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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: 10/13/2010

SUBJECT: Review of ***"A Study to Determine the Haircoat Distribution of a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs"*** (MRID 47914240).

PC Code: 106201
MRID No.: 47914240
Petition No.: NA
Assessment Type: NA
TXR No.: NA

DP Barcode: D372054
Registration No.: NA
Regulatory Action: Data Evaluation Record
Reregistration Case No.: NA
CAS No.: 33089-61-1

FROM: Ana Rivera-Lupiáñez, Chemist
Risk Assessment Branch V
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THROUGH: Jack Arthur, Branch Chief
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TO: Autumn Metzger, Risk Manager Reviewer
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Registration Division (RD) (7505P)

This document serves as a data evaluation record for the fipronil, (s) - methoprene and amitraz exposure study, "A Study to Determine the Haircoat Distribution of a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs,"submitted by Merial Limited in support of the registration of a proposed topical spot-on product for dogs and puppies containing the active ingredients fipronil, (s) - methoprene and amitraz. The study was conducted to measure the amount of each active ingredient (fipronil, (s) - methoprene and amitraz) that may be dislodged from dog's hair coat after a single treatment of the spot-on product. A primary review of this study was conducted by Versar, Inc. under the guidance of HED (see Attachment).

STUDY TYPE: Haircoat Distribution after a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs.

TEST MATERIAL: The test material was a spot-on formulation for dogs and puppies containing the active ingredients fipronil, (s) - methoprene and amitraz.referred to as ML-2,095,988 509T and ML-3,948,906.

CITATION:

Study Authors:	Théodora Mezzasalma, MSc Mireille Vila, PhD Matthias Pollmeier, DVM
Title:	A Study to Determine the Haircoat Distribution of a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs
Report Date:	October 28, 2009
Performing Laboratories:	Avogadro SA Parc de Génibrat 31470 Fontenilles France
Identifying Codes:	Avogadro Ref: A08217 Sponsor Ref: PR&D 0168601

SPONSOR: Merial 3239 Satellite Blvd.
Duluth, GA 30096-4640

EXECUTIVE SUMMARY:

This review analyzes the report "*A Study to Determine the Haircoat Distribution of a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs*,"submitted by Merial Limited in support of the registration of a proposed topical spot-on product for dogs and puppies containing the active ingredients fipronil, (s) - methoprene and amitraz. The study was conducted to measure the amount of active ingredients fipronil, (s) - methoprene and amitraz that may be dislodged from dog's hair coat after a single treatment of the spot-on product. A primary review of this study was conducted by Versar, Inc. under the guidance of HED (see Attachment).

The registrant, Merial Limited, submitted an amitraz exposure study (MRID 47914240) which was conducted to measure percent residue transfer from the treated animal to the exposed individual. The study was conducted using a pet fur clipping method, not the most advantageous "stroking" or "petting" method. The fur clipping method was recommended because the Agency was in a period of deliberation when the study sponsor requested input. Because the petting/stroking study involved human subjects who are directly exposed to a pesticide-treated animal, the Agency debated whether this implied intentional human exposure to a pesticide; which, under the Government-wide Common Rule (EPA 40 CFR 26 – Protection of Human Subjects) would not be allowable unless all appropriate criteria pertaining to ethical conduct of

the studies were adhered to. Rather than advise Merial Limited to perform a study which could have later been determined unacceptable, HED recommended an alternative transfer study method, pet fur clipping. HED recognizes that the petting/stroking studies and pet fur clipping studies differ and, therefore, the resulting data is subject to interpretation due to the noted differences in the sampling method.

