UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

June 16, 2010

MEMORANDUM

Subject:	Name of Pesticide Product:	L899 INSECTICIDE SPINETORAM
	EPA Reg. No. /File Symbol:	72642-O
	DP Barcode:	DP 379111
	Decision No.:	422561
	Action Code:	R270
	PC Code:	110009 (Spinetoram: 39.6%)
From:	Byron T. Backus, Ph.D., Toxicologist Technical Review Branch Registration Division (7505P)	Byron T. Backus 06/16/2010
To:	Samantha Hulkower/Mark Suarez RM 13 Insecticide Branch Registration Division (7505P)	M Hawkins
Registrant:	ELANCO ANIMAL HEALTH	

FORMULATION FROM LABEL:

Active Ingredient(s):		By wt.
110009 Spinetoram		39.60%
Other Ingredient(s):		59.40%*
	TOTAL	100.00%

*should be 60.40% to add up to 100%

ACTION REQUESTED: The Risk Manager requests:

"…As per the internal meeting we just had, please revise the adult [cat] companion safety study to acceptable."

BACKGROUND:

The following represents a re-review of the cat companion animal safety study in MRID 47899910 and an upgrading of this study to acceptable.

COMMENTS AND RECOMMENDATIONS:

1. It is noted that the proposed label for this product indicates the individual applicators contain 0.55 mL (0.019 fl oz) of the formulation, while the 1X dosage in the companion animal safety study in MRID 47899910 was 0.7 mL.

2. The companion animal study with adult cats (MRID 47899910) has been reclassified as acceptable. This study supports the use of this product in adult cats, with once-a-month application. We consider the death of a 5X vehicle control female on Day 33 to be the result of exposure to the vehicle on Day 30.

3. Because of the toxicity of the vehicle (deaths occurred in 1 adult and 8 kittens treated with the 5X vehicle), we recommend that the registrant consider a change in the vehicle for this product.

4. Refer to the attached DER for additional comments regarding this study.

DATA EVALUATION RECORD

SPINETORAM
COMPANION ANIMAL SAFETY STUDY- CATS – (OPPTS 870.7200)
MRID 47899910

Prepared for

Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

Prepared by

Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Number 1-37

Primary Reviewer:
H.T. Borges, Ph.D., MT(ASCP), D.A.B.T.

Signature:
Date: APR 20 2010

Secondary Reviewers:
Cheryl Bast, Ph.D., D.A.B.T.

Signature: Cheryl B Bast
Date: APR 20 2010

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: APR 20 2010

Quality Assurance:
Kimberly Slusher, M.S.

Signature: Kimberly B. Slusher
Date: APR 20 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT_Battelle, LLC., for the U.S. Department of Energy under Contract No. DE AC05 00OR22725.

EPA Reviewer: Byron T. Backus, Ph.D. Signature: Byron T. Backus
Technical Review Branch, Registration Division (7505P) Date: 06-16-2010

EPA Secondary Reviewer: Ayaad Assaad, DVM, Ph.D. Signature: A. Assaad
Toxicology and Epidemiology Branch, HED (7509P) Date: 06/16/2010

