Data Evaluation Report on the acute oral toxicity of Pyroxsulam (XDE-742) to avian species Mallard Duck *(Anas platyrhynchos)*
PMRA Submission Number 2006-4727 EPA MRID Number 469084-17 APVMA ATS 40362

Data Requirement::	PMRA DATA CODE:	9.6.2.2
	EPA DP Barcode:	D332116
	OECD Data Point:	II A 8.1.1
	EPA Guideline:	71-1 (850.2100)

Test material: **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

Primary Reviewer: David McAdam: **Date:** 15/12/2006
Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA)
D Murphy for D. McAdam 22/02/07

Secondary Reviewer: Jack Holland **Date:** 21/12/2006
(DEWHA)
22/2/08

MS 4/3/08

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

: Brigitte Lavallée (No. 1595) PMRA EAD **Date:** 6/03/2007 [DM1]
Louise Lavallee 05/03/08
for Brigitte Lavallee

PMRA study report document # 1283220
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 [DM2]: XDE-742/BAS 770 H – Avian Single-Dose LD_{50} on the Mallard Duck *(Anas platyrhynchos)*. BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany. Dow AgroSciences, unpublished report, BASF Study No. 13W0298/035028. 19th December 2003.

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EXECUTIVE SUMMARY:

The acute oral toxicity of pyroxsulam to 4-month old mallard ducks *(Anas platyrhnchos)* 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 active constituent (ac)/kg bw (mean measured concentrations were 0, 518, 1034 and 2030 mg ac/kg bw). The 14-day acute oral LD_{50} was >2030 mg ac/kg bw. The 14-day NOEL (or NOAEL) of pyroxsulam to the Mallard Duck, based on mortality was 2030 mg ac/kg bw. According to the US EPA classification, pyroxsulam would be classified as practically non toxic to mallard ducks on an acute exposure oral basis.

There was 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 mallard duck.

Results Synopsis

Test Organism Size/Age:	4 month old (before their first egg-laying season), mean weight at day 0 was 1045 g for males and 952 g for females.
LD50:	>2030 mg ac/kg bw. 95% C.I: Not reported
NOEL/NOAEL:	2030 mg ac/kg bw
Probit Slope:	Not applicable

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: US-EPA protocol "Ecological Effects Branch, 1982, Pesticides Assessment Guidelines Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, EPA-540/9-82-024, pp 33-37, 71-1 Avian single dose oral LD50 test". "EPA Standard Evaluation Procedure (SEP); EPA-540/9-85-007 of June 1985". "United States Protection Agency. 1996. Avian Acute Oral Toxicity Test, OPPTS 850.2100. Ecological Effects Test Guidelines. EPA 721-C-96-139". No deviations of significance from test guidelines or laboratory protocol.

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:	Solid (powder, 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 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	$<1 \times 10^{-7}$ 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: Mallard Duck (*Anas platyrhnchos*)
Age at study initiation: 4 months old
Weight at study initiation: Males: mean of 1045 g (range 899-1265 g)
Females: mean of 952 g (range 773-1090 g)
Source: Geflügelhof Knerr, Rieschweiler-Mühlbach, 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 ac/kg bw were selected for the definitive test.

b) Definitive Study

Table 1. Experimental Parameters

Parameter	Details	Remarks *Criteria*
Period: Conditions (same as test or not): Feeding: Health (any mortality observed):	Arrival in the laboratory on 17 Sept 2003. Acclimation to the housing conditions of birds in an air-conditioned room in one flock on a sealed floor under monitored indoor and feed conditions from arrival onwards. Adaptation to the test cages from 24 Sept to 3 Oct 2003 (dosing). Municipal water and commercial duck diet (PROVIMI KLIBA SA, Kaiseraugst, Switzerland) *ad libitum* offered before and during test with the exception of a fasting period of about 15-20 hrs prior to dosing. Mortality during the last 3 days before dosing = 0%.	Adaptation to test cages was for 10 days, less than recommended. *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.*
Pen size and construction materials	Pens made of galvanized or stainless steel wire, with stainless steel floors (mesh size 10 X 10mm), floor area 1.3 X 0.65 m (about 0.85 m^2 for 5 birds), height 1.3 m; males and females were caged separately. One female from the nominal 1000 mg ac/kg bw dose group was caged separately during the last 4 days of the experiment as it was severely attacked by other birds	Cage size corresponds to 1700 cm^2 per bird and is acceptable. *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	One day of administration and 14 days of observations.	Meets guideline requirements *EPA requires a day for dosing and at least 14 days observation.*