On April 14, 2009, HED met with Merial Limited to discuss the proposed spot on pet product. HED expressed their concerns about how the pet fur clipping study compared to petting or stroking method studies. Based upon this exchange, Merial Limited submitted a weight-of-evidence approach in a white paper to HED showing that fur clipping data were comparable to the petting study submitted by them in the past for the original Frontline® product registration. HED reviewed this submission and the result is captured in the memorandum, "HED Review of, "Residential Hazard, Exposure and Risk Assessment for a New, Topical Ectoparasiticide for Dogs that Contains Fipronil, (s)-Methoprene and Amitraz" (W. Britton, D367277)." HED concluded that, "Based upon the data submitted and reviewed, HED is satisfied that the amitraz fur clipping study is an acceptable surrogate for an amitraz petting study and, likewise, represents the amount of active ingredient which is anticipated to be available to transfer to an individual contacting an animal treated with the amitraz-containing formulation.

It should be noted that pet fur clipping studies typically result in percent transfer measures below that of petting studies, thus resulting in a less protective exposure assessment. HED currently prefers the petting method with application of the modifications as recommended by Agency ethics officials; specifically, restricting direct contact with a gloved human hand and the treated animal in favor of using a hand-held instrument, such as a mannequin hand, to mimic petting. In this instance, HED has reviewed the submitted fur clipping study and determined that it is acceptable to assess the proposed use.

HED selected the result of all measured samples from the dog with the highest percent residue transfer, due to the uncertainty in using data collected from a study using the pet fur clipping method. Using this approach, 0.0392% of total amitraz residue applied is assumed to be available for dermal transfer to humans.[1] This value was derived from the highest residue obtained of 6 dogs sampled on Day 3 after application.

A summary of the exposure study is presented below.

ATTACHMENT:

A study was conducted in Avogadro, France examining the distribution of ML-2,095,988 (fipronil), ML-3,335,716 ((s)-methoprene) and ML-3,948,906 (amitraz) on the haircoat of dogs. A spot-on topical application of a mixed liquid formulation containing 10% w/v fipronil and 9% w/v (s)-methoprene, plus a liquid formulation of amitraz was applied to each of six dogs. Hair samples were then collected at seven specified time intervals from five body zones of each dog over a period of 58 days after application. Five analytes were quantified from each hair sample. The Study Report presented the findings in micrograms active ingredient (ai) per gram of hair sample (µg ai/g) and also in µg ai/cm^2 for each body zone of the dogs tested.

[1] Refer to Table C- Additional Tables Section.

Two dogs (1 male and 1 female) were randomly chosen as the control (Group 1) and were vehicle treated (blank application). Six dogs (3 males and 3 females) were placed in Group 2 and were treated with the combined formulations. The treatment was applied using a syringe by parting the hair and concurrently applying the appropriate combination of test formulations (or two paired control vehicle formulations) directly onto the skin of each dog on two separate spots of approximately equal volume. One spot was placed on the midline of the neck, between the base of the skull and the shoulder blades, and the other spot between the shoulder blades. The treated dogs received 6.70 mg fipronil/kg body weight (bw) with 6.03 mg (s)-methoprene/kg bw (first formulation), plus 8.00 mg amitraz/kg bw (second formulation). Hair samples were collected on Day -6 (pre-application), and on Day 1, Day 3, Day 7, Day 14, Day 28, Day 42 and Day 58 after the application. Electric clippers were used to collect hair samples from five different sites on each dog: (1) lumbar zone; (2) thorax right side; (3) thorax left side; (4) middle of the back; and (5) top of the neck. A different site on the body zone was clipped at each sampling interval. The hair samples ranged in weight from 0.289 to 1.83 g, and were clipped from an area of 4 to 8 cm^2 for each sample. The samples were stored frozen until analysis. Amitraz and MFN (a degradation product of amitraz) concentrations were determined in dog hair using an LC/MS-MS method whereas fipronil, fipronil sulfone (the primary metabolite of fipronil), and (s)-methoprene were determined by HPLC/UV. The lower limit of quantification (LLOQ) was 0.10 µg/g in dog hair for fipronil and fipronil sulfone. The LLOQs for (s)-methoprene, amitraz and MFN were 0.05, 0.20, and 0.25 µg/g, respectively.