Template version 02/06

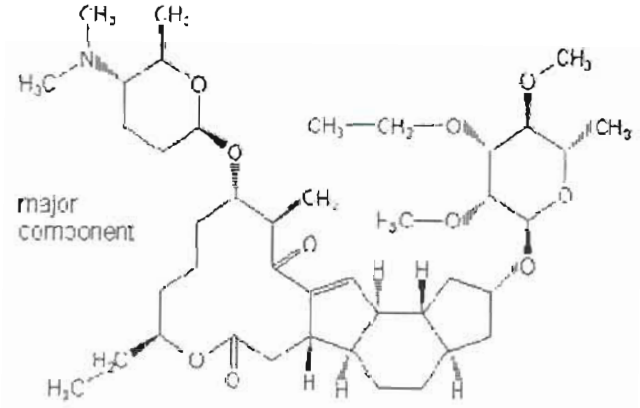
DATA EVALUATION RECORD

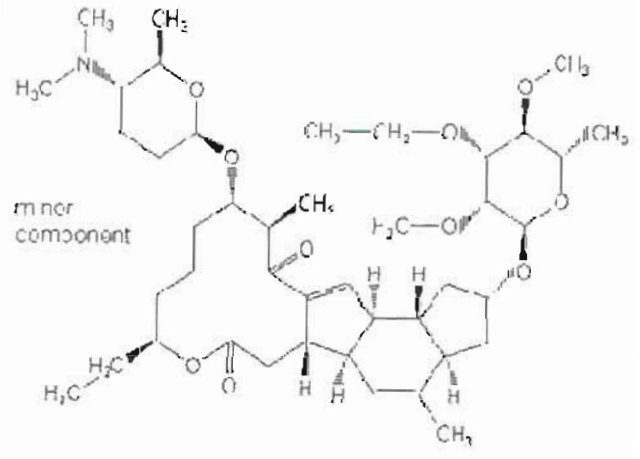
STUDY TYPE: Companion animal safety study- cats – OPPTS 870.7200

PC CODE: 110009 **DP BARCODE**: 372448

TEST MATERIAL (PURITY): L899 Insecticide (39.6% spinetoram)

STRUCTURE OF ACTIVE:





TRADE NAME: Not provided

CITATION: Lloyd, Z. (2009) Safety evaluation study of topically applied L899 insecticide on adult cats. MPI Research Inc., 54943 North Main Street, Mattawan, MI 49071-9399. Study No. 130-162. September 24, 2009. MRID 47899910. Unpublished.

SPONSOR: Elanco Animal Health, A Division of Eli Lilly & Co., 2001 W. Main Street, Greenfield, IN 46140.

EXECUTIVE SUMMARY: In a companion animal safety study (MRID 47899910), groups of six domestic short-hair cats/sex/dose (age 6 – 7.5 months) were topically administered L899 Insecticide/cat (a spot on containing 39.6% spinetoram a.i.) 29 days apart (on Days 1 and 30) at 1X (0.7 mL), 3X (2.1 mL), and 5X (3.5 mL) the recommended dose. A fourth group was dosed with vehicle control at 2 mL.

One 5X vehicle control female (#125) was found dead on Day 33, with approximately an inch and a half of its front left paw caught in the floor grate near the middle of the cage. The death was reported as accidental. However, this animal had the lowest bicarbonate and calcium levels (10 mEq/L and 6.7 mg/dL, respectively) of all adult cats on the study on Day 31, values consistent with those observed (bicarbonate: range of 7-13 mEq/L; calcium: 4.9-8.3 mg/dL) for Day 2 in the 5X vehicle control (same material used in the adult study) kittens sacrificed *in extremis* (study in MRID 47899912). It is concluded that this death in the adult female was a result of exposure to the vehicle on Day 30. It is noted that one other adult female (#133, which survived) also had a low bicarbonate value (11 mEq/L), but a normal calcium level (9.4 mg/dL), on Day 31.

Salivation was observed in two vehicle control females and one 5X female at 15 minutes postdose on day 1 and was still present at 2 hours post dose in all 3 animals, but was seen in only one vehicle control female at 4 hours, and was gone by day 2. Salivation also occurred in one 3X female and one 5X female at 15 minutes post dose (but not subsequently) on Day 30.

Slight decreases in WBC of female cats in all treated groups on Days 2 and 31 and decreases in RBC, hemoglobin and hematocrit in treated female cats in the 3X and 5X groups on Day 31 were not biologically relevant, although they may have been treatment-related. Likewise, slight increases in alkaline phosphatase activity in male cats of all treated groups on Days 2 and 31 may have been treatment-related but were not biologically relevant. No treatment-related effects were found on body weight, food consumption, or coagulation parameters following two applications applied 29 days apart.

