Data Evaluation Report on the Acute Oral Toxicity of AE F130060 Technical on Northern Bobwhite Quail (*Colinus Virginianus*)

PMRA Submission Number EPA MRID Number 45386224

01/09/04

Data Requirement:

PMRA DATA CODE	
EPA DP Barcode	D284719
OECD Data Point	
EPA MRID	45386224
EPA Guideline	§71-1

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

Primary Reviewer: Rebecca Bryan
Staff Scientist, Dynamac Corporation

Signature: Rebecca Bryan
Date: 8/22/03

QC Reviewer: Christie E. Padova, B.S.
Staff Scientist, Dynamac Corporation

Signature: C.E. Padova
Date: 8/22/03

Primary Reviewer: ~~Tim Bargar~~ Leo LaSota, Biologist
OPP/EFED/ERB - III

Date: 01/09/04 Leo LaSota

Secondary Reviewer(s):
{EPA/OECD/PMRA}

Date:

Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: 122009

Date Evaluation Completed:

Limit test only 10 birds tested ~~supplemental~~ ?

CITATION: Ebert, E. 1998. Bobwhite Quail Acute Oral Toxicity Test. Unpublished study performed by Hoechst Marion Roussel Deutschland GmbH, Frankfort, Germany. Laboratory Report No. 98.0450. Study submitted by Aventis CropScience, Research Triangle Park, NC. Study initiated April 14, 1998 completed June 24, 1998.

EXECUTIVE SUMMARY:

The acute oral toxicity of AE F130060 Technical (Mesosulfuron-methyl) to 8-month old Northern Bobwhite quail (*Colinus virginianus*) was assessed over 14 days. AE F130060 Technical was administered to the birds by oral gavage at nominal concentrations of 0 and 2000 mg/kg bw (limit dose).

No mortality was observed during the study. The acute oral LD_{50} is >2000 mg/kg, which categorizes AE F130060 Technical (Mesosulfuron-methyl) as practically non-toxic to Bobwhite quail on an acute oral basis. In addition, there were no clinical signs of toxicity, or treatment-related effects on body weight or food consumption, and terminal necropsy revealed no gross abnormalities. The NOEL was 2000 mg/kg.

Significant reduced food consumption for treated Males

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Northern Bobwhite quail (§71-1). This study is classified as CORE.

Results Synopsis

Test Organism Size/Age: 8-months old, 187-220 g (combined sexes)

LD_{50}: >2000 mg/kg
NOEL: <2000 mg/kg based on reduced (5%) food consumption in males
LOEL: >2000 mg/kg
Endpoint(s) Affected: None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The protocol followed procedures of the U.S. Environmental Protection Agency Pesticide Assessment Guidelines, Series 71-1 (1982) and OECD Draft Guideline for Testing of Chemicals "Avian Acute Toxicity Test-Oral Toxicity" (1992). The following deviations from §71-1 were noted:

1. The pre-test health observations of the birds (including mortality) was not described.
2. The photoperiod of 8-hours light/16-hours dark was less than recommended (10-hours light/14-hours dark).
3. Number of birds Tested ? Limit Test

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)

Description: Light beige powder

Lot No./Batch No.: Pfl. 35316

2

Table 1. Experimental Parameters.

Parameter	Details	Remarks *Criteria*
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	2 weeks Same as test Ssniff® Complete Diet for Ducks (Breeding) was provided *ad libitum*, except during 15 hours prior to testing. Not reported	*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	180 x 300 cm pens with smooth concrete floors (not otherwise specified)	*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	14 Days	*EPA requires a day for dosing and at least 14 days observation.*
Dose preparation Indicate method of confirmation of dose	The test substance was mixed into solution with deionized water as the vehicle. N/A	
Mode of dose administration	Gavage	*Gavage or gelatin capsule.*

4

Parameter	Details	Remarks *Criteria*
Dose levels nominal: measured:	0 and 2000 mg/kg of body weight N/A	*EPA requires 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:	Deionized water N/A	*EPA recommends that the test material 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:	 N/A 10 10	This was a single dose limit test *EPA recommends 10 birds per treatment group and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	Birds were fasted for at least 15 hours prior to dosing and 2 hours following dosing.	*EPA recommends that food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photo-period:	 20°C 30-50% 8-hours light/16-hours dark.	*EPA recommends that a 10 hr light/14 hr dark photo-period.*
Reference chemical, if used name: concentrations tested:	None used.	

5

2. Observations:

Table 2: Observations.