On each day of analysis, quality control samples were prepared in duplicate by fortifying control dog hair (untreated hair) at three concentrations ranging from 0.20 to 3.2 µg/g of fipronil and fipronil sulfone, 0.10 to 3.2 µg/g of (s)-methoprene, and 0.30 to 4.0 µg/g of amitraz and MFN. Overall average field fortification recoveries of all analytes were greater than 90%, and no field samples required correction for field fortification recovery.

The average fipronil concentration in each hair sample ranged from 0.116 µg/g (top of neck on Day 58) to 73.0 µg/g (middle of back on Day 7). The average fipronil sulfone concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 3.66 µg/g (middle of back on Day 28). The average (s)-methoprene concentration in each hair sample ranged from 0.122 µg/g (top of neck on Day 58) to 103 µg/g (middle of back on Day 7). The average amitraz concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 75.8 µg/g (middle of back on Day 7).

The results of this study demonstrate that the three active ingredients (fipronil, (s)-methoprene, and amitraz) in the combination of ML-2-2,095,988 509T and ML-3,948,906, when administered concurrently one time as topical solutions, distribute over the entire body surface with a peak on Day 7 and steadily decrease over the 58 day sampling period following treatment.

Study Parameters

Eight dogs (4 males and 4 females) ranging in age from 9.7 to 10.6 months participated in this study. The dogs were acclimated to their holding pens for 11 days prior to application of the test substance. Six days prior to the product application, the dogs were weighed to calculate the dose rate for the combined ML-2,095,988 509T (fipronil and (s)-methoprene) and ML-3,948,906 (amitraz) topical solutions. The weight of the dogs at the beginning of the study ranged from 9.07 to 13.9 kg.

Two dogs (1 male and 1 female) were randomly chosen as the control group (Group 1) and were vehicle treated (blank application). The remaining six dogs (3 males and 3 females) were placed in Group 2 and were treated with the combined formulations. The treatment was applied by parting the hair and concurrently applying the appropriate combination of test formulations (or two paired control vehicle formulations) directly onto the skin of each dog on two separate spots of approximately equal volume.

One spot was placed on the midline of the neck, between the base of the skull and the shoulder blades, and the other spot between the shoulder blades. The Group 2 dogs received 6.70 mg fipronil/kg body weight (bw), 6.03 mg (s)-methoprene/kg bw (first formulation), plus 8.00 mg amitraz/kg bw (second formulation). The actual application rates ranged from 6.78 to 7.39 mg ai/kg fipronil, from 6.10 to 6.65 mg ai/kg (s)-methoprene, and from 8.08 to 8.82 mg ai/kg amitraz.

Hair samples were collected at Day -6 (pre-application), Day 1, Day 3, Day 7, Day 14, Day 28, Day 42 and Day 58 after application of the combined formulations. Electric clippers or scissors were used at five different sites on the dog: (1) lumbar zone; (2) thorax right side; (3) thorax left side; (4) middle of the back; and (5) top of the neck. The scissors were only used if the dog was agitated. An area of 4 cm^2 was clipped for each thorax (left and right side), middle of back, and top of neck sample, while an area of 8 cm^2 was clipped for each lumbar sample. Sample weights were at least 0.5 g, except for the neck area which was at least 0.2 g. Actual average sample weights were 0.81 g, 0.74 g, 0.75 g, 0.81 g and 0.43g for the lumbar, right thorax, left thorax, middle of back and top of neck regions, respectively. After collection, the hair samples were transferred directly into a labeled container, weighed and then placed in frozen storage (approximately -80°C) until analysis. The Registrant did not provide information for how long the study samples were kept in storage prior to extraction or analysis.

