Data Evaluation Report on the Acute Oral Toxicity of Florasulam to Japanese Quail (*Coturnix japonica*)

PMRA Submission Number {.....} EPA MRID Number 468083-05

Data Requirement:

PMRA Data Code	9.6.2.3
EPA DP Barcode	D329529
OECD Data Point	{.....}
EPA MRID	468083-05
EPA Guideline	71-1

Test material: XDE-570 **Purity:** 99.2%
Common name florasulam
Chemical name: IUPAC 2',6',8-trifluoro-5-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidine-2-sulfonanilide
CAS name *N*-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidine-2-sulfonamide
CAS No. 145701-23-1
Synonyms

Primary Reviewer: Tamara Sheremata, Ph.D
PMRA **Date:** 8.15.2000

Primary Reviewer: Brian D. Kiernan, Biologist **Date:** 3.05.2007
EPA

Reference/Submission No.: {.....}

Company Code	{.....}	[For PMRA]
Active Code	{.....}	[For PMRA]
Use Site Category:	{.....}	[For PMRA]
EPA PC Code	129108	

Date Evaluation Completed: 2.28.2007

CITATION: Campbell, S.M., and J.B. Beavers (1994) XDE-570 An Acute Oral Toxicity Study with the Japanese Quail. Wildlife International Ltd., Easton, Maryland. Project number: 103-403, December 20, 1994. Unpublished.

DISCLAIMER: This document provides guidance for EPA and PMRA reviewers on how to complete a data evaluation record after reviewing a scientific study concerning the chronic toxicity of a pesticide to birds. It is not intended to prescribe conditions to any external party for conducting this study nor to establish absolute criteria regarding the assessment of whether the study is scientifically sound and whether the study satisfies any applicable data requirements. Reviewers are expected to review and to determine for each study, on a case-by-case basis, whether it is scientifically sound and provides sufficient information to satisfy applicable data requirements. Studies that fail to meet any of the conditions may be accepted, if appropriate; similarly, studies that meet all of the conditions may be rejected, if appropriate. In sum, the reviewer is to take into account the totality of factors related to the test methodology and results in determining the acceptability of the study.

2068741

EXECUTIVE SUMMARY:

The acute oral toxicity of technical XDE-570 to 8 week-old Japanese quail (*Coturnix japonica*) was assessed over 14 d. XDE-570 was administered to the animals by ingestion in corn oil as a single oral dose at nominal levels of 175, 292, 486, 810, 1350, and 2250 mg ai/kg bw. After dosing, male and female birds were separated and birds were held at 25.6 ± 1.5 °C and 77 ± 14% RH with photoperiod of 8 h light (253 lux):16 h dark and observed twice daily for 14 days. The study was conducted in accordance with Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, Section 71-1 and the EPA GLP standards.

The NOEL and LD_{50} of DE-570 to the Japanese quail were 175 and 1047 mg ai/kg bw, respectively. DE-570 would be considered slightly toxic to the DE-570 on an acute oral basis. Toxic affects were first observed at 292 mg a.i./kg, and evidently became more severe as dosing was increased to 2250 mg a.i./kg. Reported signs of toxicity were a ruffled appearance, lower limb weakness, wing droop, reduced reaction to sound and movement, prostrate posture, lethargy, opisthotonos, depression, loss of righting reflex, lower limb rigidity, shallow and rapid respiration, and walking stiffly. Mortality was 40, 60, and 100 % for 810, 1350, and 2250 mg a.i./kg dosages, respectively.

This toxicity study is classified acceptable and does contain sufficient information for the purpose of the guideline requirement for a avian acute oral toxicity study.

The PMRA DER is accepted in lieu of generating a new DER.

Results Synopsis

LD50: 1047 mg ai/kg bw
NOAEC: 175 mg ai/kg bw
Endpoint(s) Affected: survival

Appendix 9.6.2.3

PMRA Reviewer: Tamara Sheremata, Ph.D. **15-August-2000**

STUDY TYPE: Florasulam Oral LD_{50} Study;
PMRA DATA CODE: 9.6.2.3;
OECD Data Point IIA 8.1.1

TEST MATERIAL (PURITY): XDE-570 (Florasulam), 99.2 % pure.