		Remarks ***Criteria***
Dose preparation [Indicate method of confirmation of dose]	For each dose group 150 g of a preparation of the test substance in 0.5% carboxymethylcellulose (CMC) in demineralized water were prepared separately. Homogeneity and concentration control analysis of XDE-742 in CMC was carried out to confirm dose.	
Mode of dose administration	Gavage	*Gavage or gelatin capsule.*
Dose levels Nominal: Measured:	500, 1000 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). Mean analytically: 518, 1034 and 2030 mg ac/kg bw (representing ~104, ~103, and ~102% of adjusted nominal doses, respectively).	Dose levels acceptable. *EPA requires a minimum of 5 treatment levels unless LD_{50} is demonstrated to be greater than 2000 mg ai/kg bw*
Solvent/vehicle, if used Type: Amount/bw:	Carboxymethylcellulose (CMC) (0.5%)	Meets the Guideline requirements *EPA recommends that the test material be administered without a vehicle if possible. Maximum vehicle concentration 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:	Group 0 (carrier control): 5 male, 5 female Group 1: 5 male, 5 female Group 2: 5 male, 5 female Group 3: 5 male, 5 female	Meets the Guideline requirements *EPA recommends 10 birds per treatment group and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	Fasting period of 15-20 hours prior to dosing	Meets the Guideline requirements *EPA recommends that food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity:	21°C ± 2°C 35-70% relative humidity 8 h light, 16 h dark, warm-light	Meets the Guideline requirements *EPA recommends that a 10 h light/14 h dark photo-period.*

		Remarks
		Criteria
Photoperiod:	fluorescent lamps	
Reference chemical, if used Name: Concentrations tested:	Not used	

2. Observations:

Table 2: Observations

Parameters	Details	Remarks *Criteria*
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)	Mortality and clinical signs observed 3 times on the day of dosing and daily thereafter. Body weight measured at 0, 7 and 14 days after dosing. Mean feed consumption calculated from the weekly feed consumption / cage separately for male and female birds for the first and second week after dosing.	Meets the Guideline requirements *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	The birds were observed for regurgitation for at least 1 hr after dosing. No birds regurgitated test substance.	*Regurgitation is an indication that the doses was rejected. The test may have to be repeated if the problem persists.*
Groups on which necropsies were performed	No birds died during the study. All birds were sacrificed at the termination of the study. No abnormalities were detected in necropsies.	Meets the Guideline requirements *EPA recommends that gross necropsies be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	3 times on the day of dosing and daily thereafter for 14 days.	Meets the Guideline requirements
Were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

There was no mortality or sublethal effects in any control or treatment. The highest dose tested causing no mortality was 2000 mg ac/kg bw body weight (measured 2030 mg ac/kg bw) for males and females.

Table 3: Effect of Pyroxsulam (XDE-742) on mortality of Mallard Duck *(Anas platyrhynchos)*.

Treatment (mg ac/kg bw)	**No. of birds**	**Cumulative mortality**				
		day 1	**day 2**	**day 3**	**day 7**	**day 14**
Solvent/vehicle control	10	0	0	0	0	0
Test dose 518	10	0	0	0	0	0
Test dose 1034	10	0	0	0	0	0
Test dose 2030	10	0	0	0	0	0
LD_{50}	>2030 mg ac/kg bw					
NOEL/NOAEL	2030 mg ac/kg bw					
Reference chemical	Not applicable					

B. SUBLETHAL TOXICITY ENDPOINTS:

No toxic signs were observed in the control and all dose groups. No substance related impairment of feed uptake in comparison to the control was observed in any of the dose groups. There was no statistically significant substance related reduction of the body weights in any dose groups at days 7 and 14 (sacrifice) and the body weight development was not impaired in comparison to the control group. No abnormalities were detected in surviving birds.