Analytical Phase

The analytical methods used in this study were Avogadro Study Numbers A99117 (fipronil and fipronil sulfone), A99118 ((s)-methoprene), and A082182 (amitraz and MFN). Fipronil, fipronil sulfone, and (s)-methoprene concentrations were determined in dog hair using an HPLC/UV method, whereas amitraz and MFN were determined by LC/MS-MS. All of the analytical methods utilized liquid-liquid extraction. Th analytical method was validated prior to the start of the field sample analyses, to ensure that the performance (linearity, specificity, precision and accuracy) of the methods met the validation criteria on the HPLC/UV and LC/MS-MS systems. The analytical methods were validated to quantitate residues ranging between 0.10 µg/g and 4.0 µg/g in dog hair for fipronil, fipronil sulfone, between 0.05 µg/g and 4.0 µg/g for (s)-methoprene, between 0.20 µg/g and 5.0 µg/g for amitraz and between 0.25 µg/g and 5.0 µg/g for MFN. The limits of quantitation were 0.1 µg/g, 0.1 µg/g, 0.05 µg/g, 0.20 µg/g, and 0.25 µg/g for fipronil, fipronil sulfone, (s)-methoprene, amitraz and MFN, respectively. The limits of detection were 0.007 µg/g and 0.037 µg/g for amitraz and MFN, respectively. When hair sample concentrations measured in treated specimens were >15% of the highest calibration level, the specimens were re-assayed after an appropriate dilution.

Quality Control

Two dogs were randomly chosen as a control group and were vehicle treated (blank application) and sampled at the same intervals as the treated group of dogs. Field fortification samples were not prepared for this study. Control (untreated) dog hair was obtained from Avogadro for fortified concurrent and stability samples. On each day of analysis, quality control samples were prepared in duplicate by fortifying control dog hair (untreated hair) at three concentrations ranging from 0.20 to 3.2 µg/g of fipronil and fipronil sulfone, 0.10 to 3.2 µg/g of (s)-methoprene, and 0.30 to 4.0 µg/g of amitraz and MFN.

Freeze and thaw stability of fipronil, fipronil sulfone and (s)-methoprene in hair samples were prepared by fortifying control matrix with working solution. The prepared samples were immediately frozen for approximately 24 hours at -80°C, then thawed at room temperature for approximately 2 hours and frozen again for approximately 12 hours. The stability samples were extracted after 15 minutes of thawing.

The short term stability of fipronil, fipronil sulfone, (s)-methoprene, amitraz, and MFN in hair samples stored at approximately 4 hours at room temperature was tested at 2 concentration levels (4 replicates per level).

Long term stability of fipronil, (s)-methoprene and amitraz in hair samples stored at -80°C for a storage duration that covered at least the maximum storage duration of the actual study samples was evaluated at three concentrations (4 replicates per level) in order to validate the specimen storage. The maximum storage duration of the actual study samples was not reported in the study.

Results and Calculations

Samples collected from each of the dogs six days prior to the application date, confirmed that all of the dogs (Groups 1 and 2) were not exposed to fipronil, fipronil sulfone, (s)-methoprene, amitraz or MFN before dosing.

After the application, residual levels of fipronil, (s)-methoprene and amitraz were found on the control dogs (Group 1) from Day 3 to Day 42 with the highest concentrations found between Day 7 and Day 14. Fipronil residues in the control samples ranged from 0.106 µg/g (Day 3) to 0.435 µg/g (Day 7) with a corresponding LOQ of 0.10 µg/g. (s)-Methoprene residues in the control samples ranged from 0.055 µg/g (Day 3) to 0.757 µg/g (Day 14) with a corresponding LOQ of 0.05 µg/g. Amitraz residues in the control samples ranged from 0.209 µg/g (Day 14) to 0.780 µg/g (Day 7) with a corresponding LOQ of 0.20 µg/g. MFN residues were found in the control samples on Days 1, 28 and 42, ranging from 0.274 µg/g (Day 28) to 1.43 µg/g (Day 42) with a corresponding LOQ of 0.250 µg/g. According to the Registrant, the low level contamination could have resulted from a number of factors which include the following: (1) hair shedding from treatment dogs; (2) accidental cross contamination after handling treated dogs; and (3) laboratory contamination. It was determined that the overall impact of the contamination on the results of the study was negligible and that no corrections were required.