Parameter	Details	Remarks/Criteria
Parameters measured		
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/others)	- Mortality - Clinical signs of toxicity - Individual body weight - Average feed consumption - Necropsy	*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	No regurgitation was reported.	*Regurgitation is an indication that the dose was rejected. The test may have to be repeated if the problem persists.*

Parameter	Details	Remarks/Criteria
Groups on which necropsies were performed	All birds from the control and treatment group were subject to a gross pathological examination.	*EPA recommends that gross necropsies be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	Mortality: Daily Signs of Toxicity: Determined three times during the first hour, every two hours during the first six hours, and daily thereafter. Body Weight: Days 1, 4, 8, and 15. Feed consumption: Days 1-4, 4-8, and 8-15.	Where Day 1 is the day of dosing.
Were raw data included?	Raw data were included for feed consumption and body weight.	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality occurred during the study (Table 1, p. 14)

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

Treatment (mg/kg bw)		No. of birds	Cumulative mortality[1]							
			day 1	day 3	day 5	day 7	day 9	day 11	day 13	day 15
Control		10	0	0	0	0	0	0	0	0
2000 (limit dose)		10	0	0	0	0	0	0	0	0
NOEL		2000 mg/kg								
LD_{50}		>2000 mg/kg								
Reference chemical	mortality	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	LD_{50}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NOEL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

[1] Where Day 1 is the day of dosing.

B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity, or treatment-related effects on body weight or food consumption were observed Tables 2-4, pp. 15-18). In addition, post-mortem examination revealed no treatment-related findings (Table 5, p. 19).

Table 4: Sub-lethal effects of AE F130060 on *Colinus virginianus*.

Mean Body Weight, g[1]					
Treatment, mg/kg bw		**Males**		**Females**	
		Day 1	**Day 15**	**Day 1**	**Day 15**
Control		1250	1308	1072	1152
2000 (limit dose)		1278	1369	1068	1191
NOEL		2000 mg/kg			
EC_{50}		>2000 mg/kg			
Reference chemical	effect: NOEL: LD_{50}	N/A	N/A	N/A	N/A

[1] Where Day 1 is the day of dosing.

Mean Feed Consumption, g/bird/day[1]				
Treatment, mg/kg bw		**Days 1-4**	**Days 4-8**	**Days 8-15**
Control		203	161	191
2000		203	172	159
NOEL		2000 mg/kg		
EC_{50}		>2000 mg/kg		
Reference chemical	effect NOEL LD_{50}	N/A		N/A

[1] Where Day 1 is the day of dosing.

C. REPORTED STATISTICS:

Because there were no mortalities or sublethal effects, the LD_{50} and NOEL were visually determined.

9

D. VERIFICATION OF STATISTICAL RESULTS:

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

LD_{50}: >2000 mg/kg
NOEL: 2000 mg/kg
LOEL: >2000 mg/kg
Endpoint(s) Affected: None

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA guideline §71-1 that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions agreed with the study authors'.

G. CONCLUSIONS:

This toxicity study is scientifically sound, fulfills the guideline requirements for an acute toxicity study using the Mallard duck (§71-1), and is classified CORE. There were no significant effects of AE F130060 Technical on mortality, body weight, or food consumption. No clinical signs of toxicity were observed, and necropsy revealed no gross abnormalities. The 14-day LD_{50} was >2000 mg/kg bw, which categorizes AE F130060 Technical (Mesosulfuron-methyl) as practically non-toxic to Mallard duck.

LD_{50}: >2000 mg/kg
NOEL: 2000 mg/kg
Endpoint(s) Affected: None

III. REFERENCES:

A reference list was not provided.

Purity: 94.6%

Stability of Compound Under Test Conditions: Analysis of trial mixes (5 and 25%, w:v) were stable and homogeneous over 4 hours, with recoveries of 95-98% of nominal (p. 12).

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: Bobwhite quail (*Colinus virginianus*)

Age at study initiation: Approximately 8 months old

Weight at study initiation: 188-220 g (males) and 187-219 g (females)

Source: Morris Quail Farm, Goulds, Florida

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:	2 weeks	
Conditions (same as test or not):	Same as test	
Feeding:	Ssniff® Complete Diet for Quails was provided *ad libitum*, except during 15 hours prior to testing.	*EPA recommends that birds be pre-conditioned to the test facilities for at least 15 days:*
Health (any mortality observed):	Not reported Probably observations	*OECD recommends that birds be pre-conditioned to the test facilities for at least 7 days.*

Parameter	Details	Remarks *Criteria*
Pen size and construction materials	Wire-mesh cages; 81 cm long, 78 cm wide, and 22 cm high.	eliminate *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	14 Days	*EPA requires a day for dosing and at least 14 days observation.*
Dose preparation Indicate method of confirmation of dose	The test substance was mixed into solution with deionized water as the vehicle. N/A	
Mode of dose administration	Gavage	*Gavage or gelatin capsule.*
Dose levels nominal: measured:	0 and 2000 mg/kg of body weight N/A	This was a single treatment limit test *EPA requires 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:	Deionized water N/A	*EPA recommends that the test material be administered without a vehicle if possible. Maximum vehicle should not exceed 0.1 to 1.0% of body weight.*

Parameter	Details	Remarks / *Criteria*
Number of birds per groups/treatment for negative control: for solvent/vehicle control: for treated:	N/A 10 10	This was a limit test with only 10 birds treated *EPA recommends 10 birds per treatment group and 10 birds for each control and vehicle group.*
No. of feed withholding days before dosing	Birds were fasted for at least 15 hours prior to dosing and 2 hours following dosing.	*EPA recommends that food should be withheld for at least 15 hours prior to dosing.*
Test conditions Temperature: Relative humidity: Photo-period:	20˚C 50-70% 8-hours light/16-hours dark.	*EPA recommends that a 10 hr light/14 hr dark photo-period.*
Reference chemical, if used name: concentrations tested:	None used.	