SYNONYMS: XR-570 (1990-Jan. 1994), XDE-570 (Jan. 94 - Jan. 97), DE-570 (Feb. 1997-?), Florasulam.

CITATION: Campbell, S.M., and J.B. Beavers (1994) XDE-570 An Acute Oral Toxicity Study with the Japanese Quail. Wildlife International Ltd., Easton, Maryland. Project number: 103-403, December 20, 1994. Unpublished.

SPONSOR: The Dow Chemical Company, Health & Environmental Sciences, Environmental Toxicology & Chemistry Research Laboratory, Midland Michigan.

EXECUTIVE SUMMARY:

The acute oral toxicity of technical XDE-570 to 8 week-old Japanese quail (*Coturnix japonica*) was assessed over 14 d. XDE-570 was administered to the animals by ingestion in corn oil as a single oral dose at nominal levels of 175, 292, 486, 810, 1350, and 2250 mg ai/kg bw. After dosing, male and female birds were separated and birds were held at 25.6 ± 1.5 °C and 77 ± 14% RH with photoperiod of 8 h light (253 lux) : 16 h dark and observed twice daily for 14 days. The study was conducted in accordance with Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, Section 71-1 and the EPA GLP standards.

The NOEL and LD_{50} of DE-570 to the Japanese quail were 175 and 1047 mg ai/kg bw, respectively. DE-570 would be considered slightly toxic to the DE-570 on an acute oral basis.

Toxic affects were first observed at 292 mg a.i./kg, and evidently became more severe as dosing was increased to 2250 mg a.i./kg. Signs of toxicity were a ruffled appearance, lower limb weakness, wing droop, reduced reaction to sound and movement, prostrate posture, lethargy, opisthotonos, depression, loss of righting reflex, lower limb rigidity, shallow and rapid respiration, and walking stiffly. Mortality was 40, 60, and 100 % for 810, 1350, and 2250 mg a.i./kg dosages, respectively.

This toxicity study is classified acceptable and does satisfy the guideline requirement for a Japanese quail oral LD_{50} study (DATA CODE: 9.6.2.3).

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging

statements were provided. ?flagging statement?

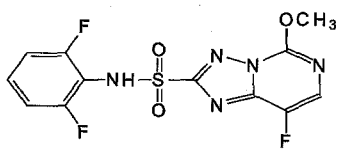
I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, Section 71-1.

A. MATERIALS:

1. Test Material: DE-570

Description: white powder received from The Dow Chemical Company on 24/2/94, grade and stability were not specified.
Lot/Batch #: WIL-2851
Purity: 99.2 % ai.5
Stability of compound: not specified
CAS #: 145701-23-1
IUPAC name: 2′,6′,8-trifluoro-5-methoxy-s-triazolo[1,5-c]pyrimidine-2-sulphonanilide
Structure:



2. Test organism:

Species: Japanese quail (*Coturnix japonica*)
Age at study initiation: 8 wks
Weight at study initiation: 139-195 g
Source: Northwest Gamebirds, Kennewick, Washington 99337-7012.
Housing: pen
Acclimation period: 17 d to caging and facilities 17 d prior to test initiation.

B. STUDY DESIGN:

1. Experimental conditions:

Table 1: Experimental conditions.

Criteria	Details	Remarks
Dose levels	175, 292, 486, 810, 1350, and 2250 mg a.i./kg	
Number of birds per dose	5 male and 5 female quail were assigned to each treatment group	
Number of birds in negative control group	5 male and 5 female	
Positive control (if used) *(chemical)*	not used	
Pen size	78 x 51 cm and 20-25 cm high	Each dosage group was assigned two pens. One pen contained 5 males and the other 5 females.
Photoperiod	8 h per day	Maintained during acclimation and throughout the test.
Temperature (°C)	25.6 °C ± 1.5 °C (SD)	
Relative humidity (%)	77 % ± 14 % (SD)	
Dose preparation	Test substance was dispersed in corn oil.	