Tables 1 through 5 provide a summary of the concurrent QC sample recoveries. All of the average recoveries for each concentration level were >90%, therefore, the field samples did not require correction for concurrent fortification recoveries. The overall average percent recovery for fipronil was 99.2% ± 4.91 (n=104). The overall average percent recovery for fipronil sulfone was 97.0% ± 4.74 (n=73). The overall average percent recovery for (s)-methoprene was 103% ± 8.15 (n=80). The overall average percent recovery for amitraz was 96.5% ± 5.81 (n=73). The overall average percent recovery for MFN was 98.6% ± 6.56 (n=66).

Tables 6 through 10 provide a summary of the levels (µg/g) of fipronil, fipronil sulfone, (2)-methoprene, amitraz and MFN detected in dog hair for each of five body zones at each sampling interval. The average fipronil concentration in each hair sample ranged from 0.116 µg/g (top of neck on Day 58) to 73.0 µg/g (middle of back on Day 7). The average fipronil sulfone concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 3.66 µg/g (middle of back on Day 28). The average (s)-methoprene concentration in each hair sample ranged from 0.122 µg/g (top of neck on Day 58) to 103 µg/g (middle of back on Day 7). The average amitraz concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 75.8 µg/g (middle of back on Day 7). The average MFN concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 1.93 µg/g (middle of back on Day 7).

Table 11 provides the weight and body area of each hair sample collection. This information was used to convert the residues from µg/g to µg/cm^2. Tables 12 through 16 provide a summary of the levels (µg/cm^2) of fipronil, fipronil sulfone, (2)-methoprene, amitraz and MFN detected in dog hair for each of five body zones at each sampling interval. The µg/g concentration values (Tables 6 through 10) were converted to µg/cm^2 (Tables 12 through 16) using the area of each clipping (8 cm^2 for lumbar zone and 4 cm^2 for the

remaining zones) and the weight of each hair sample in grams as presented in Table 11. The following equation was used:

Concentration ($\mu g/cm^2$) = Concentration ($\mu g/g$) x Wt (g) / A (cm^2)

Where: Wt = weight of hair sample collected (g)
A = area of body surface sampled (8 or 4 cm^2)

The average fipronil concentration in each hair sample ranged from 0.010 $\mu g/cm^2$ (top of neck on Day 58) to 14.4 $\mu g/cm^2$ (middle of back on Day 7). The average fipronil sulfone concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 0.614 $\mu g/cm^2$ (middle of back on Day 28). The average (s)-methoprene concentration in each hair sample ranged from 0.012 $\mu g/cm^2$ (top of neck on Day 58) to 20.2 $\mu g/cm^2$ (middle of back on Day 7). The average amitraz concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 15.3 $\mu g/cm^2$ (middle of back on Day 7). The average MFN concentration in each hair sample ranged from <LOQ (top of neck on Day 58) to 0.372 $\mu g/cm^2$ (middle of back on Day 7).

Tables 12 through 16 summarize the arithmetic mean and geomean concentrations ($\mu g/g$) for each body part and each sampling interval (Days 1 through 58) of the 5 analytes.

Tables 17 through 21 summarize the arithmetic mean and geomean fipronil concentrations ($\mu g/cm^2$) for each body part and each sampling interval (Days 1 through 58). Average fipronil residue concentrations ranged from 0.172 $\mu g/cm^2$ (Day 58) to 3.00 $\mu g/cm^2$ (Day 7) for the lumbar zone, from 0.173 $\mu g/cm^2$ (Day 58) to 6.22 $\mu g/cm^2$ (Day 7) for the right side of thorax, from 0.214 $\mu g/cm^2$ (Day 58) to 5.06 $\mu g/cm^2$ (Day 7) for the left side of thorax, from 1.46 $\mu g/cm^2$ (Day 58) to 14.4 $\mu g/cm^2$ (Days 7) for the middle of the back and from 0.01 $\mu g/cm^2$ (Day 58) to 2.61 $\mu g/cm^2$ (Day 7) for the top of the neck.

