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WASHINGTON, D.C. 20460

CASWELL FILE

011772

OPP OFFICIAL RECORD  
HEALTH EFFECTS DIVISION  
SCIENTIFIC DATA REVIEWS  
EPA SERIES 361  
JAN 30 1996

OFFICE OF  
PREVENTION, PESTICIDES, AND  
TOXIC SUBSTANCES

**MEMORANDUM:**

**SUBJECT: FIPRONIL** Subchronic Neurotoxicity Screening Battery - Rats  
[OPPTS 870.6200, §82-7]

**EPA ID NOs.:** MRID No.: 432917-03  
DP Barcode:: D214926  
Submission No.: S476260  
P.C. Code: 129121  
TOX Chem No.: none

**FROM:** Robert F. Fricke, Ph.D. *Robert F. Fricke 25 Jan 96*  
Toxicology Branch II, Section II  
Health Effects Division (7509C)

**TO:** Rick Keigwin  
Product Manager (10)  
Registration Division (7505C)

**THRU:** K. Clark Swentzel *K. Clark Swentzel 1/29/96*  
Toxicology Branch II, Head Section II  
Health Effects Division (7509C)

and

Stephanie Irene, Ph.D. *Stephanie R. Irene 1/26/96*  
Acting Branch Chief, Toxicology Branch II  
Health Effects Division (7509C)

**REGISTRANT:** Rhône-Poulenc Ag Company, 2 T.W. Alexander Drive, Research  
Triangle Park, NC

**CHEMICAL:** M&B 46030, Fipronil (96.7%):

**ACTION REQUESTED:** Review subchronic neurotoxicity study in the rat.

**EXECUTIVE SUMMARY:** Driscoll, C.D. and Hurley, J.M. (15 September 1993),  
M&B 46030: Ninety-day dietary neurotoxicity study in Sprague-Dawley rats,

Bushy Run Research Center, Export, PA, Report No.: 92N1074, MRID No.: 43291703, Unpublished

In this subchronic neurotoxicity study, male and female Sprague-Dawley rats (15/sex/dose) were fed test diets containing M&B 46030 at 0 (basal diet), 0.5, 5.0, or 150 ppm (equivalent to 0, 0.0297, 0.301, or 8.89 mg/kg/day, males; 0, 0.0354, 0.351 or 10.8 mg/kg/day, females). Neurobehavioral screening, consisting of Functional Observational Battery and motor activity evaluations, was performed at pretreatment, and during Weeks 4, 9 and 13. At terminal sacrifice, six animals/sex/dose were anesthetized and perfusion fixed *in situ* for neuropathological evaluation.

With the exception of one low-dose female which was found dead on Day 16, all remaining animals survived to terminal sacrifice without the appearance of any treatment-related clinical signs.

Decreases in mean body weight, observed in high-dose males and females at Week 1 of treatment, were judged to be slight (6.5%, males; 6.9%, females). The decrease in body weight was accompanied by a concomitant decrease in food consumption, which would suggest a palatability problem, rather than a treatment-related effect.

FOB findings revealed minimal effects in high-dose animals at the Weeks 4, 9 and 13 evaluations. High-dose males had a decreased incidence of no urination and an increased incidence of exaggerated tail pinch response. High-dose males and females had an increased incidence of exaggerated startle responses in the manipulative observations. High-dose females had increased forelimb grip strength at Week 13. The mean body weights of treated males were significantly greater than the concurrent control values.

Necropsy findings did not reveal any treatment-related gross pathological or histopathological findings. Although histopathological lesions were observed, incidences were low and attributed by the study pathologist to animal variation and artifactual changes.

Based on the results (FOB findings) of this study, the LOEL was established at 150 ppm (8.89 mg/kg/day, males; 10.8 mg/kg/day, females); the NOEL was established at 5.0 ppm (0.301 mg/kg/day, males; 0.351 mg/kg/day, females).

This study is classified as **Core - Acceptable** and satisfies guideline requirements (§82-7) for a subchronic neurotoxicity screening battery in the rat.