It is concluded that the margin of safety in adult cats administered 0.7 mL applications of topical L899 Insecticide (containing 39.6% a.i. spinetoram) is at least 5X the recommended dose (equivalent to 342 mg/kg bw for males and 517 mg/kg bw for females). The proposed label indicates the dosage rate (amount in an applicator) is 0.55 mL.

This companion animal safety study in male and female adult short-hair cats is **Acceptable/ Guideline** and **does satisfy** the guideline requirement for a companion animal safety study (OPPTS 870.7200) in the cat.

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

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test material: L899

Description:	Liquid
Batch #:	PP-09-192-L899-09-03-22
% Active Ingredient:	39.6% Spinetoram
Density	1.061
Date of Manufacture	April 25, 2009
Storage:	Received in amber vials. Stored at room temperature.
Compound Stability:	The test material was stable for the duration of the study
CAS #:	Not provided

Vehicle control

Description:	Not provided
Batch #:	09-01-81
% Active Ingredient:	None [information as to composition is Confidential Business Information]
Date of Manufacture	May 3, 2009
Storage:	Received in amber vials. Stored at room temperature.
CAS #:	Not provided

2. Test animals:

Species:	Feline
Strain:	Domestic short-hair
Age/weight	6-7.5 months/Males 3.68-4.78 kg; Females 2.02-3.81 kg
Source:	Liberty Research, Waverly, NY
Housing:	Individually in stainless steel cages
Diet:	Block Lab Diet® (Feline Diet #5003), PMI Nutrition Int, Inc., *ad libitum*
Water:	Tap water, *ad libitum*
Environmental conditions:	
Temperature:	64-84°F
Humidity:	30-70%
Air changes:	Not reported
Photoperiod:	12 hours light/dark
Acclimation period:	15 days

B. STUDY DESIGN:

1. **In life dates**: Start: May 28, 2009; End: July 13, 2009

2. **Animal assignment**: Twenty four cats of each sex were chosen for the study (Table 1). A standard, by weight, block randomization procedure was used to assign the cats to the control and treatment groups. Male cats had body weights within ± 20.0% of the mean body weight while that of female cats was ± 34.21%.

TABLE 1. Study design				
Test Group	Number of cats	Treatment	Amount of test article (mg spinetoram/kg bw)[a]	Dose volume (mL)
1	12 (6 M and 6 F)	Placebo control	0.0/0.0	2.0
2	12 (6 M and 6 F)	1x	65/105	0.7
3	12 (6 M and 6 F)	3x	211/305	2.1
4	12 (6 M and 6 F)	5x	342/517	3.5

Data from page 15 of MRID 47899910

[a]Calculated by reviewer using a density of 1.061, the average body wt/sex/group on day -1, and 39.6% active ingredient. Presented as M/F.

3. **Dose selection rationale**: The 1X dose of the test material is 0.7 mL/cat, although the proposed label indicates individual applicators would contain 0.55 mL. The doses chosen for this study were to provide 1, 3, and 5 times the proposed *ad usum* in cats to evaluate the margin of safety for the test material.

4. **Preparation and treatment**: The placebo and test substance were applied on Days 1 and 30 at the doses and volumes shown in Table 1. The appropriate amount of placebo (2.0 mL placebo) or test material (0.7 mL for the 1X group, 2.1 mL for the 3X group and 3.5 mL for the 5X group) was drawn into a dosing syringe; a new syringe for each animal. The animal was restrained such that the shoulder blades were accessible. The placebo or test substance was administered on the unshaved dorsal midline between the shoulder blades, extending cranially or caudally, as needed, to prevent runoff. The study was blinded, with only individuals responsible for dosing and the study director knowing study groups and treatment.

