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DATA EVALUATION RECORD

PROPAZINE

**CHRONIC ORAL TOXICITY: DOG [OPPTS 870.4100b (§83-1b)]
MRID 46654401**

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Prepared by

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OPPTS 870.4100/ OECD 452409

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DATA EVALUATION RECORD

TXR#: 0053788**STUDY TYPE:** Chronic Oral Toxicity Feeding - Dog
[OPPTS 870.4100b (§83-1b)]; OECD 452.**PC CODE:** 080808**DP BARCODE:** D322219**SUBMISSION NO.:** N/A**TEST MATERIAL (PURITY):** Propazine (96.9 %)**SYNONYMS:** 2,4-Bis(isopropylamino)-6-chloro-s-triazine; 2-chloro-4,6-bis(isopropylamino)-s-triazine**CITATION:** Saunders M.D. (2005). Propazine Toxicity Study by Dietary Administration to Beagle dogs for 52 weeks, Huntingdon Life Sciences Ltd., Woolley Road, Alconbury, Huntingdon, Cambridgeshire, PE28 4HS, England. Study No. GFN/031. August 17, 2005. MRID 46654401. Unpublished.**SPONSOR:** Griffin LLC, P.O. Box 30, Elkton Road, Newark, DE 19714-0030**EXECUTIVE SUMMARY:** In a 52-week oral chronic toxicity study (MRID 46654401), Propazine (96.9 % ai, Batch # SG90502205) was administered to 4 beagle dogs/sex/dose in the diet at concentrations of 0, 50, 200, or 750 ppm daily (1.64, 6.50, and 23.94 mg/kg/day for males and 1.65, 6.72, and 23.98 mg/kg/day for females, respectively).

There were no treatment related mortalities and no clinical signs. There were no differences between the controls and the Propazine treated groups in ophthalmology and urinalysis. Food consumption in male dogs was comparable to that of the controls, but was decreased in females at 750 ppm. At termination, the treated male dogs had body weight and body weight gains were comparable with those of the controls. In contrast, the female dogs had decreases in body weight (86% of the control) and body weight gain (53% of the control) at 750 ppm. Treated dogs showed slight increases in absolute and adjusted weight (to terminal body weight) of the liver at 750 ppm in both sexes, but only the males attained statistical significance at $p < 0.01$ (adjusted to terminal B.W.). In addition, the absolute kidney weight was increased slightly only in the male dogs in the 750 ppm group. Hematology analyses in the high dose group showed very minor decreases in hemoglobin and hematocrit from the control. However, the decreases in high dose females correlated with the findings of hemosiderosis in 4/4/dogs. Blood chemistry and EKG analyses showed minor incidental variations in the treated beagle dogs. None of these changes were of toxicological significance.

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Chronic (52-week) Oral Toxicity Study (non-rodents) (2005) Page 3 of 14
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Two female dogs from the 200 ppm group and two females and three males from the 750 ppm groups that had skin lesions mainly on the hind legs. The terminal histological examination showed skin lesions from one male dog each from the 50 and 200 ppm groups and two from the 750 ppm group. None were found in the female. These skin lesions appeared to be two separate incidental events and had no toxicological significance.

Under the conditions of this study, the LOAEL for Propazine in beagle dogs was not established for males and was 750 ppm (23.98 mg/kg/day) for females based on decreases in body weight and body weight gain. The NOAEL for males is \geq 750 ppm (23.04 mg/kg/day) and for females is 200 ppm (6.72 mg/kg/day).

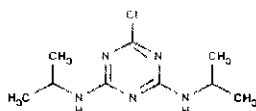
This chronic study is **Acceptable/Guideline** and satisfies the requirement for a chronic oral study [OPPTS 870.4100, OECD 452] in the dog.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Data Flagging statements were provided.

I. MATERIALS AND METHODS:

A. MATERIALS:

- 1. Test material:** Propazine
Description: White powder
Lot/Batch #: SG90502205
Purity: 96.9%.
Compound Stability: Stable in diet for 22 days under conditions of study
CAS # if TGA1: 139-40-2
Structure:



- 2. Vehicle and/or positive control:** dietary.