Fipronil

Subchronic Neurotoxicity §82-7

011772

EPA Reviewer: Robert F. Fricke, Ph.D. *Robert F. Fricke 25 Jan 96*  
Review Section II, Toxicology Branch II, HED (7509C)

EPA Secondary Reviewer: K. Clark Swentzel *K. Clark Swentzel 1/25/96*  
Review Section II, Toxicology Branch II, HED (7509C)

### DATA EVALUATION RECORD

**STUDY TYPE:** Subchronic Neurotoxicity Screening Battery - Rats  
[OPPTS 870.6200, §82-7]

**DP BARCODE:** D214926

**SUBMISSION NO.:** S476260

**P.C. CODE:** 129121

**TOX CHEM NO.:** none

**TEST MATERIAL** M&B 46030, Fipronil (96.7%):  
5-Amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-(1,R,S)-  
(trifluoromethyl)sulfinyl-1H-pyrazole-3-carbonitrile

**CITATION:** Driscoll, C.D. and Hurley, J.M. (15 September 1993), M&B  
46030: Ninety-day dietary neurotoxicity study in  
Sprague-Dawley rats, Bushy Run Research Center, Export, PA,  
Report No.: 92N1074, MRID No.: 43291703, Unpublished

**SPONSOR:** Rhône-Poulenc Ag Company, 2 T.W. Alexander Drive, Research  
Triangle Park, NC

**EXECUTIVE SUMMARY:** In this subchronic neurotoxicity study, male and female Sprague-Dawley rats (15/sex/dose) were fed test diets containing M&B 46030 at 0 (basal diet), 0.5, 5.0, or 150 ppm (equivalent to 0, 0.0297, 0.301, or 8.89 mg/kg/day, males; 0, 0.0354, 0.351 or 10.8 mg/kg/day, females). Neurobehavioral screening, consisting of Functional Observational Battery and motor activity evaluations, was performed at pretreatment, and during Weeks 4, 9 and 13. At terminal sacrifice, six animals/sex/dose were anesthetized and perfusion fixed *in situ* for neuropathological evaluation.

With the exception of one low-dose female which was found dead on Day 16, all remaining animals survived to terminal sacrifice without the appearance of any treatment-related clinical signs.

Decreases in mean body weight, observed in high-dose males and females at Week 1 of treatment, were judged to be slight (6.5%, males; 6.9%, females). The decrease in body weight was accompanied by a concomitant decrease in food consumption, which would suggest a palatability problem, rather than a treatment-related effect.

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Necropsy findings did not reveal any treatment-related gross pathological or histopathological findings. Although histopathological lesions were observed, incidences were low and attributed by the study pathologist to animal variation and artifactual changes.

**Based on the results (FOB findings) of this study, the LOEL was established at 150 ppm (8.89 mg/kg/day, males; 10.8 mg/kg/day, females); the NOEL was established at 5.0 ppm (0.301 mg/kg/day, males; 0.351 mg/kg/day, females).**

This study is classified as **Core - Acceptable** and satisfies guideline requirements (§82-7) for a subchronic neurotoxicity screening battery in the rat.

**Regulatory Compliance:** Quality assurance was documented by signed and dated GLP and quality assurance statements. This study neither meets nor exceeds any of the applicable criteria; and a statement of "no confidentiality claims" was provided.

## I. MATERIALS

### A. Test Material: M&B 46030, Fipronil

**Description:** White powder

**Batch No:** 78/GC/90

**Purity:** 96.7%

**CAS No.:** 120068-37-3

### B. Test Animals

**Species (Strain):** Rat (Sprague-Dawley)

**Age at Initiation:** Approximately 8 weeks

**Weight at Initiation:** 251.2-279.9 g (males), 162.6-192.3 g (females)

**Source:** Harlan Sprague-Dawley, Indianapolis, IN

**Housing:** one/cage during study

**Feed:** Ground Purina Rodent Chow #5002, *ad libitum*

**Water:** Tap water, *ad libitum*

**Environment:** Temperature: 67-77°F; Humidity: 40-70%

**Air changes:** Not stated; **Light/dark cycle:** 12 hr/12 hr

**Acclimation Period:** 3 Weeks

## II. STUDY DESIGN

**A. In-Life Study Dates:** 22 June 1992 to 23-25 September 1992

**B. Animal Assignment:** Animals were randomly assigned to study groups as presented in Table 1. Weight variations at initiation of the study were limited to  $\pm 20\%$  of the population mean for each sex.