5. **Statistics**: Multiple endpoint analyses, such as body weight, food consumption, hematology, coagulation, and clinical chemistry, were analyzed using a repeated measures analysis of covariance model blocked on treatment, sex, and time. The pre-treatment value or the average of the pre-treatment values closest to dosing was used as the covariate. If the Treatment × Sex × Time interaction was significant at $p<0.05$, the Treatment × Time interaction was examined for each Sex at $\alpha = 0.10$. In addition, detailed qualitative analyses such as profile plots and descriptive statistics were done. Regardless of whether Treatment × Sex interaction was significant, if the Treatment × Time interaction was significant, pair-wise contrasts at each time using the "time by dose group" least squares mean was evaluated at $\alpha = 0.10$.

C. METHODS:

1. Observations:

a. **Cageside**: All cats were observed for morbidity, mortality, and clinical signs of toxicity at least twice daily through the study.

b. **Clinical**: Detailed clinical examinations were done twice daily on non-dosing days beginning on Day -7. The animals were also examined immediately prior to dosing and 1, 2, 3, and 4 hours post-dose on days 1 and 30. The examinations included evaluation of the skin, fur, eyes, ears, nose, oral cavity, thorax, abdomen, external genitalia, limbs and

feet, respiratory system, circulatory system, autonomic and nervous system, somatomotor activity, and behavior.

2. **Body weight:** The animals were weighed on receipt, and on Days -1, 7, 14, 21, 28, 30 (pre-dose), 36, and 43.

3. **Food consumption:** Food consumption was measured daily beginning on Day -7 and reported weekly.

4. **Hematology and clinical chemistry**: Blood was collected from the jugular vein for hematology and clinical chemistry assessments of fasted animals on the following days: - 6, 2, and 31. The CHECKED (X) parameters were examined.

a. Hematology

X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count*	X	Reticulocyte count
	Blood clotting measurements*		
X	(Thromboplastin time)		
	(Fibrinogen)		
X	(Prothrombin time)		

*Recommended for companion animals safety evaluation based on OPPTS 870.7200

b. Clinical chemistry

	ELECTROLYTES		OTHER
X	Calcium*	X	Albumin*
X	Chloride*	X	Creatinine*
X	Magnesium	X	Urea nitrogen*
X	Phosphorus *	X	Total Cholesterol
X	Potassium* (K)	X	Globulins*
X	Sodium* (NA)	X	Glucose*
	ENZYMES (more than 2 hepatic enzymes, eg., *)	X	Total bilirubin *
X	Alkaline phosphatase (AP)*	X	Total protein*
X	Lactic acid dehydrogenase (LDH)	X	Triglycerides
X	Alanine aminotransferase (ALT/also SGPT)*	X	Albumin/Globulin ratio
X	Aspartate aminotransferase (AST/also SGOT)*	X	Direct bilirubin*
X	Gamma glutamyl transferase (GGT)	X	Bicarbonate
	Cholinesterase (ChE)		
X	Creatine kinase		
X	Amylase		

* Recommended for a companion animal safety evaluation based on OPPTS 870.7200

5. **Urinalysis:** Urinalysis was not done.

6. **Fecal samples:** Fecal ova and parasite evaluations were done during the acclimation period. All animals included in the study were negative.

6. **Sacrifice and pathology**: The study did not have a scheduled necropsy.

II. RESULTS

A. OBSERVATIONS:

1. **Clinical signs of toxicity**: No treatment-related clinical signs of toxicity were observed in the animals exposed to 1X, 3X or 5X the Spinetoram-containing formulation.

2. **Application site examination**: Slight yellowish hair discoloration was noted on some cats, particularly females. In addition, hair sparseness was observed at the application site on occasion sporadically throughout the study; most notably on two females in the 3X group and one male and one female in the 5X group.

3. **Mortality**: One placebo control female was found dead during the study with its front paw caught in the floor grate near the middle of the cage. This animal had the lowest bicarbonate and calcium levels (10 mEq/L and 6.6 mg/dL, respectively) of all adult cats on the study on Day 31, values consistent with those observed (bicarbonate: range of 7-13 mEq/L; calcium: 4.9-8.3 mg/dL) for Day 2 in the 5X vehicle control (same control as used in the adult study) kittens sacrificed *in extremis* (study in MRID 47899912). It is concluded that this death in the adult female was a result of exposure to the vehicle on Day 30. All other cats survived until scheduled sacrifice, although it is noted that one other 5C vehicle control female (#133) had a low bicarbonate value (11 mEq/L), but a normal calcium level (9.4 mg/dL) on Day 31.