2. Observations:

Table 2: Observations.

Parameter	Details	Remarks/Criteria
Parameters measured		
Parameters measured (mortality/individual body weight at test initiation and termination, mean feed consumption/others)	- Mortality - Clinical signs of toxicity - Individual body weight - Average feed consumption - Necropsy	*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.*

Parameter	Details	Remarks/Criteria
Indicate if the test material was regurgitated	No regurgitation was reported.	*Regurgitation is an indication that the dose was rejected. The test may have to be repeated if the problem persists.*
Groups on which necropsies were performed	All birds from the control and treatment group were subject to a gross pathological examination.	*EPA recommends that gross necropsies be performed with inspections of the GI tract, liver, kidneys, heart, and spleen.*
Observation intervals	Mortality: Daily Signs of Toxicity: Determined three times during the first hour, every two hours during the first six hours, and daily thereafter. Body Weight: Days 1, 4, 8, and 15. Feed consumption: Days 1-4, 4-8, and 8-15.	Where Day 1 is the day of dosing.
Were raw data included?	Raw data were included for feed consumption and body weight.	

6

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality occurred during the study (Table 1, p. 14)

Table 3: Effect of AE F130060 Technical on mortality of *Colinus virginianus*.

Treatment (mg/kg bw)		No. of birds	Cumulative mortality[1]							
			day 1	day 3	day 5	day 7	day 9	day 11	day 13	day 15
Control		10	0	0	0	0	0	0	0	0
2000 (limit dose)		10	0	0	0	0	0	0	0	0
NOEL		2000 mg/kg								
LD_{50}		>2000 mg/kg								
Reference chemical	mortality	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	LD_{50}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	NOEL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

[1] Where Day 1 is the day of dosing.

B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity, or treatment-related effects on body weight or food consumption were observed Tables 2-4, pp. 15-18). In addition, post-mortem examination revealed no treatment-related findings (Table 5, p. 19).

Table 4: Sub-lethal effects of AE F130060 on *Colinus virginianus*.

Mean Body Weight, g[1]					
Treatment, mg/kg bw		**Males**		**Females**	
		Day 1	**Day 15**	**Day 1**	**Day 15**
Control		211	217	194	195
2000 (limit dose)		201	207	203	204
NOEL		2000 mg/kg			
EC_{50}		>2000 mg/kg			
Reference chemical	effect: NOEL: LD_{50}	N/A	N/A	N/A	N/A

[1] Where Day 1 is the day of dosing.

Mean Feed Consumption, g/bird/day[1]							
Treatment, mg/kg bw		**Males**			**Females**		
		Days 1-4	**Days 4-8**	**Days 8-15**	**Days 1-4**	**Days 4-8**	**Days 8-15**
Control		40.4	40.4	39.9	34.0	34.1	45.3
2000		21.9	21.9	26.9	29.9	29.9	45.2
NOEL		2000 mg/kg					
EC_{50}		>2000 mg/kg					
Reference chemical	effect NOEL LD_{50}	N/A	N/A	N/A	N/A	N/A	N/A

[1] Where Day 1 is the day of dosing.

C. REPORTED STATISTICS:

Because there were no mortalities or sublethal effects, the LD_{50} and NOEL were visually determined.

4

D. VERIFICATION OF STATISTICAL RESULTS:

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

LD_{50}: >2000 mg/kg
NOEL: 2000 mg/kg
LOEL: >2000 mg/kg
Endpoint(s) Affected: None

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA guideline §71-1 that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions agreed with the study authors'.

G. CONCLUSIONS:

This toxicity study is scientifically sound, fulfills the guideline requirements for an acute toxicity study using the Northern Bobwhite quail (§71-1), and is classified CORE. There were no significant effects of AE F130060 Technical on mortality, body weight, or food consumption. No clinical signs of toxicity were observed, and necropsy revealed no gross abnormalities. The 14-day LD_{50} was >2000 mg/kg bw, which categorizes AE F130060 Technical (Mesosulfuron-methyl) as practically non-toxic to Northern Bobwhite quail.

LD_{50}: >2000 mg/kg
NOEL: 2000 mg/kg
Endpoint(s) Affected: None

III. REFERENCES:

A reference list was not provided.

Page ___ is not included in this copy.

Pages 10 through 24 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.