**Table 1: Study Design**

Study Group	Dose Level (ppm)	Animals Assigned	
		Males	Females
Control	0	15	15
Low	0.5	15	15
Mid	5.0	15	15
High	150	15	15

**C. Dose Selection Rationale:** Dose selection was based on a chronic toxicity/carcinogenicity study (MRID No.: 429186-48, HED Doc. No.: 011086) in which rats were fed diets containing 0, 0.5, 1.5, 30, or 300 ppm M&B 46030. At 300 ppm, three males and two females died within the first week of treatment. Convulsions were observed in these animals prior to death. Two additional animals were found dead during Weeks 3

and 9, and another sacrificed for humane reasons (loss of use of hindlimbs) during Week 25. No mortalities were observed at 30 ppm or lower.

**D. Dose Preparation:** A concentrated premix was prepared and diluted with basal diet to yield the high-dose level. Lower dose test diets were prepared serial dilutions of the high-dose test diet. The concentration of test compound in the test diets was not corrected for percent purity of the a.i. Test diets were evaluated for homogeneity, stability and concentration.

**E. Statistical Evaluations:** Levene's test was used to evaluate homogeneity of variances. Homogeneous data were initially analyzed using a one-way analysis of variance (ANOVA). If the ANOVA result was significant (F-test), pair-wise comparisons were carried out using pooled t-test. Heterogeneous data were first evaluated using an ANOVA for unequal variances, followed, when necessary, by pair-wise comparisons using separate variance t-tests. Incidence data were evaluated using Fischer's Exact Test. Incidence data, graded for severity, were analyzed for group differences using Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somer's D measurements of association. Motor activity data were evaluated using repeated measures ANOVA accompanied by the epsilon-adjustment procedure (Greenhouse-Geisser correction).

#### IV. METHODS

**A. Observations:** Animals were observed twice daily for signs of mortality and moribundity. Detailed physical examinations were performed once weekly.

**B. Body Weight:** Body weights were measured at the start of the study, at weekly intervals, thereafter, and at terminal sacrifice. Body weights were also determined in conjunction with the neurobehavioral evaluations.

**C. Food Consumption:** Food consumption was measured on a weekly basis. Achieved compound intakes were determined from analytical chemistry and food consumption results.

**D. Neurobehavioral Tests:** Neurobehavioral tests consisted of the Functional Observational Battery (FOB) and evaluation of motor activity. Because of the complexity of these tests, animals were randomly divided into two subgroups which were counterbalanced according to treatment group across test days, test sessions, and motor activity test enclosure. FOB and motor activity were evaluated at prestudy and after 4, 9, and 13 weeks of treatment.

**1. Functional Observational Battery:** The following parameters were evaluated in 10 animals/sex/group by a trained observer at each test session:

<p><b>CAGESIDE OBSERVATIONS</b></p> <ul style="list-style-type: none"> <li>Posture</li> <li>Convulsions</li> <li>Tremors</li> <li>Palpebral closure</li> </ul> <p><b>OPEN-FIELD OBSERVATIONS</b></p> <ul style="list-style-type: none"> <li>Reactivity to handling</li> <li>Convulsions</li> <li>Tremors</li> <li>Vocalizations</li> <li>Piloerection</li> <li>Abnormal/stereotypic behavior</li> <li>Gait abnormalities</li> <li>Body position</li> <li>Breathing pattern</li> <li>Arousal</li> <li>Palpebral closure</li> <li>Quantity of urine</li> <li>Number of fecal pellets</li> <li>No. of rears</li> </ul>	<p><b>MANIPULATIVE OBSERVATIONS</b></p> <ul style="list-style-type: none"> <li>Approach response</li> <li>Startle response</li> <li>Tail pinch response</li> <li>Pupil response</li> <li>Muscle tone</li> <li>Lacrimation</li> <li>Salivation</li> <li>Exophthalmus</li> <li>Emaciation</li> <li>Dehydration</li> <li>Fur appearance</li> <li>Crusts</li> <li>Visual placing</li> </ul> <p><b>MEASUREMENTS/COUNTS</b></p> <ul style="list-style-type: none"> <li>Body weight</li> <li>Body temperature</li> <li>Air righting</li> <li>Hind/Forelimb grip strengths</li> <li>Landing foot splay</li> </ul>
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**2. Motor Activity:** Following the FOB evaluations, 15 animals/sex/group were evaluated for motor activity using an automated, figure-eight shaped activity chamber. Animals were monitored individually during a 90-minute session, consisting of nine, 10-minute intervals. Motor activity of control animals was asymptotic during the last 20 minutes of the evaluation.