3. Test animals:

- Species:** Dog
Strain: Beagle
Age/weight at study initiation: Age: 18 to 22 weeks old. Weight: males -- 7.3-10.7 kg; females -- 7.2-9.4 kg
Source: Harlan, U.K.
Housing: Two dogs/pen according to United Kingdom Home Office Code of Practice for the Housing and Care of Animals used on Scientific Procedures. Animals were housed individually following the removal of food, in metabolism cages for urine collection.
Diet: Dry powder diet (SDS Lab A for dogs), 1000 g/day which consisted 400 g dry diet containing either 50, 200, or 750 ppm of Propazine and 600 ml ml tap water.
Water: Not described.

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Environmental conditions:	Temperature:	15-24°C
	Humidity:	NA
	Air changes:	10 times/hour
	Photoperiod:	12 hrs dark/ 12 hrs light
Acclimation period:	At least 4 weeks	

B. STUDY DESIGN:

- In life dates:** Start: August 6, 2002; End: August 6-8, 2003
- Animal assignment:** Animals were randomly assigned to the test groups noted in Table 1 after stratification by body weight.

Test group	Concentration in diet (ppm)	Dose to animals (mg/kg/day)		# Males	# Females
		Males	Females		
Control	0	0	0	4	4
1	50	1.64	1.65	4	4
2	200	6.50	6.72	4	4
3	750	23.94	23.98	4	4

^a Data from page 13 and Table 3, pages 46-47, MRID 46654401

- Dose selection rationale:** The doses were selected based on an earlier 90-day study with dogs. That study showed decreased body weight gain was lower at 1000 ppm, and the no effect level was 200 ppm. In addition, a 52-week dog study with a similar compound revealed moderate to severe cardiac toxicity at 1000 ppm and a NOAEL of 150 ppm. (No additional information was provided for these two studies in MRID 46654401). Therefore 750 ppm was selected to be the high dose level; 200 ppm was selected as an intermediate dose level; and 50 ppm was considered low enough to be a no observed effect level.
- Diet preparation and analysis:** A premix was prepared by grinding the Propazine directly into 355 µm sieved SDS Lab A diet for dogs. The premix was then made to final weight and mixed in a Turbula mixer for at least five minutes. The required concentrations were then prepared by direct dilution of the premix with appropriate quantities of untreated diets and mixed in a Turbula mixer for at least five minutes. The diets were prepared between 3 and 12 days prior to use and were stored at ambient temperature.

Homogeneity was verified for the nominal concentrations of 50 and 1000 ppm diet prior to treatment. Duplicate samples were taken and analyzed from the top, middle, and bottom levels of the Turbula drum. Stability of diets was determined by taking subsamples of the homogeneity samples. Subsamples of the homogeneity samples were pooled, subdivided, and treated as follows: storage at ambient temperature for 1, 8, or 22 days, and storage at 20°C for 21 days.

Results:

Homogeneity analysis: Mean concentrations of duplicate samples of top, middle, and bottom were 50.4 ppm (100.8%), 48.8 ppm (97.6%), and 48.8 ppm (97.6%) of the 50 ppm nominal concentration and 996.5 ppm (99.7%), 992.5 ppm (99.3%) and 992.5 (99.3%) of the 1000 ppm nominal concentration. The coefficients of variation are 3.85 and 0.64%, for the nominal concentrations of 50 and 1000 ppm, respectively.

Stability analysis: The average concentrations of samples stored at ambient temperature for 0 to 22 days or at below -20°C for 21 days were 47.5 ppm (94.9%) and 50.5 ppm (101%), respectively, for the nominal concentration of 50 ppm. The samples from the 1000 ppm diet stored under the identical conditions had average concentrations of 965.3 ppm (96.5%) and 988 ppm (98.8%), respectively.

Concentration analysis: The mean concentrations of samples taken at five different dates during the study period were 50.7 ppm (101.4%); 203 ppm (101.5%); and 764.2 ppm (101.9%) for the nominal concentrations of 50, 200, and 750 ppm, respectively.

The analytical data indicated that the mixing procedure was adequate. The variance between nominal concentration and actual dosage to the animals was acceptable.

5. **Statistics:** Data from male and female dogs were analyzed separately. Statistical analyses were conducted on food consumption, body weight, blood chemistry, clinical pathology, electrocardiography, and organ weight data. The homogeneity of variance between treatment groups was performed by Bartlett's test. If no significant heterogeneity was detected, Williams and Dunnett tests were carried out. If significant heterogeneity of variance was present, the Shirley and Steel tests were used. For incidence data, Fisher's Exact test was applied. Statistical significance was set at $p \leq 0.05$ and 0.01.