2. Observations:

Table 2: Observations

Criteria	Details
Test duration	17 d acclimation 15 h fasting prior to test dosing (one event) Post-dosing observation-14 d
Test dates: start end	June 24, 1994 July 8, 1994
Observation intervals	Daily during acclimation. Twice daily following dosing
Observations at each time interval	mortality, signs of toxicity, and abnormal behaviour
Others	Body weights were measured individually at the initiation of the test and on Day 14. Feed consumption was determined for each dosing group.

Mortality data were analyzed using a computer program (developed by C.E. Stephan, 1978, U.S. EPA Environmental Research Laboratory, Duluth Minnesota). The program calculated the LD50 and the 95 % confidence interval by probit analysis.

II. RESULTS AND DISCUSSION:

A. Mortality:

Table 3: Effect of *chemical* on mortality of the [*common name*]. *[expand table to include all dose levels]*

Treatment	% Mortality in Observation period														
	0d	1d	2d	3d	4d	5d	6d	7d	8d	9d	10d	11d	12d	13d	14d
Negative control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
175 mg a.i./kg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
292 mg a.i./kg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
486 mg a.i./kg	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
810 mg a.i./kg	20	20	40	40	40	40	40	40	40	40	40	40	40	40	40
1350 mg a.i./kg	0	0	20	50	60	60	60	60	60	60	60	60	60	60	60
2250 mg a.i./kg	0	20	90	100	100	100	100	100	100	100	100	100	100	100	100
NOEL	175														
LD_{50} (95 % C.L.)	1046 (824-1337)														

B. Other toxicity endpoints:

Table 4: Effect of DE-570 on mean body weight and feed consumption of the Japanese Quail during acute oral toxicity study.

Treatment	sex	% increase in mean body weights between 0 and 14 days	Feed consumption (g/bird/day)	
			Days 0-7	Days 8-14
Negative control	M F	18 18	45 47	35 36
175 mg a.i./kg	M F	20 24	41 42	33 35
292 mg a.i./kg	M F	19 23	42 41	33 37
486 mg a.i./kg	M F	17 23	41 41	35 37
810 mg a.i./kg	M F	26 10	49 54	48 45
1350 mg a.i./kg	M F	14 18	23 28	46 49
2250 mg a.i./kg	M F	- -	- -	- -

- denotes mortality

Statistical tests were not conducted to determine differences in the averages reported in the above Table. However, it would appear that the increases in body weights were not effected by DE-570 dosing. Between 0 and 7 days, it appears that feed consumption was lower at the 1350 mg a.i./kg dose, as compared to the 0 to 810 mg a.i./kg dosages. However, between 8 and 14 days, there appears to be slightly greater feed consumption at 810 and 1350 mg a.i./kg dosages, as compared to the the 0 to 486 mg a.i./kg dosages. The possible increases in feed consumption just noted, do not appear to have resulted in overall increases in body weights.

C. Other effects:

There were no reported toxic affects in the control group and in the 175 mg a.i./kg dose group. Between 292 and 2250 mg a.i./kg dosing groups, signs of toxicity were a ruffled appearance, lower limb weakness, wing droop, reduced reaction to sound and movement, prostrate posture, lethargy, opisthotonos, depression, loss of righting reflex, lower limb rigidity, shallow and rapid respiration, and walking stiffly.

IV. Study deficiencies: There were no major deficiencies in this study.

Template author: *M. Segstro*
Template dated: *October 20, 1998*
Template name: *av-or-sp.wpd*

Study review filename: *X:\EDO\CRO\OECD\Review Exchange\MISC REVIEWS\Florasulam for EPA by DOW Request\Environment\9.6.2.3 (9621) Other avian species_oral.wpd*