Tables 22 through 26 summarize the arithmetic mean and geomean fipronil sulfone concentrations ($\mu g/cm^2$) for each body part and each sampling interval (Days 1 through 58). Average fipronil sulfone residue concentrations ranged from 0.017 $\mu g/cm^2$ (Day 1) to 0.155 $\mu g/cm^2$ (Day 28) for the lumbar zone, from 0.048 $\mu g/cm^2$ (Day 1) to 0.374 $\mu g/cm^2$ (Day 14) for the right side of thorax, from 0.018 $\mu g/cm^2$ (Day 1) to 0.232 $\mu g/cm^2$ (Day 14) for the left side of thorax, from 0.093 $\mu g/cm^2$ (Day 1) to 0.756 $\mu g/cm^2$ (Day 28) for the middle of the back and from <LOQ (Day 58) to 0.107 $\mu g/cm^2$ (Day 7) for the top of the neck.

Tables 27 through 31 summarize the arithmetic mean and geomean (s)-methoprene concentrations ($\mu g/cm^2$) for each body part and each sampling interval (Days 1 through 58). Average (s)-methoprene residue concentrations ranged from 0.362 $\mu g/cm^2$ (Day 58) to 4.04 $\mu g/cm^2$ (Days 7 and 14) for the lumbar zone, from 0.323 $\mu g/cm^2$ (Day 58) to 9.60 $\mu g/cm^2$ (Day 14) for the right side of thorax, from 0.363 $\mu g/cm^2$ (Day 58) to 7.35 $\mu g/cm^2$ (Day 7) for the left side of thorax, from 2.09 $\mu g/cm^2$ (Day 58) to 20.2 $\mu g/cm^2$ (Day 7) for the middle of the back and from 0.012 $\mu g/cm^2$ (Day 58) to 3.64 $\mu g/cm^2$ (Day 7) for the top of the neck.

Tables 32 through 36 summarize the arithmetic mean and geomean amitraz concentrations ($\mu g/cm^2$) for each body part and each sampling interval (Days 1 through 58). Average amitraz residue concentrations ranged from 0.048 $\mu g/cm^2$ (Day 58) to 2.89 $\mu g/cm^2$ (Day 7) for the lumbar zone, from 0.056 $\mu g/cm^2$ (Day 58) to 6.14 $\mu g/cm^2$ (Day 7) for the right side of thorax, from 0.063 $\mu g/cm^2$ (Day 58) to 5.09 $\mu g/cm^2$ (Day 7) for the left side of thorax, from 0.471 $\mu g/cm^2$ (Day 58) to 15.3 $\mu g/cm^2$ (Day 7) for the middle of the back and from <LOQ (Day 58) to 4.06 $\mu g/cm^2$ (Day 7) for the top of the neck.

Tables 37 through 41 summarize the arithmetic mean and geomean MFN concentrations ($\mu g/cm^2$) for each body part and each sampling interval (Days 1 through 58). Average MFN residue concentrations

ranged from <LOQ (Day 58) to 0.161 µg/cm^2 (Day 7) for the lumbar zone, from <LOQ (Day 58) to 0.214 µg/cm^2 (Day 7) for the right side of thorax, from <LOQ (Day 58) to 0.153 µg/cm^2 (Day 7) for the left side of thorax, from <LOQ (Day 58) to 0.372 µg/cm^2 (Day 7) for the middle of the back and from <LOQ (Day 58) to 0.070 µg/cm^2 (Day 7) for the top of the neck. Figures 1 through 5 provide a graphical representation of the average concentrations for each chemical at each body location and at each sampling interval.