B. BODY WEIGHT AND WEIGHT GAIN:

As shown in Tables 2 and 3, no treatment-related effects on body weight or body weight gain were found.

Table 2: Body weight (kg) ± S.D.

Group	Males			
	Day -1	Day 7	Day 21	Day 43
Placebo	4.313 ± 0.3869	4.405 ± 0.4962	4.730 ± 0.4621	5.072 ± 0.6128
1X	4.293 ± 0.3595	4.380 ± 0.3769	4.622 ± 0.4182	4.817 ± 0.4867
3X	4.187 ± 0.3833	4.272 ± 0.3526	4.532 ± 0.4693	4.712 ± 0.5294
5X	4.300 ± 0.2955	4.418 ± 0.3020	4.657 ± 0.1806	4.888 ± 0.2109
	Females			
Placebo	2.810 ± 0.5898	2.788 ± 0.5402	2.882 ± 0.6341	3.026 ± 0.5744
1X	2.807 ± 0.5468	2.812 ± 0.5303	2.850 ± 0.5771	2.817 ± 0.5854
3X	2.897 ± 0.5395	2.907 ± 0.5434	2.945 ± 0.6076	3.017 ± 0.7092
5X	2.842 ± 0.4811	2.847 ± 0.4411	3.005 ± 0.4561	3.077 ± 0.4731

Data from pages 195-198 of MRID 47899910
N = 6/group

Table 3: Body weight gains (kg) ± S.D.					
Group	Males				
	Day -1 to 7	Day 7 to 28	Day 28 to 36	Day 36 to 43	Day -1 to 43
Placebo	0.092 ± 0.229	0.487 ± 0.149	0.125 ± 0.094	0.055 ± 0.103	0.758 ± 0.341
1X	0.087 ± 0.044	0.303 ± 0.149	0.128 ± 0.162	0.005 ± 0.052	0.523 ± 0.321
3X	0.085 ± 0.139	0.328 ± 0.261	0.103 ± 0.053	0.008 ± 0.104	0.525 ± 0.317
5X	0.118 ± 0.071	0.282 ± 0.247	0.140 ± 0.115	0.048 ± 0.084	0.588 ± 0.370
	Females				
Placebo	-0.022 ± 0.088	0.137 ± 0.153	*0.024 ± 0.057	*-0.028 ± 0.117	*0.146 ± 0.076
1X	0.005 ± 0.060	0.005 ± 0.129	0.002 ± 0.5771	-0.002 ± 0.018	0.010 ± 0.071
3X	0.010 ± 0.091	0.093 ± 0.131	0.027 ± 0.062	-0.027 ± 0.078	0.120 ± 0.272
5X	0.005 ± 0.065	0.162 ± 0.070	0.050 ± 0.035	-0.017 ± 0.068	0.235 ± 0.132

Calculated from data on pages 487-491 of MRID 47899910
*N = 5/group; otherwise N = 6/group

C. **FOOD CONSUMPTION:** No treatment-related effects on food consumption were found.

D. **CLINICAL PATHOLOGY ANALYSES:**

1. **Hematology**: As shown in Table 4, female cats in the 1X, 3X, and 5X groups had slight, but statistically significant decreases in the WBC count on Day 2 and Day 31. This was attributed by the study author to mild decreases in neutrophils in female cats in all treatment groups and intervals with minimal contributions by decreases in lymphocytes. Although the decreases in WBC and neutrophils in female cats were not dose-related, they may be treatment-related. However, they were within the published normal range for domestic cats and not of biological concern.

