]
Use Site Category:	13 and 14 [For PMRA]
EPA PC Code	108702

CITATION: Zok, S. 2003. XDE-742/BAS 770 H – Avian Single-Dose LD_{50} [DM3] on the Bobwhite Quail (*Colinus virginianus*). BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany. Dow AgroSciences, unpublished report, BASF Study No. 11W0298/035027. 19th December 2003.

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EXECUTIVE SUMMARY:

The acute oral toxicity of XDE-742 to 5-month old Bobwhite Quail (*Colinus virginianus*) was assessed over 14 days in accordance with the US-EPA protocols OPP §71-1, OPPTS 850.2100, and EPA 721-C-96-139. Pyroxsulam was administered to the birds (5 males and 5 females per dose group) by gavage into the crop at nominal doses of 0 (control), 500, 1000 and 2000 mg ac/kg bw (mean measured doses of 0, 508, 1062, and 2105 mg ac/kg bw). The 14-day acute oral LD_{50} was > 2105 mg ac/kg bw. The 14 day NOEL/NOAEL of pyroxsulam to the Bobwhite Quail, based on mortality was ≥ 2105 mg ac/kg bw. According to the US EPA classification, pyroxsulam would be classified as practically non-toxic to Bobwhite Quail on an acute oral exposure basis. There were no compound related toxicity effects (survival or sublethal) during this 14-day study.

This toxicity study is classified as acceptable and is consistent with the guideline requirement for an acute oral toxicity study on the Bobwhite Quail.

Results Synopsis

Test Organism Size/Age:	5 months old (before their first egg-laying season), mean weight at day 0 was 189 g for males and 189 g for females.
LD_{50}:	> 2105 mg ac/kg bw 95% C.I: Not reported
NOEL/NOAEL:	2105 mg ac/kg bw
Endpoint(s) Effected:	There were no compound related effects (survival or sublethal) noted during this study.
Probit Slope:	Not applicable.

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 (EPA 540/9-82-0254) and United States Protection Agency. 1996. Avian Acute Oral Toxicity Test, OPPTS 850.2100. Ecological Effects Test Guidelines. EPA 721-C-96-139". No deviations from test guidelines or laboratory protocol.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with the U.S. EPA Good Laboratory Practice Standards (40 CFR Part 160).

A. MATERIALS:

1. Test Material Pyroxsulam (XDE-742)

Description: Solid, white beige
Lot No./Batch No. : E0952-52-01
Purity: 98% active constituent

Stability of compound under test conditions: Not reported (not required for an acute oral test).

Storage conditions of test chemicals: Stored at ambient temperature.

Physicochemical properties of XDE-742 *(from company's report)*

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 × 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: Northern bobwhite quail (*Colinus virginianus*)

Age at study initiation: Approximately 5 months old

Weight at study initiation: Male: mean:189 g; range 173-209 g
Female: mean 189 g, range 167-214 g

Source: H & E Küberich, Wiesentheid/Geesdorf, Germany

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding study: A range finding study was conducted prior to the definitive test. The results of this study indicated a LD_{50} >2000 mg ac/kg bw and, consequently, treatment levels of 500, 1000 and 2000 mg/kg were selected for the definitive test.

b. Definitive study

Table 1: Experimental Parameters

Parameter	Details	Remarks *Criteria*
Acclimation Period: Conditions: (same as test or not) Feeding: Health: (any mortality observed)	 18 days in laboratory and 7 days in before test Same as test Municipal water and commercial quail diet (a meal form provided by PROVIMI KLIBA SA, Kaiseraugst, Switzerland) *ad libitum* before and during test with the exception of a fasting period of about 15-20 h prior to dosing. Mortality during the last 3 days before dosing = 0%.	The birds were housed in the same cages as used in the test from arrival in the laboratory. Meets US EPA 850.2100 Guideline requirements *The recommended acclimation period is a minimum of 15 days. OECD recommends a minimum of 7 days.*
Pen size and construction materials	Stainless steel cages measuring 0.59 m length X 0.45 m width X 0.26 m height with wire mesh floors (10 X 15 mm, 0.27 m^2).	Floor area is 2655 cm^2 for 5 birds, 530 cm^2 per bird. Meets US EPA 850.2100 Guideline requirements. *Pen size and construction should conform to good husbandry practices and should not create crowding stress.* *OECD recommends that pens be suitable for the captive rearing of that species.*
Test duration	14 days	Meets requirements *Recommended test duration is one day for dosing and at least 14 days observation.*
Dose preparation [Indicate method of confirmation of dose]	The appropriate dose of test substance (mg) was mixed into 0.5% carboxymethyl cellulose (CMC) in bidistilled water.	
Mode of dose administration	Gavage into the crop	 *Gavage or gelatin capsule is recommended*