C. METHODS:**1. Observations:**

1a. Cageside observations: Animals were inspected visually at least twice daily for signs of toxicity and mortality.

1b. Clinical examinations: Clinical examinations (not specified) were conducted daily until termination of the study.

2. **Body weight:** Animals were weighed prior to treatment initiation, on the treatment day (Week 0), weekly throughout the study, and on the day of necropsy.

3. **Food consumption and compound intake:** Dry powder diet (SDS Lab A for dogs), 1000 g/day which included 400 g treated dry diet and 600 ml water was given to each animal every day. Intake was measured daily for the whole study period.

4. **Water consumption:** 600 ml of tap water was mixed with the dry diet daily. No other water was specified.

5. **Ophthalmoscopic examination:** The eyes of each animal were examined once before treatment initiation and in Week 52. Mydriasis was induced with a 1% Tropicamide ophthalmic solution. Eyes were examined with a binocular indirect ophthalmoscope.
6. **Electrocardiology:** All animals were examined during pre-treatment, Weeks 39 and 52. In addition, animals in Groups 1 and 4 were examined with the three standard limb leads and the three augmented limb leads tests during Weeks 13 and 26. The EKG traces were evaluated visually for any abnormalities and the following wave intervals were calculated: P, PR, QRS, ST, QT, and QTc.
7. **Hematology and clinical chemistry:** Fasting blood samples were collected from the jugular vein of each animal prior to treatment and at Weeks 13, 26, and 52 for hematology and clinical chemistry. The CHECKED (X) parameters were examined. Hematology parameters were examined using EDTA as the anticoagulant and sodium citrate for the prothrombin measurement. Blood film by Romanowsky stain was examined by light microscopy for abnormal morphology and unusual cell types. Lithium heparin was used as the anticoagulant for clinical chemistry.

a. **Hematology:**

X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpuscular HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpuscular volume (MCV)*
X	Platelet count*		Reticulocyte count
	Blood clotting measurements*		Methemoglobin (MET)
	(Thromboplastin time)		Sulphemoglobin (SHB)
	(Clotting time)		Heinz bodies
X	(Prothrombin time)	X	Large unstained cells (LUC)

* Recommended for 90-day chronic studies based on Guideline 870.4100

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b. Clinical chemistry:

ELECTROLYTES		OTHER	
X	Calcium*	X	Albumin*
X	Chloride*	X	Creatinine*
	Magnesium	X	Urea nitrogen*
X	Phosphorus*	X	Total Cholesterol*
X	Potassium*	X	Globulins
X	Sodium*	X	Glucose*
	ENZYMES (more than 2 hepatic enzymes suggested)*	X	Total bilirubin*
X	Alkaline phosphatase (ALK)*	X	Total protein (TP)*
	Cholinesterase (ChE)	X	Triglycerides
	Glutamate dehydrogenase		Serum protein electrophoresis
X	Lactic acid dehydrogenase (LDH)	X	Albumin/globulin (A/G) ratio
X	Alanine aminotransferase (also SGPT)*	X	Ornithine carbamyl transferase
X	Aspartate aminotransferase (also SGOT)*		Creatine phosphokinase
	Sorbitol dehydrogenase*		
	Gamma glutamyl transferase (GGT)*		

* Recommended for chronic studies based on Guideline 870.4100

8. **Urinalysis:** Urine was collected before the start of treatment and during Weeks 13, 26, and 52 from all animals. The CHECKED (X) parameters were examined.

X	Appearance*	X	Glucose*
X	Volume*	X	Ketones
X	Specific gravity /osmolality*	X	Bilirubin
X	pH*	X	Blood /blood cells*
X	Sediment (microscopic)		Nitrate
X	Protein*		Urobilinogen

* Recommended for chronic studies based on Guideline 870.4100

9. **Sacrifice and pathology:** Animals were fasted overnight prior to sacrifice by an intravenous injection of sodium pentobarbitone (200 mg/ml iv) followed by exsanguination. All sacrificed animals were subjected to a gross pathological examination. The CHECKED (X) tissues were examined histologically. In addition, the (XX) organs were weighed. The gall bladder was weighed with the liver, and the parathyroids were weighed with the thyroid.

Testes and epididymides were fixed in Bouin's solution. Eyes with optic nerve were fixed in Davidson's fluid; only one was examined histologically. All other tissue samples from all animals were preserved in 10% neutral buffered formalin.

