Data Evaluation Report on the Acute Dietary Toxicity of AE F130060 Technical to Mallard Duck (*Anas Platyrhynchos*)

PMRA Submission Number EPA MRID Number 45386227

Data Requirement:

PMRA DATA CODE	
EPA DP Barcode	D284719
OECD Data Point	
EPA MRID	45386227
EPA Guideline	§71-2b

Test material: AE F 130060 Technical **Purity:** 94.6%
Common name: Mesosulfuron-methyl
Chemical name: IUPAC: Methyl 2-[3-(4,6-dimethoxyprimidin-2-yl)ureidosulfonyl]-4-methanesulfonamidomethylbenzoate
CAS name: Not reported
CAS No.: Not reported
Synonyms: Code: AE F130060 00 1C95 0001

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Staff Scientist, Dynamac Corporation

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Date: 8/22/03

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{EPA/OECD/PMRA}

Date:

Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: 122009

Date Evaluation Completed:

CITATION: Ebert, E. 1998. Mallard Duck Dietary LC_{50} Study. Unpublished study performed by Hoechst Marion Roussel Deutschland GmbH, Hattersheim, Germany. Laboratory Report No. 98.0436. Study submitted by Aventis CropScience, Research Triangle Park, NC. Study initiated May 7, 1998 and completed August 24, 1998.

EXECUTIVE SUMMARY:

The acute dietary toxicity of AE F130060 Technical (Mesosulfuron-methyl) to 10-day-old Mallard duck (*Anas Platyrhynchos*) was assessed over 8 days. AE F130060 Technical was administered to the birds in the diet at nominal concentrations of 0 (two negative control groups), 312.5, 625, 1250, 2500, and 5000 ppm. Mean-measured concentrations were <LOD (controls), 309. 650, 1150, 2325, and 4750 ppm.

No mortality was observed during the study. The acute dietary LC_{50} is >4750 ppm. which categorizes AE F130060 Technical (Mesosulfuron-methyl) as slightly toxic to Mallard duck on an acute dietary basis. There were no clinical signs of toxicity, effects on body weight, or gross abnormalities observed at terminal necropsy. Feed consumption was reduced (based on visual determination) during the treatment phase in all test groups compared to the controls. Feed consumption averaged 75.9 and 75.1 g/bird/day for the two negative control groups, and averaged 55.6, 50.6, 53.1, 47.2, and 57.9 g/bird/day for the 309, 650, 1150, 2325, and 4750 ppm groups, respectively. Consumption during the recovery period was comparable for all groups. Based on reduced feed consumption, the NOEC is <309 ppm.

This toxicity study is scientifically sound and fulfills the guideline requirements for an avian dietary study using the Mallard duck (§71-2b). This study is classified as CORE.

Results Synopsis

Test Organism Size/Age: 10-days old, 157.2 ± 19.8 g

LC_{50}: >4750 ppm
NOEC: <309 ppm
LOEC: 309 ppm
Endpoint(s) Affected: Feed consumption during the treatment phase.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The protocol followed procedures of the U.S. Environmental Protection Agency Pesticide Assessment Guidelines, Series 71-2 (1982) and OECD Draft Guideline for Testing of Chemicals "Avian Dietary Toxicity Test" (1984). The following deviations from §71-2 were noted:

1. Raw (individual) body weight and feed consumption data were not provided.
2. Specific details pertaining to treated feed preparation were not reported.

COMPLIANCE: Signed and dated GLP. Quality Assurance. and Data Confidentiality statements were provided. This study was conducted in accordance with OECD principles of GLP (p. 3).

A. MATERIALS:

1. Test Material AE F 130060 Technical (Mesosulfuron-methyl)

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Description:	Light beige powder
Lot No./Batch No.:	Pfl. 35316
Purity:	94.6%
Stability of Compound Under Test Conditions:	Stability of the test material in avian diet was assessed after 12 days of room temperature storage in treated feed prepared at 312.5 and 5000 ppm. Recoveries averaged 93-98% of nominal concentrations (p. 26). In addition, samples of each test level were analyzed for concentration verification after 12 days of deep frozen storage, just prior to test initiation. Recoveries averaged 92-104% of nominal concentrations (p. 27).
Storage conditions of test chemicals:	Stored at 25 ± 5°C in the dark.