Parameter	Details	Remarks *Criteria*
Dose levels nominal: measured:	500, 100, and 2000 mg ac/kg bw. Since purity of the test substance was 98%, doses of 510, 1020 and 2041 mg ac/kg bw were given to birds to adjust for purity. 508, 1062, and 2105 mg ac/kg bw, representing 100, 104 and 103% of adjusted nominal doses, respectively.	Measurement of dose levels not a requirement for US EPA Guideline; acceptable. *Dose levels should be 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:	Carboxymethylcellulose (0.5%) 10 g of preparation/kg bw Representing 1% of bodyweight	*The test material should 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:	10 N/A 10 10	5 males and 5 females per treatment group. *Recommended number of birds in a treatment group is 10 and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	15-20 hours	*Food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photoperiod:	21°C ± 2°C 35-70% relative humidity 8 h light, 16 h dark, warm-light fluorescent lamps	Meets Guideline requirements. *The recommended photoperiod is 8 hours of light and 16 hours of dark.*
Reference chemical, if used name: concentrations tested:	Not applicable	

2. Observations:

Table 2: Observations

Criteria	Details	Remarks *Criteria*
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)	- Mortality - Clinical signs of toxicity - Mean feed consumption (g/bird/day) - Mean body weight	Meets Guideline requirements *Body weight should be measured at test initiation, on day 14 and at the end of the test if the test is extended beyond 14 days. Mortality should not be more than 10% in controls.* *Feed consumption should be measured as average daily food consumption.*
Indicate if the test material was regurgitated	No regurgitation was reported.	*Regurgitation is an indication that the dose was rejected. If this problem persists, the test should be repeated.*
Groups on which necropsies were performed	All surviving birds.	No abnormalities were detected in the surviving birds. *Gross necropsies should be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	Mortality and signs of toxicity: Determined three times on Day 0 and daily thereafter. Feed consumption: Determined Days 7 and 14 Body Weight: Days -0, 7, and 14	Meets Guideline requirements.
Were raw data included?	Yes	Meets US EPA 850.2100 Guideline requirements.

II. RESULTS AND DISCUSSION:

A. MORTALITY:

By 14 days, there were no mortalities in the control or treatment groups. The LD_{50} based on mortality was >2105 mg ac/kg bw and the NOEL/NOAEL was 2000 mg ac/kg bw (nominal) or 2105 mg ac/kg bw (mean, measured).

Table 3: Effect of Pyroxsulam on Mortality of Northern bobwhite quail, *Colinus virginianus*

Treatment (mg ac/kg bw)	No. of Birds	Cumulative Mortality		
		day 1	day 7	day 14
Control	10	0	0	0
500 (nominal) 508 (mean, measured)	10	0	0	0
1000 (nominal) 1062 (mean, measured)	10	0	0	0
2000 (nominal) 2105 (mean, measured)	10	0	0	0
NOEL/NOAEL	2000 (nominal) or 2105 (mean, measured) mg ac/kg bw			
LD_{50}	> 2000 (nominal) or >2105 (mean, measured) mg ac/kg bw			
Reference chemical	Not applicable.			

B. SUBLETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were observed. No adverse effects on bodyweight or feed consumption were observed. There were no statistically significant differences in bodyweight or feed consumption on any tested day. Liquid stools were observed in all test groups including control on the day of dosing. The study author considered this to be caused by fasting of the animals and was not considered to be a toxic effect. DEH notes this is acceptable as it does not appear to be due to the test compound but could be due to the solvent/vehicle used. The NOEL/NOAEL based on all sublethal endpoints was >2000 mg ac/kg bw (nominal) or >2105 mg ac/kg bw (mean, measured and corrected for method recovery).