DIGESTIVE SYSTEM		CARDIOVASC./HEMAT.		NEUROLOGIC	
X	Tongue	X	Aorta, thoracic*	XX	Brain*+
X	Salivary glands*	XX	Heart*+		Peripheral nerve*
X	Esophagus*	X	Bone marrow*	X	Spinal cord (3 levels)*
X	Stomach*	X	Lymph nodes*	XX	Pituitary*
		XX	Spleen*+	X	Eyes (optic nerve)*
X	Duodenum*	XX	Thymus*+	X	Sciatic nerve
X	Jejunum*				GLANDULAR
X	Ileum*			XX	Adrenal gland*+
X	Cecum*				Lacrimal gland
X	Colon*				Parathyroid*+
X	Rectum*	XX	UROGENITAL		Thyroid*+
XX	Liver*+	X	Kidneys*+	XX	
XX	Gall bladder*+	XX	Urinary bladder*	XX	OTHER
X	Pancreas*	XX	Testes*+		Bone (sternum and/or femur)
	RESPIRATORY	XX	Epididymides*+	X	Skeletal muscle
X	Trachea*	XX	Prostate*	X	Skin*
X	Lung*++	X	Ovaries*+		All gross lesions and masses*
X	Nasal Turbinates*	XX	Uterus*+		
X	Pharynx*		Mammary gland*		
X	Larynx*	XX	Vagina & cervix		

* Recommended for 90-day oral non-rodent studies based on Guideline 870.4100

+ Organ weight required for non-rodent studies.

++ Organ weight required if inhalation route.

II. RESULTS:

A. OBSERVATIONS:

1. **Clinical signs of toxicity:** Hair loss and reddening and scabbing of the skin, mainly on the hind limbs, were observed in two females treated with 200 ppm and in three males and two females treated with 750 ppm Propazine. These signs persisted through the study but were not exacerbated with increased duration of dosing. In addition, some animals in the 50 ppm group as well as controls showed similar signs which were less severe or persistent.

2. **Mortality:** No unscheduled deaths occurred during the study.

B. **BODY WEIGHT AND WEIGHT GAIN:** Body weight and body weight gain data are shown in Table 2. At study termination, the body weight and body weight gain for males were comparable to those of the controls. At the high dose the body weight for females was slightly decreased (ranged from 89 to 97% of the control) during Weeks 2-36, resulting in a lower final body weight (86% of the control). Total body weight gain was decreased to 53% ($p < 0.01$) of the control in the high dose female group. The body weight gain was also less in all female groups in the second week after treatment, but all groups recovered except for the high concentration group which persisted to termination.

TABLE 2: Body weight and body weight gain in dogs during 52 weeks of treatment with Propazine ^{a,b}								
Group, ppm	Body weight, kg						Weight gain, kg Weeks 0-2	Weight gain,kg Weeks 0-52
	Week 0	Week 2	Week 12	Week 24	Week 36	Week 52		
Males								
Control	9.0	9.7	11.8	12.7	13.3	13.2	0.7	4.2
50	9.4	9.9	11.8	12.4	13.0	13.4 (102)	0.6 (86)	4.0 (95)
200	9.2	9.9	12.0	12.8	13.0	13.3 (101)	0.7 (100)	4.1 (98)
750	9.2	9.7	11.7	12.8	13.4	13.5 (102)	0.5 (71)	4.3 (102)
Females								
Control	8.3	9.1	10.7	11.6	12.2	12.3	0.8	4.0
50	8.5	9.0	11.0	12.1	12.6	12.7 (103)	0.5 (63)*	4.2 (105)
200	8.3	8.7	10.3	11.6	11.8	11.8 (96)	0.5 (63)*	3.5 (88)
750	8.5	8.8 (97)	9.7 (91)	10.4 (90)	11.0 (90)	10.6 (86)	0.3 (38)**	2.1 (53)**

^a Data from page 42-3, MRID 46654401.

^b Number in parenthesis represents % of control value, calculated by reviewer.

* p<0.05, ** p<0.01

C. FOOD CONSUMPTION AND COMPOUND INTAKE:

- Food consumption:** The food consumption of males was comparable to that of the controls during the study; however, in females, especially in the 750 ppm group, the food consumption rate was reduced from Week 2 till termination, with a mean average food consumption rate of 83% (p<0.01) of that of the control (Table 3). The mean food consumption value was slightly reduced (88% of the control values) for females in the 200 ppm group.

TABLE 3. Food consumption group mean values in dogs during 52 weeks of treatment with Propazine ^a							
Group, ppm	Food, g (correction for water content x 0.4)						Mean value Weeks 0-52
	Week 1	Week 2	Week 12	Week 24	Week 36	Week 52	
Males							
Control	2594	2671	2687	2794	2800	2800	2731
50	2701	2727	2803	2803	2800	2800	2794(102) ^b
200	2685	2746	2802	2805	2800	2800	2794(102)
750	2479	2766	2686	2803	2739	2737	2749(101)
Females							
Control	2728	2688	2794	2776	2737	2709	2744
50	2505	2704	2802	2804	2751	2426	2685(98)
200	2426	2534	2573	2787	2723	2148	2592(94)
750	1942(71)	2019(75)	2307(83)	2336(84)	2119(77)	2142(79)	2270(83)**

^a Data from page 44-5, MRID 46654401.

^b Number in parenthesis represents % of control value, calculated by reviewer.

** p<0.01

2. **Water consumption:** Water consumption was not reported.

3. **Compound consumption:** Compound consumption is shown in Table 1.

4. **Food efficiency:** Food efficiency was not reported.

D. **OPHTHALMOSCOPIC EXAMINATION:** No treatment related lesions were observed in the treated animals.

E. **ELECTROCARDIOGRAPHY:** Minor sporadic changes were found in the EKGs of the treated dogs (prevalent in the 750 ppm groups) during the study period. These changes included respiratory sinus arrhythmia, sinus tachycardia and variations in atrial activity due to excitement or muscle tone. However, these nonspecific changes could not be definitively associated with treatment with Propazine.

F. **BLOOD ANALYSES:**

1. **Hematology:** Very minor changes were found in several hematological parameters, such as hematocrit and hemoglobin in males in the 200 and 750 ppm groups and in females in the 750 ppm group. These decreases were in the range of 7-10% less than the control value. In addition, very minor sporadic increases were found in the neutrophil and platelet counts in the males treated with 200 and 750 ppm Propazine. Although these changes attained statistical significance (p<0.05 or p<0.01), they were of no biological or toxicological significance.

2. **Clinical chemistry:** Although there were several slight decreases in blood chemistry parameters that attained statistical significance, such as creatinine concentrations in both

males and females in the 750 ppm groups (both 87% of the control at 52 weeks), these changes were not considered biologically or toxicologically significant.

G. URINALYSIS: There were no findings in the urinalysis of treated dogs that could be attributed to the test chemical Propazine.

H. SACRIFICE AND PATHOLOGY:

- 1. Organ weight:** All treated male dogs showed slight increases in absolute kidney weight which attained statistical significance ($p < 0.05$) in the 750 ppm group; in contrast the female dogs showed a slight decrease (8-9% of the control) (Table 4). Slight increases in absolute and adjusted (to terminal BW) of liver weight were found in all treated dogs. The adjusted liver weight in males at 750 ppm attained statistical significance when compared to that of the control. There was no dose-response relationship for liver weight in males or kidney weight in females. None of these changes were considered toxicologically significant.

TABLE 4. Selected absolute and adjusted organ weights, and standard deviation in dogs treated with Propazine for 52 weeks ^{a,b}				
Organ	Group and concentration in diet, ppm			
	0	50	200	750
Males				
Kidney, g absolute	54.9± 2.7	58.2± 6.1(106)	60.7± 7.7(111)	65.2±4.4(119)*
Liver, g absolute	370± 44	410±11(111)	381±51(103)	414±30(112)
adjusted to terminal BW	372	409(110)	386(104)	409(110)**
Females				
Kidney, g absolute	52.7±4.1	48.7±2.5(92)	48.7±3.4(92)	47.8±2.5(91)
Liver, g absolute	334±44	352±35(105)	335±6(100)	349±42(104)
adjusted to terminal BW	324	333(103)	337(104)	376(116)

^a Data from pages 101-106, MRID 46654401.

^b Number in parenthesis represents % of control value, calculated by reviewer.