   Female cats had a mild dose-related decrease in hemoglobin and hematocrit in the 3X and 5X groups on Days 2 and 31. While the changes may be treatment related, they were not biologically relevant and were well within the published normal range for domestic cats. No treatment-related effects were found on examined coagulation parameters.

Table 4. Selected hematology results						
Group	Male			Female		
	Day -6	Day 2	Day 31	Day -6	Day 2	Day 31
WBC (10^3/µL)						
Placebo	20.32 ± 4.65	16.73 ± 6.12	13.98 ± 5.55	16.97 ± 1.52	15.18 ± 2.77	16.46 ± 6.06
1X	18.98 ± 5.84	13.33 ± 5.21	13.83 ± 4.58	14.53 ± 5.68	10.05 ± 2.48**	9.43 ± 2.22**
3X	16.37 ± 2.29	12.63 ± 1.42	13.37 ± 3.21	14.72 ± 4.77	9.35 ± 2.71**	9.02 ± 2.95**
5X	18.75 ± 2.95	14.58 ± 4.00	12.65 ± 3.71	14.25 ± 2.32	9.33 ± 1.55**	9.74 ± 1.51**
RBC (10^6/µL)						
Placebo	9.73 ± 1.16	9.13 ± 0.95	9.82 ± 1.52	10.12 ± 1.13	9.81 ± 1.17	10.18 ± 1.96
1X	8.86 ± 0.72	9.16 ± 1.08	9.72 ± 0.73	9.76 ± 0.94	9.40 ± 0.72	9.09 ± 1.28
3X	8.72 ± 0.66	9.24 ± 0.53	9.96 ± 0.79	10.00 ± 0.99	9.00 ± 1.21	8.84 ± 0.81
5X	9.33 ± 0.64	9.52 ± 9.62	9.46 ± 0.88	9.20 ± 1.19	8.92 ± 0.63	8.36 ± 0.70
Hemoglobin (g/dL)						
Placebo	12.6 ± 1.08	12.1 ± 1.14	12.8 ± 1.51	13.8 ± 1.14	13.6 ± 1.31	13.9 ± 1.90
1X	11.4 ± 0.83	12.0 ± 1.45	12.6 ± 0.82	13.0 ± 1.02	12.6 ± 0.84	11.9 ± 1.21*
3X	11.4 ± 1.26	12.3 ± 1.26	13.2 ± 1.36	13.4 ± 0.65	12.2 ± 1.09	11.9 ± 0.56*
5X	11.9 ± 1.19	12.4 ± 0.89	12.2 ± 1.49	12.1 ± 1.17	11.9 ± 0.87	10.7 ± 0.90**
Hematocrit (%)						
Placebo	39.7 ± 3.52	37.1 ± 3.18	37.8 ± 36.9	43.4 ± 3.59	41.0 ± 4.17	40.6 ± 5.98
1X	35.7 ± 2.40	36.8 ± 4.68	37.0 ± 2.66	41.5 ± 3.48	38.4 ± 2.63	35.1 ± 4.34*
3X	36.0 ± 4.03	38.0 ± 3.30	39.6 ± 4.66	43.1 ± 2.00	37.6 ± 4.16	35.0 ± 1.74*
5X	37.4 ± 3.34	38.0 ± 2.23	35.5 ± 3.79	38.3 ± 3.58*	36.8 ± 2.22	31.9 ± 2.49**

Data from pages 212 – 228 of MRID 47899910
*p<0.05; **p<0.01 calculated be reviewer

2. Clinical Chemistry: No biologically or toxicologically relevant treatment-related effects were found on measured clinical chemistry parameters. The study author reported a dose-dependent increase in alkaline phosphatase activity in male cats in the 1X, 3X, and 5X groups (Day 2 – 69.0, 85.2, 87.2, and 99.5 IU; Day 31 – 71.8, 73.8, 93.7, 111.5 IU in the control, low, mid, and high-dose groups, respectively); however, the very slight increases in activity were not biologically or toxicologically relevant. Other statistically significant effects were present, but were unrelated to dose and/or well within the established normal range for domestic cats.