No treatment-related findings were observed during necropsy.

Table 4: Sublethal Effects of Pyroxsulam on Northern bobwhite quail, *Colinus virginianus*

Mean Body Weight (g)						
Treatment (mg ac/kg bw) Nominal (mean, measured) results.	**Males**			**Females**		
	Day 0	**Day 7**	**Day 14**	**Day 0**	**Day 7**	**Day 14**
Control	190.16	198.56	200.2	188.96	196.38	198.06
500 (508)	189.50	201.96	205.10	191.52	201.02	204.16
1000 (1062)	189.36	199.96	203.18	188.52	199.84	202.52
2000 (2105)	188.30	200.50	205.08	185.22	196.46	199.90
NOEL/NOAEL	2000 (nominal) or 2105 (mean, measured) mg ac/kg bw			2000 (nominal) or 2105 (mean, measured) mg ac/kg bw		
EC_{50}	Not determined			Not determined		
Reference chemical	Not applicable					

Mean Feed Consumption, g/bird/day					
Treatment (mg ac/kg bw) Nominal (mean, measured) results)		**Males**		**Females**	
		Day 7	**Day 14**	**Day 7**	**Day 14**
Control		13	12	12	11
500 (508)		13	12	13	12
1000 (1062)		13	12	14	13
2000 (2105)		13	12	14	13
NOEL/NOAEL		2000 (nominal) or 2105 (mean, measured) mg ac/kg bw		2000 (nominal) or 2105 (mean, measured) mg ac/kg bw	
EC_{50}		Not determined		Not determined	
Reference chemical	effect NOEL/ NOAEL LD_{50}	N/A		N/A	

C. REPORTED STATISTICS:

No statistical calculation of the LD_{50} was performed since there were no mortalities. For body weight data a parametric one-way analysis of variance was done via the F-test (ANOVA). A comparison of each dose group with the control group was carried out via Dunnett's test for the hypothesis of equal means (two sided test).

D. VERIFICATION OF STATISTICAL RESULTS:

No verification of statistical results was performed as there were no mortalities and there was no adverse change in body weights or feed consumptions based on visual inspection nor reported by the study author.

LD_{50}: >2000 (nominal) or >2105 (mean, measured)mg ac/kg bw
95% C.I.: N/A

NOEL/NOAEL: 2000 (nominal) or 2105 (mean, measured)mg ac/kg bw

Probit Slope: Not applicable

E. STUDY DEFICIENCIES:

There were no study deficiencies.

F. REVIEWER'S COMMENTS:

The DEW reviewer's conclusions were identical to the study author's.

PMRA Comments
The PMRA EAD reviewer agrees with the conclusions reached by the study Author and the DEH reviewers.

G. CONCLUSIONS:

The study is scientifically sound and is consistent with US EPA Guideline 850.2100; the studyis classified as **ACCEPTABLE**. The NOEL/NOAEL is 2000 (nominal) 2105 (mean, measured) mg ac/kg bw based on all endpoints. The 14-day acute oral toxicity LD_{50} was estimated as >2000 (nominal) or 2105 (mean, measured) mg ac/kg bw, which categorizes pyroxsulam as practically non-toxic to Northern bobwhite quail on an acute oral exposure basis.

LD_{50}: >2000 (nominal) or >2105 (mean, measured) mg ac/kg bw 95% C.I.: N/A
Probit slope: Not determined 95% C.I.: N/A
NOEL/NOAEL: 2000 (nominal) or 2105 (mean, measured) mg ac/kg bw

Endpoint(s) Affected: None

PMRA Conclusions
The PMRA EAD considers this study scientifically valid and acceptable. This study satisfies the guideline requirements for an avian acute study with the Northern Bobwhite (DACO 9.6.2.1). For Northern Bobwhite exposed to Pyroxsulam (XDE 742), the LD50 is > 2105 mg ac/kg bw, and the NOEL is 2105 mg ac/kg bw. According to the US EPA classification, Pyroxsulam would be classified as practically non-toxic to Bobwhite Quail on an acute oral basis.

III. REFERENCES:

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