**E. Neuropathology:** During Week 14 of treatment, 10 animals/sex/group (11 in the high-dose female group) were anesthetized and perfused *in situ* with 10% neutral buffered formalin. Gross examination of the thoracic and peritoneal cavities were performed on all animals. Neuropathological examinations were performed on 6 animals/sex from the control and high-dose groups. Brains were weighed prior to sectioning. The following tissues were examined:

**GROSS LESIONS**

**BRAIN:** Cerebral cortex, cerebellar cortex, medulla/pons

**SPINAL CORD:** Cervical, thoracic & lumbar regions

**CENTRAL NERVOUS SYSTEM:** Dorsal root ganglia, dorsal & ventral nerve roots, & gasserian ganglion

**PERIPHERAL NERVES:** Sciatic, tibial, sural, & peroneal nerves

**THYROIDS**

**LIVER**

**TAIL** (animal identification only)

## VI. RESULTS

**A. Analytical Chemistry:** Analytical chemistry results for the prepared test diets are summarized in Table 2. Fipronil was homogeneously distributed and stable for 21 days at room temperature in an open or closed container. The achieved concentrations were all within  $\pm 10\%$  of the target levels.

**Table 2: Analytical Chemistry of Test Diets<sup>a</sup>**

Observation	Dose Level (ppm)	% of Nominal		
Homogeneity (Coefficient of Variation)	0.5	92.6 (2.6%)		
	5.0	95.5 (1.3%)		
	150	93.6 (1.3%)		
	300	95.6 (1.0%)		
Concentration	0.5	97.4		
	5.0	99.9		
	150	94.6		
Stability <sup>b</sup>	Day 0	0.5, 300	103.1, 95.6	
	Day 7	Open	0.5, 300	94.4, 94.8
		Closed	"	97.3, 94.9
	Day 14	Open	0.5, 300	90.1, 94.7
		Closed	"	97.0, 93.0
	Day 21	Open	0.5, 300	96.5, —
		Closed	"	95.6, 93.0

<sup>a</sup> Data summarized from Tables 3-5 of Appendix 1 (pp 86-92)

<sup>b</sup> Stability was determined in open and closed containers

**B. Clinical Signs and Mortality:** One low-dose female, not showing any previous overt signs of toxicity, was found dead on Day 16. All remaining animals survived to terminal sacrifice without the appearance of any treatment-related clinical signs.

**C. Body Weights:** Mean body weight and body weight gain data for male and female rats are summarized in Table 3. High-dose males and females had statistically significant decreases in mean body weight at Week 1 only. Slight (6.5%, males; 6.0% females) decreases in mean body weight were observed only at Week 1. Significant decreases in body weight gain were observed for Week 0-1. Week 13 mean body weights and body weight gain for Weeks 0 to 13 of treated animals were comparable to control values.

Table 3: Mean Body Weight (% Change from Control) and Body Weight Gain<sup>a</sup>

Observation	Week	Dose Level (ppm)			
		0	0.5	5.0	150
<b>MALES</b>					
Body Weight (g)	0	266.4	268.1	266.6	266.4
	1	295.4	300.9	296.9	277.4 <sup>**</sup> (-6.5)
	13	421.8	434.4	435.6	442.2 (+4.8)
Gain (g)	0-1	28.9	32.8	30.4	11.0 <sup>**</sup>
	0-2	49.1	57.1 <sup>**</sup>	52.6	40.9 <sup>**</sup>
	0-13	155.4	166.3	169.1	175.8
<b>FEMALES</b>					
Body Weight (g)	0	177.1	176.9	178.1	175.6
	1	191.3	193.1	192.5	179.9 <sup>**</sup> (-6.0)
	13	263.8	261.9	262.9	262.5 (-0.5)
Gain (g)	0-1	14.2	16.2	14.3	4.2 <sup>**</sup>
	0-13	86.6	84.4	84.8	86.9

<sup>a</sup> Data summarized from Table 3, 4, 5, and 6 (pp 21, 23, 24, and 26) of the study.

<sup>\*\*</sup> p < 0.01

#### D. Food Consumption and Achieved Dosage

1. **Food Consumption:** Mean food consumption data are summarized in Table 4. Mean food consumption of high-dose animals was significantly lower than controls for Week 0-1 in males and females. Food consumption for high-dose animals returned to control levels at Week 1-2 and all other intervals, thereafter, through the end of the study.

Table 4: Mean Food Consumption (grams/animal/day)<sup>a</sup>

Sex	Week	Dose Level (ppm)			
		0	0.5	5.0	150
Males	0-1	22.4	22.7	22.6	17.2 <sup>**</sup>
	1-2	22.1	22.5	22.5	22.8
Females	0-1	16.5	16.8	16.3	12.5 <sup>**</sup>
	1-2	16.7	16.4	16.3	17.1

<sup>a</sup> Data summarized from Table 3, 4, 5, and 6 (pp 21, 23, 24, and 26) of the study.

<sup>\*\*</sup> p < 0.01

**2. Achieved Dosage:** The achieved dosages of test compound are summarized in Table 5.

**Table 5: Overall (Weeks 1 to 13) Achieved Dosage (mg/kg/day)<sup>a</sup>**

Sex	Dose Level (ppm)		
	0.5	5.0	150
Male	0.0297	0.301	8.89
Female	0.0354	0.351	10.8

<sup>a</sup> Data summarized from Tables 9 and 10 (pp 29-30) of the study.

### E. Neurobehavioral Evaluations

**1. FOB Evaluations:** FOB findings revealed minimal effects in high-dose animals (Table 6) at the Week 4, 9 and 13 FOB evaluations. High-dose males had an increased incidence of no urination during the open field observations. High-dose males and females had an increased incidence of exaggerated tail pinch and startle responses in the manipulative observations. High-dose females had increased forelimb grip strength at Week 13. The mean body weights of treated males were significantly greater than the concurrent control values.

**2. Motor Activity:** No treatment-related differences in motor activity were observed.

**3. Neurobehavioral Positive Controls:** Appendix 10 of the study certifies the experience and capabilities of the FOB observers.

### G. Pathology

**1. Gross Pathology:** Gross pathological examination did not reveal any treatment-related effects. The one low-dose female, which was found dead of Day 16, had a lower urinary tract infection with associated obstruction.

**2. Neuropathology:** Lesions present in the central and peripheral nervous systems are summarized in Table 8. The study pathologist did not attribute any of the observed histopathological changes to treatment and offered the following explanation (Appendix 2, pg 102): "...histomorphological changes were recorded in the spirit of being as thorough as possible in the documentation of any microscopic alterations which were present. Even when sections are

prepared from adequately perfused and properly dissected nervous system tissues, artifactual changes such as vacuolation or myelin sheath swelling may be present. Also, some variations exists from animal to animal and from section to section in the amount of endoneurial connective tissue present within the peripheral nerves."

### 3. Neuropathology Positive Controls: Not included with study.

Table 6: Summary of FOB Findings<sup>a</sup>

Observation		Dose Level (ppm)			
		0	0.5	5.0	150
MALES					
Urine, None	Prestudy	7/10	7/10	7/10	5/10
	Week 4	5/10	4/10	1/10	0/10*
	Week 9	5/10	6/10	3/10	1/10
	Week 13	5/10	5/10	6/10	1/10
Startle Response, Exaggerated	Prestudy	1/10	0/10	1/10	1/10
	Week 4	0/10	0/10	0/10	4/10
	Week 9	0/10	0/10	1/10	2/10
	Week 13	0/10	0/10	0/10	2/10
Tail Pinch Response, Exaggerated	Prestudy	3/10	1/10	2/10	1/10
	Week 4	0/10	0/10	0/10	4/10
	Week 9	0/10	0/10	1/10	2/10
	Week 13	0/10	0/10	0/10	0/10
Body Weight (g)	Prestudy	229.9	228.1	235.4	229.1
	Week 4	331.8	350.0**	352.2**	337.0
	Week 9	394.4	411.5*	418.7**	410.9*
	Week 13	423.2	437.7	450.5**	447.2*
FEMALES					
Startle Response, Exaggerated	Prestudy	0/10	0/10	0/10	0/10
	Week 13	0/10	0/10	0/10	1/10
Forelimb Grip Strength (kg)	Prestudy	0.52	0.47	0.50	0.57
	Week 13	0.61	0.68	0.70	0.88*

<sup>a</sup> Data summarized from study Tables 11, 12, 13, 14, 15, and 18 (pp 31-45).

\*  $p < 0.05$ , \*\*  $p < 0.01$



FOB findings revealed minimal effects in high-dose animals at the Weeks 4, 9 and 13 evaluations. High-dose males had a decreased incidence of no urination and an increased incidence of exaggerated tail pinch response. High-dose males and females had an increased incidence startle responses in the manipulative observations. High-dose females had increased forelimb grip strength at Week 13. The mean body weights of treated males were significantly greater than the concurrent control values.

Necropsy findings did not reveal any treatment-related gross pathological or histopathological findings. Although histopathological lesions were observed, incidences were low and attributed by the study pathologist to animal variation and artifactual changes.

## **VI. REVIEWER'S COMMENTS and CONCLUSIONS**

The dosages selected in this subchronic neurotoxicity study appeared to be adequate to evaluate the neurotoxic effects of Fipronil. Although the neurobehavioral effects in this study appeared to be borderline at the high-dose tested (150 ppm), they are consistent with clinical signs observed in a chronic toxicity study/oncogenicity study in rats (MRID No.: 429186-48, HED Doc. No.: 011086) submitted by the Registrant.

The FOB evaluations from the subchronic neurotoxicity study indicated that the rats were hyperexcitable with exaggerated startle and tail pinch responses observed in males and/or females. For the first 13 weeks of the chronic toxicity study, hyperexcitable behavior was also observed and summarized in Table 8. Clinical signs of rats dosed at 300 ppm (12.68 mg/kg/day, males; 16.75 mg/kg/day, females) included the following behavioral changes: aggressiveness, irritability, and hyperactivity and excessive vocalizations (females). Convulsions were observed in males, and to a lesser extent in females. Dosing the rats at 300 ppm also produced borderline toxicity, with slight decreases in mean body weight (92%, males; 95% females) and body weight gain (89%, males; 93%, females), and increased incidence in mortality (4/80, males; 1/80, females).

Although the neurobehavioral effects observed in the neurotoxicity study are slight, taken in conjunction with the results at 300 ppm of the chronic toxicity study, the high-dose tested (150 ppm) appears to be a valid LOEL for neurobehavioral effects.

**Based on the results (FOB findings) of this study, the LOEL was established at 150 ppm (8.89 mg/kg/day, males; 10.8 mg/kg/day, females); the NOEL was established at 5.0 ppm (0.301 mg/kg/day, males; 0.351 mg/kg/day, females).**

This study is classified as **Core - Acceptable** and satisfies guideline requirements (§82-7) for a subchronic neurotoxicity screening battery in the rat.

**Table 8: Clinical Signs , Mortality and Body Weight and Body Weight Gains for Weeks 0 to 13 Summarized from Chronic Toxicity/Oncogenicity Study<sup>a</sup>**

Observation		Dosage (Males)		Dosage (Females)	
		0 ppm	300 ppm	0 ppm	300 ppm
Behavior	Aggressive	0/80	2/80	0/80	8/80
	Irritable	0/80	1/80	0/80	11/80
	Overactive	0/80	2/80	0/80	4/80
	Vocalizations	0/80	0/80	0/80	9/80
Muscles	Convulsions	0/80	6/80	0/80	1/80
Mortality		0/80	4/80	0/80	1/80
Body Weight	Week 0	192	190	162	158
	Week 13	607	558 (92%) <sup>b</sup>	337	320 (95%)
Body Weight Gain Week 0-13		415	368 <sup>**</sup> (89%)	175	162(93%)

<sup>a</sup> Data summarized from study (MRID No.: 429186-48) Tables 4A (pp. 96 to 101), Appendix 3 (412 to 452) and Appendix 4 (pp 453 to 855) and Data Evaluation Record (HED Doc. No.: 011086) Table 3.

<sup>b</sup> Values in parentheses are the percent of control value

<sup>\*\*</sup>  $p < 0.01$



13544



009230

<b>Chemical:</b>	<b>Fipronil</b>
<b>PC Code:</b>	<b>129121</b>
<b>HED File Code</b>	<b>13000 Tox Reviews</b>
<b>Memo Date:</b>	<b>01/30/1996</b>
<b>File ID:</b>	<b>TX011772</b>
<b>Accession Number:</b>	<b>412-01-0170</b>

**HED Records Reference Center**  
**05/22/2001**