III. DISCUSSION AND CONCLUSIONS

A. INVESTIGATORS' CONCLUSIONS: The study author concluded that L899 Insecticide was well tolerated when administered topically to adult cats at 1X, 3X, and 5X the proposed clinical dose of 0.7 mL by two single topical applications applied 29 days apart.

B. REVIEWER COMMENTS: In this study, four groups of six adult domestic short-hair cats/sex/dose received a placebo, or 1, 3, or 5 times the proposed *ad usum* for cats of L899 Insecticide (39.6% spinetoram a.i.). Slight decreases in WBC of female cats in all treated groups on Days 2 and 31 and decreases in RBC, hemoglobin and hematocrit in treated female cats in the 3X and 5X groups on Day 31 were not biologically relevant, although they may have been treatment-related. Likewise, slight increases in alkaline phosphatase activity in male cats of all treated groups on Days 2 and 31 may have been treatment-related but were

not biologically relevant. No treatment-related effects were found on body weight, food consumption, or coagulation parameters following two applications applied 29 days apart.

One 5X vehicle control female (#125) was found dead on Day 33, with approximately an inch and a half of its front paw caught in the floor grate near the middle of the cage. The death was reported as accidental. However, this animal had the lowest bicarbonate and calcium levels (from p. 651 of MRID47899910 10 mEq/L and 6.7 mg/dL, respectively) of all adult cats on the study on Day 31, values consistent with those observed (bicarbonate: range of 7-13 mEq/L; calcium: 4.9-8.3 mg/dL) for Day 2 in the 5X vehicle control (same material used in the adult study) kittens sacrificed *in extremis* (study in MRID 47899912). It is concluded that this death in the adult female was a result of 5X exposure to the vehicle on Day 30. It is noted that one other adult female (#133, which survived) also had a low bicarbonate value (11 mEq/L), but a normal calcium level (9.4 mg/dL) on Day 31.

It is concluded that the margin of safety in adult cats administered 0.7 mL applications of topical L899 Insecticide (containing 39.6% a.i. spinetoram) is at least 5X the recommended dose (equivalent to 342 mg/kg bw for males and 517 mg/kg bw for females). The proposed label dosage rate (amount in an applicator) is 0.55 mL.

C. STUDY DEFICIENCIES:

None that would preclude interpretation of the study results.

1. **DP BARCODE:** 372448
2. **PC CODE:** 110009 (Spinetoram)
3. **CURRENT DATE:** May 25, 2010
4. **TEST MATERIALS:** Controls (Group 1): 5X (2.0 mL) vehicle (L899 Insecticide Placebo, Lot No. 09-01-81, containing the same solvents and inerts in the same relative proportions as L899 Insecticide); Groups 2, 3, 4: 1X (0.7 mL), 3X (2.1 mL) and 5X (3.5 mL): L899 Insecticide [39.58% (w/w) Spinetoram; Lot No. PP-09-192-L899-09-03-22]

Study/Species/Lab Study # / Date	MRID	Results	Tox. Cat.	Core Grade
Companion Animal Safety Study/6-7.5 month old Cats MPI Research Inc., Mattawan, Michigan Elanco Animal Health, A Division of Eli Lilly & Company, Greenfield, Indiana	47899910	Four groups (each 6M & 6F) of 6-7.5 month old cats were treated on Day 0. Group 1 (5X controls) was treated with 2.0 mL vehicle, Group 2 with 1X (0.7 mL) L899 Insecticide; Group 3 with 3X (2.1 mL) L899 Insecticide; Group 4 with 5X (3.5 mL) L899 Insecticide. All groups were treated again at the same doses on Day 29. One placebo control female was found dead with its paw caught in a floor grate on Day 33; clinical chemistry findings from this cat on day e were no mortalities in any of the other groups and there were no dose-related signs of toxicity.	N/A	A

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived