

**Data Evaluation Report on the Acute Dietary Toxicity of Pyrasulfotole to Avian Species
{*Colinus virginianus*}**

PMRA Submission Number 2006-2445

EPA MRID Number 468017-30

Data Requirement:	PMRA Data Code	9.6.2.4
	EPA DP Barcode	D328639
	OECD Data Point	IIA 8.1.2
	EPA MRID	468017-30
	EPA Guideline	850.2200

Test material: Pyrasulfotole

Purity: 95.4%

Common name: AE 0317309**Chemical name:** IUPAC: (5-hydroxy-1,3-dimethylpyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone
CAS name: Not reported
CAS No.: Not reported
Synonyms: Not reported**Primary Reviewer:** Rebecca Bryan
Staff Scientist, Dynamac Corporation**Signature:** *Rebecca L. Bryan*
Date: 5/17/06**Secondary Reviewer:** Teri S. Myers
Senior Scientist, Cambridge Environmental Inc.**Signature:** *Teri S. Myers*
Date: 5/22/06**Primary Reviewer:** Melissa Panger
EPA**Date:** 7-7-06**Secondary Reviewer:** J.D. Whall (Officer No. 1268)
PMRA**Date:** 11/21/06**Secondary Reviewer(s):** David McAdam
Australian Government Department of the Environment and Heritage (DEH).**Date:** 6 Nov 2006**Reference/Submission No.:** {.....}**Company Code** BCZ
Active Code PSA
Use Site Category: 13, 14
EPA PC Code 000692**Date Evaluation Completed:** 11-27-2006

CITATION: Stoughton, T.L. 2005. Technical AE0317309: A Subacute Dietary LC₅₀ with Northern Bobwhite. Unpublished study performed by Bayer Corporation, Agriculture Division, Research and Development Department, Environmental Research and Toxicology, Stilwell, Kansas. Study No. A9721701/EBAIM002. Study sponsored by Bayer CropScience, Research Triangle Park, NC. The final report issued October 3, 2005.

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 acute dietary toxicity of a pesticide to avian species. 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



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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.

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EXECUTIVE SUMMARY:

The acute dietary toxicity of Pyrasulfotole to 10-day old Northern bobwhite quail, *Colinus virginianus*, was assessed over 8 days (5 days on treated feed and 3 day recovery period). Pyrasulfotole was administered to the birds in the diet at mean measured concentrations of 591, 1247, 2813, and 4911 mg a.i./kg of diet (mean daily dietary dose = 58, 109, 232, 517, and 892 mg a.i./kg bw, respectively). The acute dietary LC₅₀ was >4911 mg ai/kg diet. The NOEC based on all endpoints was ≥4911 mg a.i./kg diet. According to the US EPA classification, Pyrasulfotole would be classified as practically non-toxic to Northern bobwhite quail on an acute dietary basis.

There were no mortalities in the control or treatment groups. No treatment-related clinical signs of toxicity were observed during the study. There were no effects on body weights or feed consumption during the study.

This toxicity study is scientifically sound, is classified as **ACCEPTABLE**, and does satisfy the guideline requirement for acute dietary toxicity study for Northern bobwhite quail.

Results Synopsis

Test Organism Size/Age (Mean Weight): 10 days old, 29.8-31.1 g (treatment means) and 25.6-34.7 g (range)

LC₅₀: >4911 mg ai/kg diet 95% C.I.: N/A

NOAEC: ≥4911 mg a.i./kg diet

Probit Slope: Not calculable 95% C.I.: N/A

Endpoint(s) affected: None

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I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was based on procedures of the EPA 71-2, OPPTS 850.2200 and OECD Guideline No. 205. The following deviations from U.S. Environmental Protection Agency Series 850-Ecological Effects Test Guidelines (*draft*), OPPTS Number 850.2200, *Avian dietary toxicity test* were noted:

No deviations were noted.

COMPLIANCE: Signed and dated GLP, Quality Assurance and No Data Confidentiality statements were provided. The test was conducted according to the US EPA-FIFRA Good Laboratory Practice (40 CFR Part 160).

A. MATERIALS:

1. Test Material Pyrasulfotole (AE 0317309)

Description: Light brown powder

Lot No./Batch No. : OP 1-4

Purity: 95.4%

Stability of Compound Under Test Conditions: Stability of the test material was determined in the 313 and 5000 mg a.i./kg feed after one day. The recoveries were 88-97% of the initial concentrations.

Storage Conditions of Test Chemicals: Stored under ambient conditions ($25 \pm 5^{\circ}\text{C}$).

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Physicochemical properties of Pyrasulfotole

Parameter	Value	Comment
Molecular weight	362.3 g/mol	
Water Solubility (g/L) at 20°C	4.2 at pH 4 69.1 at pH 7 49.0 at pH 9	Very soluble
Vapor Pressure/Volatility	2.7×10^{-7} Pa at 20°C 6.8×10^{-7} Pa at 25°C	Non-volatile
UV Absorption	water $\lambda_{\text{max}} = 264$ 0.1M HCl $\lambda_{\text{max}} = 241$ 0.1M NaOH $\lambda_{\text{max}} = 216$	Not likely to undergo photolysis.
Pka	4.2 ± 0.15	
log K _{ow} at 23°C	0.276 at pH 4 -1.362 at pH 7 -1.58 at pH 9	Not likely to bioaccumulate
Stability of compound at room temperature, if provided		No significant degradation over 12 months at ambient temperatures.

Data obtained from pyrasulfatole chemistry review of Submission 2006-2445.

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2. Test organism:

Species (common and scientific names): Northern bobwhite quail, *Colinus virginianus*
(EPA recommends using either bobwhite quail or mallard duck.)

Age at study initiation: 10 days old
(EPA recommends: 10-14 days old)

Weight at study initiation (mean and range): 29.8-31.1 g (treatment means), 25.6-34.7 g (range)

Source: Barrett's Quail Farm, Houston, Texas.

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
<u>Acclimation</u> Period: Conditions: (same as test or not) Feeding: Health: (any mortality observed)	6 days Same as test Teklad Bayer Starter Ration and local tap water were provided <i>ad libitum</i> . Birds that appeared healthy were used for testing. There was <3% mortality (4 birds) during acclimation.	
Pen size and construction materials	Galvanized steel brooders (91L×81W×25H cm).	Recommended pen size is about 35 x 100 x 24 cm
Test duration	5 days with treated feed, and 3 days with untreated feed.	Recommended test duration is 5 days with treated feed and at least 3 days observation with "clean" feed.
<u>Test concentrations</u> nominal: measured:	313, 625, 1250, 2500, and 5000 mg a.i./kg 308, 591, 1247, 2813, and 4911 mg a.i./kg	Five or six test concentrations should be used in a geometric scale, unless the LC ₅₀ > 5000 mg ai/kg diet.

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Parameter	Details	Remarks
		Criteria
Solvent/vehicle, if used type: amount:	N/A	<i>Recommended solvents include distilled water, corn oil, propylene glycol, 1% carboxymethylcellulose, or gum arabic. The solvent should not be more than 2%.</i>
Diet preparation and feeding	The appropriate amount of test chemical and feed were added into mixing bowl and blended for 5 minutes in laboratory mixer. The premix was added to additional feed and mixed in laboratory mixers for a total of 20 minutes. Fresh food was presented daily from a mixed batch stored under frozen conditions.	<i>The control group should be tested with a diet containing the maximum amount of vehicle used in treated diets.</i>
Feed withholding period	None	
Stability and homogeneity of test material in the diet determined (Yes/No)	Stability was determined after one day in the brooder.	
Number of birds per replicate/groups for negative control: for vehicle control: for treated:	10 N/A 10	<i>The recommended number of birds per replicate is a minimum of ten.</i>
Number of replicates/group (if used) for negative control: for vehicle control: for treated:	1 N/A 1	
Test conditions temperature: relative humidity(%): photoperiod:	22EC for room temperature and 32-38EC for brooder temperatures. 52% 14 hours light/10 hours dark	<i>Recommended brooder temperature is about 35EC (95EF) Recommended room temperature is 22-27EC (71-81 EF) Recommended relative humidity is 30-80% Recommended photoperiod is a minimum of 14 hours of light.</i>
Reference chemical, if used	None	

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2. Observations:

Table 2: Observations

Parameters	Details	Remarks
Parameters measured (mortality/body weight/ mean feed consumption/ others)	- Mortality - Clinical signs of toxicity - Mean feed consumption (g/bird/day) - Mean body weight	
Indicate the stability and homogeneity of test chemical in the diet	Stability of the test material in feed was assessed in treated feed prepared at 313 and 5000 ppm from one day in the brooder during the test. The brooder recoveries were 88-97% of the initial concentrations.	Freezer stability and homogeneity were not determined during this test. Historical homogeneity and freezer stability data indicates homogeneous feed and stability for up to 14 days.
Indicate if the test material was regurgitated	No regurgitation was reported.	
Treatments on which necropsies were performed	All 5000 mg a.i./kg birds and 40% of the other treatment group birds were necropsied.	
Observation intervals	Mortality and signs of toxicity: Determined three times on Day 0 and daily (1 to 2 times) thereafter. Feed consumption: Determined daily Body Weight: Days -3, 0, 5, and 8	
Were raw data included?	Yes	

II. RESULTS AND DISCUSSION:

A. MORTALITY:

There were no mortalities in the control or treatment groups. The NOAEC based on mortality was ≥ 4911 mg a.i./kg.

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Table 3: Effect of Pyrasulfotole on Mortality of *Colinus virginianus*

Treatment (mg ai/kg diet) measured (nominal) conc.	No. of birds per treatment	Cumulative mortality							
		day 1	day 2	day 3	day 4	day 5	day 6	day 7	day 8
Control	10	0	0	0	0	0	0	0	0
308 (313)	10	0	0	0	0	0	0	0	0
591 (625)	10	0	0	0	0	0	0	0	0
1247 (1250)	10	0	0	0	0	0	0	0	0
2813 (2500)	10	0	0	0	0	0	0	0	0
4911 (5000)	10	0	0	0	0	0	0	0	0
NOAEC	≥4911 mg a.i./kg								
LC ₅₀	>4911 mg a.i./kg								
Reference chemical	mortality	N/A							
	LC ₅₀	N/A							
	NOEC	N/A							

B. SUB-LETHAL TOXICITY ENDPOINTS:

No treatment-related clinical signs of toxicity were observed during the study. There were no effects on body weights or feed consumption during the study. The NOAEC based on body weights or feed consumption was ≥4911 mg a.i./kg.

No treatment-related findings were observed in postmortem examinations.

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Table 4: Sublethal Effect of Pyrasulfotole on *Colinus virginianus*

Treatment (mg ai/kg diet) measured (nominal) conc.		Observation			
		Mean body weight (g)			Food consumption (g/bird/day)
		Day			Day
		0	5	8	0-5 6-8
Control		30.8	51.8	64.3	7.5 8.2
308 (313)		30.0	50.3	64.5	7.5 8.5
591 (625)		29.8	50.5	63.0	7.4 8.3
1247 (1250)		30.7	52.2	65.9	7.7 8.9
2813 (2500)		31.1	51.6	64.0	7.6 8.8
4911 (5000)		29.8	51.7	64.9	7.4 8.8
NOAEC		≥4911 mg a.i./kg			≥4911 mg a.i./kg
EC ₅₀		Not determined			Not determined
Reference chemical	NOEC	N/A			
	EC ₅₀	N/A			

C. REPORTED STATISTICS:

The LD₅₀ could not be calculated because there were no mortalities. The bodyweight and growth data were analyzed using the chi-square test for normality and the Levene's test for homogeneity of variance. The body weight treatment group data was compared to the control using Dunnett's one-tailed test (p>0.05). The statistical analyses on body weight were conducted using the TOXSTAT version 3.4 computer program. Nominal concentrations were used in all estimations. Feed consumption data were not analyzed statistically.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Percent body weight gain was calculated during the day 0-5 and 5-8 intervals; data were statistically analyzed for the day 0-5 interval only because there were no significant effects during that interval and it could be visually determined that effects did not occur during the recovery time interval (days 5-8). Analyzed data satisfied the assumptions of normality and homogeneity of variances. The NOAEC values were determined using ANOVA via Toxstat statistical software. Replicate feed consumption data were not provided, so this endpoint was not statistically analyzed; it could be determined visually that there were no adverse effects on this parameter.

LC₅₀: >4911 mg ai/kg diet 95% C.I.: N/A

NOAEC: ≥4911 mg a.i./kg diet

Probit Slope: Not calculable 95% C.I.: N/A

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E. STUDY DEFICIENCIES:

There were no study deficiencies identified.

F. REVIEWERS' COMMENTS:

Results of the reviewers' statistical verification were identical to those of the study author.

G. CONCLUSIONS:

This study is scientifically sound and is classified **ACCEPTABLE**. The NOAEC was ≥ 4911 mg a.i./kg diet and the LC₅₀ was > 4911 mg a.i./kg diet, the highest treatment group, which categorizes pyrasulfotole as practically non-toxic to Northern bobwhite quail on an acute dietary basis.

LC₅₀: > 4911 mg ai/kg diet 95% C.I.: N/A
NOAEC: ≥ 4911 mg a.i./kg diet
Endpoint(s) affected: None

III. REFERENCES:

- American Society of Testing and Materials (ASTM). 1993. Standard Practice for Conducting Subacute Dietary Tests with Avian Species. ASTM Standard E857-87.
- Conover, W.J. 1980. Practical Nonparametric Statistics, 2nd Edition, John Wiley and Sons, New York.
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- Snedecor, G.W. and W.G. Cochran. 1971. Statistical Methods, 6th Edition, The Iowa State Press, Ames, Iowa.
- Stephan, C.E. 1977. Methods for Calculating an LC50. Aquatic Toxicology and Hazard Evaluation, ASTM STP 634. F.L. Mayer and J.L. Hamelink, eds. American Society for Testing Materials, Philadelphia, PA. 65-84.
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- West, Inc. and D.D. Gulley. 1994. TOXSTAT, version 3.4. WEST, Inc., Western EcoSystems Technology, Inc., Cheyenne, Wyoming.

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APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:

body weight gain

File: 1730b

Transform: NO TRANSFORMATION

ANOVA TABLE

SOURCE	DF	SS	MS	F
Between	5	343.217	68.643	1.317
Within (Error)	54	2813.798	52.107	
Total	59	3157.015		

Critical F value = 2.45 (0.05,5,40)

Since $F < \text{Critical } F$ FAIL TO REJECT H_0 :All groups equal

body weight gain

File: 1730b

Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 1 OF 2

H_0 :Control<Treatment

GROUP	IDENTIFICATION	TRANSFORMED MEAN	MEAN CALCULATED IN ORIGINAL UNITS	T STAT	SIG
1	control	68.337	68.337		
2	308	67.506	67.506	0.257	
3	591	69.738	69.738	-0.434	
4	1247	70.331	70.331	-0.618	
5	2813	66.337	66.337	0.620	
6	4911	73.789	73.789	-1.689	

Dunnett table value = 2.31 (1 Tailed Value, $P=0.05$, $df=40,5$)

body weight gain

File: 1730b

Transform: NO TRANSFORMATION

DUNNETTS TEST - TABLE 2 OF 2

H_0 :Control<Treatment

GROUP	IDENTIFICATION	NUM OF REPS	Minimum Sig Diff (IN ORIG. UNITS)	% of CONTROL	DIFFERENCE FROM CONTROL
1	control	10			
2	308	10	7.457	10.9	0.831
3	591	10	7.457	10.9	-1.401
4	1247	10	7.457	10.9	-1.994
5	2813	10	7.457	10.9	2.000
6	4911	10	7.457	10.9	-5.452

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body weight gain

File: 1730b

Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 1 OF 2

GROUP	IDENTIFICATION	N	ORIGINAL MEAN	TRANSFORMED MEAN	ISOTONIZED MEAN
1	control	10	68.337	68.337	67.922
2	308	10	67.506	67.506	67.922
3	591	10	69.738	69.738	68.802
4	1247	10	70.331	70.331	68.802
5	2813	10	66.337	66.337	68.802
6	4911	10	73.789	73.789	73.789

body weight gain

File: 1730b

Transform: NO TRANSFORMATION

WILLIAMS TEST (Isotonic regression model) TABLE 2 OF 2

IDENTIFICATION	ISOTONIZED MEAN	CALC. WILLIAMS	SIG P=.05	TABLE WILLIAMS	DEGREES OF FREEDOM
control	67.922				
308	67.922	0.129		1.68	k= 1, v=54
591	68.802	0.144		1.76	k= 2, v=54
1247	68.802	0.144		1.79	k= 3, v=54
2813	68.802	0.144		1.80	k= 4, v=54
4911	73.789	1.689		1.80	k= 5, v=54

s = 7.219

Note: df used for table values are approximate when v > 20.

body weight gain

6

10

10

10

10

10

10

control

69.51

59.32

68.55

78.77

64.4

73.8

63.24

66.46

68.63

70.69

308

66.67

62.93

53.16

66.67

69.14

71.93

69.04

71.94

72.2

71.38

591

74.43

70.69

71.74

71.33

65.31

75.7

73.54

64.01

59.01

71.62

1247

60.95

71.33

73.29

73.39

62.93

60.38

86.32

71.19

79.8

63.73

2813

69.37

61.86

63.82

59.34

59.06
59.72
83.39
65.02
79.25
62.54
4911
76.49
61.87
72.57
89.84
66.15
74.76
62.35
82.03
76.51
75.32

	d0	d5	d8	% body weight gain	
				d 0-5	d 5-8
control	30.5	51.7	65.8	69.51	27.27
	29.5	47	65.2	59.32	38.72
	33.7	56.8	68.2	68.55	20.07
	29.2	52.2	66.5	78.77	27.39
	32.3	53.1	63.8	64.40	20.15
	31.3	54.4	65.1	73.80	19.67
	27.2	44.4	52.9	63.24	19.14
	32.8	54.6	67.7	66.46	23.99
	32.2	54.3	67.4	68.63	24.13
	29	49.5	60.6	70.69	22.42
308	28.8	48	63.9	66.67	33.13
	29.4	47.9	64	62.93	33.61
	30.1	46.1	58.6	53.16	27.11
	30.9	51.5	67.5	66.67	31.07
	32.4	54.8	67.8	69.14	23.72
	28.5	49	62.7	71.93	27.96
	32.3	54.6	68.5	69.04	25.46
	27.8	47.8	58.3	71.94	21.97
	29.5	50.8	67.7	72.20	33.27
	30.4	52.1	65.7	71.38	26.10
591	30.9	53.9	67.1	74.43	24.49
	29	49.5	63.2	70.69	27.68
	27.6	47.4	59.7	71.74	25.95
	27.9	47.8	59.1	71.33	23.64
	32	52.9	63.6	65.31	20.23
	28.4	49.9	62.5	75.70	25.25
	29.1	50.5	61.6	73.54	21.98
	31.4	51.5	63.9	64.01	24.08
	32.2	51.2	65.5	59.01	27.93
	29.6	50.8	63.7	71.62	25.39
1247	31.5	50.7	65.1	60.95	28.40
	29.3	50.2	63.8	71.33	27.09
	32.2	55.8	71.4	73.29	27.96
	32.7	56.7	70.5	73.39	24.34
	32.1	52.3	64.9	62.93	24.09
	31.3	50.2	64.4	60.38	28.29
	28.5	53.1	67.2	86.32	26.55
	29.5	50.5	61.1	71.19	20.99
	30.2	54.3	70.2	79.80	29.28
	29.5	48.3	60.5	63.73	25.26
2813	33.3	56.4	69	69.37	22.34
	31.2	50.5	61.1	61.86	20.99
	34	55.7	69.2	63.82	24.24
	27.3	43.5	55.2	59.34	26.90
	32	50.9	63.5	59.06	24.75
	28.8	46	57.2	59.72	24.35

	29.5	54.1	69.9	83.39	29.21
	30.3	50	62.8	65.02	25.60
	29.4	52.7	63.2	79.25	19.92
	34.7	56.4	68.5	62.54	21.45
4911	28.5	50.3	63.8	76.49	26.84
	29.9	48.4	59.5	61.87	22.93
	28.8	49.7	63.3	72.57	27.36
	25.6	48.6	63.1	89.84	29.84
	32.5	54	67.6	66.15	25.19
	30.9	54	64.6	74.76	19.63
	32.4	52.6	65.9	62.35	25.29
	30.6	55.7	71.5	82.03	28.37
	28.1	49.6	62	76.51	25.00
	30.8	54	67.9	75.32	25.74