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:	Mallard duck (*Anas platyrhynchos*)
Age at study initiation:	10 days
Weight at study initiation:	157.2 ± 19.8 g (individual data not provided)
Source:	Zuchtgeflugelhof B. Franzsander, Schoneck-Oberdorfelden, FRG

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: Conditions (same as test or not): Feeding: Health (any mortality observed):	3 days Same as test Water and Ssniff® Complete Diet for Ducks(Rearing) was provided *ad libitum*. No mortality occurred.	Diet composition is provided on p. 24.
Pen size and construction materials	Wire mesh cages, 81 x 78 x 22 cm.	*EPA requires: about 35 x 100 x 24 cm*
Test duration	5 days with treated feed, and 3 days with"clean" feed.	*EPA requires: 5 days with treated feed and at least 3 days observation with "clean" feed.*
Test concentrations nominal: measured:	0 (negative controls), 312.5, 625, 1250, 2500, and 5000 ppm <LOD (controls), 309, 650, 1150, 2325, and 4750 ppm	Mean-measured concentrations were reviewer-calculated from data provided on p. 27. Batches had been stored deep frozen for 12 days prior to analysis. *Four minimum, 5 or 6 strongly recommended, in a geometric scale, unless LC_{50} > 5000 ppm.*
Solvent/vehicle, if used type: amount:	N/A N/A	*EPA requires: Distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic. Solvent not more than 2%.*

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Parameter	Details	Remarks *Criteria*
Diet preparation and feeding	5 kg final mixtures of each concentration were prepared and stored deep frozen for 12 days prior to study initiation (not further specified).	Homogeneity was assessed at the low and high levels on the day of preparation, stability was assessed at the low and high levels after 12 days of room temperature storage, and concentration verification was assessed at all levels after 12 days of deep frozen storage. *EPA requires: Control group tested with diet containing the maximum amount of vehicle used in treated diets?*
Feed withholding period	None	
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	
Number of birds per replicate/group for negative control: for vehicle control: for treated:	 10 N/A 10	 *EPA requires: 10 (strongly recommended)*
Number of replicates/group (if used) for negative control: for vehicle control: for treated:	 2 N/A 1	
Test conditions temperature: relative humidity(%): photoperiod:	 Brooder: 28-33°C Room: 21-24°C 60-80% 17 hours light/7 hours dark	The light intensity in the cage was approximately 100-300 lux. ***Brooder temperature:*** *about 35°C (95°F)* ***Room temperature:*** *22-27°C (71-81°F)* ***Relative humidity:*** *30-80%* ***Photoperiod:*** *Minimum of 14 h of light.*
Reference chemical, if used	None used.	

2. Observations:

Table 2: Observations

Criteria	Details	Remarks *Criteria*
Parameters measured (mortality/body weight/ mean feed consumption/ others)	- Mortality - Clinical signs of toxicity - Mean feed consumption (g/bird/day) - Body weight - Necropsy	
Indicate the stability and homogeneity of test chemical in the diet	Stability: Stability of the test material in avian diet was assessed after 12 days of room temperature storage in treated feed prepared at 312.5 and 5000 ppm. Recoveries averaged 93-98% of nominal concentrations (p. 26). Homogeneity: Homogeneity was assessed on the day of preparation in treated feed prepared at 312.5 and 5000 ppm. Three samples were collected from each of the prepared batches. Coefficients of Variation (C.V.) were 1.0% for the 312.5 ppm level and 5.2% for the 5000 ppm level (reviewer-calculated from data provided on p. 26).	In addition, samples of each test level were analyzed for concentration verification after 12 days of deep frozen storage, just prior to test initiation. Recoveries averaged 92-104% of nominal concentrations (p. 27).
Indicate if the test material was regurgitated	Regurgitation was not reported.	
Treatments on which necropsies were performed	None	

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Observation intervals	Mortality and signs of toxicity were measured at least once daily (twice daily during work-days). Food consumption was recorded on Days 1-6 and 6-9. Body weights were determined on Days 1, 6, and 9.	The day of treatment was Day 1.
Were raw data included?	Raw data were included.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality occurred during the 8-day study (Table 1, p. 17).

Table 3: Effect of AE F130060 Technical on mortality of *Anas platyrhynchos*.

Treatment, ppm mean-measured (and nominal)		No. of birds per treatment	Cumulative mortality								
			Days								
			1	2	3	4	5	6	7	8	9
Negative control		20	0	0	0	0	0	0	0	0	0
309 (312.5)		10	0	0	0	0	0	0	0	0	0
650 (625)		10	0	0	0	0	0	0	0	0	0
1150 (1250)		10	0	0	0	0	0	0	0	0	0
2325 (2500)		10	0	0	0	0	0	0	0	0	0
4750 (5000)		10	0	0	0	0	0	0	0	0	0
NOEC		4750 ppm									
LC_{50}		>4750 ppm									
Reference chemical	mortality	N/A									
	LC_{50}	N/A									
	NOEC	N/A									

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B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were observed during the study (Table 2, pp. 18-19), and no effect on body weight was observed (Table 3, p. 20). Based on visual inspection, food consumption was lower during the treatment period in all test groups compared to the two control groups (Tables 4-5, pp. 21-22). Intake was comparable to controls during the recovery phase. The study author reported that in the absence of any dose-dependent relationship and impairment of body weight, that these differences were not biologically significant (p. 15). No gross abnormalities were observed upon terminal necropsy (Table 6, p. 23).

Table 4: Sublethal effects of AE F130060 Technical on *Anas platyrhynchos*.

Treatment, ppm mean measured (and nominal)		Observation				
		Mean body weight (g)			Food consumption (g/bird/day)	
		Day			Day	
		1	6	9	1-6	6-9
Negative control		161.7	282.2	367.1	75.9	81.1
Negative control		162.6	285.7	367.3	75.1	81.0
309 (312.5)		158.8	289.8	350.9	55.6	76.7
650 (625)		156.9	279.0	316.0	50.6	65.6
1150 (1250)		142.7	264.9	334.3	53.1	69.7
2325 (2500)		154.7	279.2	352.7	47.2	75.1
4750 (5000)		163.1	316.3	391.4	57.9	80.7
NOEC		<309 ppm				
EC_{50}		Not determined				
Reference chemical	NOEC	N/A				
	EC_{50}	N/A				

C. REPORTED STATISTICS:

Because there were no mortalities or sublethal effects, the NOEC was visually determined.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical analyses were not required for mortality, as this endpoint could be visually determined. Replicate data were not provided for body weight or food consumption, and these endpoints could not be statistically verified.

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LC_{50}: >4750 ppm
NOEC: <309 ppm
LOEC: 309 ppm
Endpoint(s) Affected: Feed consumption during the treatment phase.

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA guideline §71-2 that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions generally agreed with the study authors'. Although the reviewer agrees that the differences in feed consumption may not be biologically significant, the effects were not dismissed and considered to be a treatment-related effect.

Since the highest mean-measured concentration was below the required limit level of 5000 ppm, a more conservative Toxicity Category was assigned.

Based on the feed consumption and concentration in the diet, the mean daily uptake of the test compound was calculated (Table 5, p. 22). Uptake of AE F130060 Technical averaged 77.5, 145.1, 236.3, 545.0, and 1210.0 mg/kg bw/day for the 312.5, 625, 1250, 2500, and 5000 ppm groups, respectively.

G. CONCLUSIONS:

This toxicity study is scientifically sound and fulfills the guideline requirements for an avian dietary LC_{50} study using the Mallard duck (§71-2b). There were no significant effects of AE F130060 Technical on mortality or body weight. Food consumption was reduced at all test levels compared to the controls during the treatment phase; intake was comparable to controls during the recovery phase. No clinical signs of toxicity were observed, and necropsy revealed no gross abnormalities. The acute dietary LD_{50} was >4750 ppm, which categorizes AE F130060 Technical (Mesosulfuron-methyl) as slightly toxic to Mallard duck.

LC_{50}: >4750 ppm
NOEC: <309 ppm
LOEC: 309 ppm
Endpoint(s) Affected: Feed consumption during the treatment phase.

III. REFERENCES:

A reference list was not provided.

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