Liquid stools were observed in all test groups including control about 1 hour following administration of the doses, and about 4 hours following administration of the doses for the 2070 mg ac/kg bw dose group only. The study author considered this to be caused by fasting of the animals and was not considered to be a toxic effect. This could be due to the solvent/vehicle used.

Table 4: Sublethal effect of Pyroxsulam (XDE-742) on Mallard Duck *(Anas platyrhynchos).*

Treatment (mg ac/kg bw)	**Observation**						
	Mean body weight for male and female, (g)			**Mean food consumption (g/bird/day) for male and female**			**other endpoint**
	day 0	**day 7**	**day 14**	**day 0**	**day 7**	**day 14**	**% affected**
Solvent/vehicle control	1046 923	1105 1019	1126 1069	-	179 159	222 149	nil
Test dose 518	1015 927	1099 1018	1104 1032	-	171 145	158 116	nil
Test dose 1034	1020 976	1091 1039	1139 1073	-	182 131	174 117	nil
Test dose 2030	1098 984	1162 1089	1231 1122	-	177 174	164 148	nil
ED_{50}	>2030 mg ac/kg bw						
NOEL/NOAEL	2030 mg ac/kg bw						
Reference chemical	Not applicable						

C. REPORTED STATISTICS: For body weight data a parametric one-way analysis of variance was done via the F-test (ANOVA) (Winer, 1971). A comparison of each dose group with the control group was carried out via Dunnett's test for the hypothesis of equal means.

D. VERIFICATION OF STATISTICAL RESULTS BY THE REVIEWER: The results of the ANOVA using the body weight data were verified as correct (Microsoft Excel), ie no statistically difference between control and each dose group.

Statistical Method:

LD_{50}: >2030 mg ac/kg bw No mortalities;
NOEL: 2030 mg ac/kg bw. No statistically difference in body weight
Probit Slope: n/a

E. STUDY DEFICIENCIES: No deviations from the Guideline (US EPA 850.2100) were noted except for one minor deviation which was adaptation to the test cages was 9 days rather than the required 10 days.

F. REVIEWERS COMMENTS: The reviewer's comments are the same as the study author's.

PMRA Comments
The PMRA EAD reviewer agrees with the conclusions reached by the study author and the DEW reviewers.

G. CONCLUSIONS: The study is classified as acceptable. The LD_{50} was >2070 mg ac/kg bw and the NOEC/NOAEL was 2030 mg ac/kg bw. Pyroxsulam is practically non-toxic to mallard duck in this acute oral toxicity study.

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 Mallard duck (DACO 9.6.2.2). For Mallard duck exposed to Pyroxsulam (XDE-742), the LD_{50} is > 2030 mg ac/kg bw, and the NOEL is 2030 mg ac/kg bw. According to the US EPA classification, Pyroxsulam would be classified as practically non-toxic to Mallard duck on an acute oral basis.

III. REFERENCES:

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VERIFICATION OF STATISTICAL ANALYSES

Males

	1029.1	1047.6	1201.2	1174.4
	1082.2	1198.2	1184.2	1259.5
Day 14	1263.8	1240.8	1022.1	1241.6
	1302.3	1080.1	1216.8	1438.7
	952.3	951.8	1071.4	1039.7

Females

	928.7	986.2	954.9	1006.8
Day 14	1134.7	993	1032	1169.4
	1162.2	1045.4	1143	1104.9
	1114	1234.5	1163.7	1234.3
	1005.1	901.2	1072.9	1094.5

Anova: Single Factor Males Day 14

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
control	5	5629.7	1125.94	22887.56
500	5	5518.5	1103.7	13626.11
1000	5	5695.7	1139.14	7549.998
2000	5	6153.9	1230.78	20965.73

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	46829.37	3	15609.79	0.960168	0.435456	3.238872

Within Groups	260117.6	16	16257.35
Total	306947	19	

Anova: Single Factor Females Day 14

SUMMARY

Groups	*Count*	*Sum*	*Average*	*Variance*
Control	5	5344.7	1068.94	9698.753
500	5	5160.3	1032.06	15478.27
1000	5	5366.5	1073.3	7188.665
2000	5	5609.9	1121.98	7294.437

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	20435.59	3	6811.863	0.687024	0.572995	3.238872
Within Groups	158640.5	16	9915.031			
Total	179076.1	19				