* $p < 0.05$; ** $p < 0.01$

- 2. Gross pathology:** At termination, examinations revealed scabbing, hair loss, or swelling of the skin on the inner part of the hind leg or forelimb in 1/4, 1/4 and 2/4 male dogs in the 50, 200, and 750 ppm groups, respectively. No microscopic examinations were performed on these lesions. Some of the skin lesions were attributed to the attachment of the EKG leads.
- 3. Microscopic pathology:** Hemosiderosis was detected in females: 1/4, 2/4, 2/4, and 4/4/ in the control through the high dose groups, respectively (Table 5). Severity was higher in females in 750 ppm group. Findings of hemosiderosis were sporadic in the male dogs. There were no microscopic lesions that correlated with the increased and decreased kidney weights in males and females, respectively.

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TABLE 5. Histopathology findings in dogs receiving Propazine for 52-weeks ^a				
Organ	Group and concentration in diet, ppm			
	Control	50	200	750
Males				
Spleen - Hemosiderosis, total	1/4	4/4	1/4	0/4
Females				
Spleen - Hemosiderosis, total	1/4	2/4	2/4	4/4

^a Data from pages 104-114, MRID 46654401**III. DISCUSSION AND CONCLUSIONS:**

- A. INVESTIGATORS' CONCLUSIONS:** The study author concluded that chronic oral administration of Propazine in the diet to beagle dogs produced evidence of mild toxicity, but was tolerated without any mortality. Treatment related changes were apparent in dogs treated with 750 ppm and included lower food consumption and body weight gain, reduced hemoglobin, hematocrit, platelet counts, and splenic hemosiderosis, EKG changes, and skin lesions. Both minor EKG changes and skin lesions were also observed in animals at 200 ppm. There were no treatment related effects seen in dogs at 50 ppm. The study author concluded that the NOEL of Propazine for the male and female beagle dogs was 50 ppm.
- B. REVIEWER COMMENTS:** There were no treatment related mortalities or clinical signs. There were no differences between the controls and the Propazine treated groups in ophthalmology and urinalysis. Food consumption in male dogs was comparable to that of the controls and significantly decreased in female dogs at 750 ppm. At termination, the treated male dogs had body weights and body weight gain comparable with the controls. In contrast, high dose female dogs had decreases in body weight (86% of the control) and body weight gain (53% of the control). The effect on body weight in females in the 750 ppm group appears to be the result of lower food intake.

No biologically significant effects were seen in organ weights. Hematology analyses showed very minor decreases in hemoglobin and hematocrit at 750 ppm and these appeared to be correlated with the microscopic finding of the hemosiderosis in females. Blood chemistry and EKG analyses showed minor incidental variations in the treated beagle dogs. All these changes found from the study were considered of no toxicological significance.

Two female dogs from the 200 ppm group and two females and three males from the 750 ppm groups had skin lesions, primarily on the hind legs. The terminal histological examination showed skin lesions in one male dog each from the 50 and 200 ppm groups and two from the 750 ppm group. None were found in the females. These skin lesions appeared

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to be incidental events; however, the study author suggested they could be caused by a urine excreted metabolite or irritation from the EKG leads, but provided no evidence.

Under the conditions of this study, the LOAEL for Propazine in beagle dogs was not established for males and was 750 ppm (23.98 mg/kg/day) for females based on decreases in body weight and body weight gain. The NOAEL for males is \geq 750 ppm (23.04 mg/kg/day) and for females is 200 ppm (6.72 mg/kg/day).

C. STUDY DEFICIENCIES: There were no serious study deficiencies that invalidated the study results.

DATA FOR ENTRY INTO ISIS

Subchronic Oral Study - dog (870.3150)

PC code	MRID	Study	Species	Duration	Route	Admin	Conc./Dose range ppm/mg/kg/day	Doses ppm/mg/kg/day	NOAEL ppm/mg/kg/day	LOAEL ppm/mg/kg/day	Target organ	Comments
080808	46654401	chronic	beagle dog	52 weeks	oral	diet	0-750 Males: 0-23.94 Females: 0-23.98	0, 50, 200, 750 Males: 0, 1.64, 6.50, and 23.94 Females: 0, 1.65, 6.72, and 23.98	Males: ≥750/ ≥23.94 Females: 200/6.72	Males: Not identified Females:750/ 23.98	body weight and body weight gain	



13544

R154898

Chemical:

PC Code:

HED File Code: 258 **Contractor DER TOX Warning:** This Document (review) was completed by a contractor and has not undergone secondary review. This document may not reflect Agency policies

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