Table 42 provides a summary of the results from the storage stability studies. Results from the long term stability study showed that no degradation occurred during the storage period of hair samples at -80°C. Fipronil and (s)-methoprene were stable for 183 days and amitraz was stable for 172 days. According to the Registrant, these storage durations covered the entire storage duration of the actual field samples. The storage duration for the actual samples was not reported in the study. The overall average percent recoveries for fipronil, (s)-methoprene and amitraz were 89.9%, 111%, and 105%, respectively. Short term stability was determined for the fipronil, fipronil sulfone, (s)-methoprene, amitraz, and MFN. Average percent recoveries after 4 hours storage at room temperature were 102%, 92.3%, 104%, 101%, and 96.7% for and fipronil, fipronil sulfone, (s)-methoprene, amitraz, and MFN, respectively. Freeze and thaw stability were determined for fipronil, fipronil sulfone, and (s)-methoprene after two freeze/thaw cycles. The samples were frozen for 20 to 24 hours at -80°C, then thawed at room temperature for approximately 2 hours and then frozen again for approximately 12 hours. The samples were analyzed after 15 minutes of thawing at room temperature. The overall percent recoveries were 91.8%, 100%, and 100% for fipronil, fipronil sulfone, and (s)-methoprene, respectively.

Figures 1 through 5 illlustrate the residue levels determined for each analyte over the sampling period broken out for the different body parts.

Conclusion

The results of this study demonstrate that the three active ingredients (fipronil, (s)-methoprene, and amitraz) in the combination of ML-2-2,095,988 509T and ML-3,948,906, when administered once concurrently as topical solutions, rapidly distribute over the entire body surface with a peak on Day 7 and steadily decrease over the 58 day sampling period following treatment.

Average fipronil levels peaked at Day 7 for the lumbar, thorax right and left sides, middle of back and top of the neck. After reaching a maximum, levels decreased, but were detectable even at Day 58 for all zones.

Average fipronil sulfone levels peaked at Day 7 for the top of neck, Day 14 for the thorax right and left sites and at Day 28 for the lumbar and middle back zones. After reaching a maximum, levels decreased, but were detectable even at Day 58 for all zones except for the top of the neck.

Average (s)-methoprene levels peaked at Day 7 for the lumbar, thorax left, middle of back and top of neck zones. The (s)-methoprene residues on the right side of the thorax peaked at Day 14. After reaching a maximum, levels decreased, but were detectable even at Day 58 for all zones.

Average amitraz levels peaked at Day 7 for the lumbar, thorax right and left sides, middle of back and top of the neck. After reaching a maximum, levels decreased, but were detectable even at Day 58 for all zones with the exception of the top of neck.

Average MFN levels peaked at Day 7 for the lumbar, thorax right and left sides, middle of back and top of the neck. After reaching a maximum, levels decreased to below the LOQ (0.25 µg/g) by Day 28 for the top of neck, by Day 42 for the right and left thorax zones, and by Day 58 for all remaining zones.

Issues

- *Type of residue detected:* Due to the porous nature of hair, it is possible that some of the residues detected after liquid extraction of the hair samples might be residues contained inside the hair shaft as well as those on the surface of the hair.

- *Method limits/correction of residue levels*: The analytical method was validated to be able to quantitate residues ranging between 0.1 µg/g and 4.0 µg/g for fipronil, fipronil sulfone, and (s)-methoprene, between 0.2 µg/g and 5.0 µg/g for amitraz and between 0.25 µg/g and 5.0 µg/g for MFN. Most of the field samples had fipronil, (s)-methoprene and/or amitraz residue levels requiring dilution to fall within the quantifiable range. The Study Report does not specify which samples were diluted, what dilution factor was used, or which samples contain what they consider very high residues.

- *Storage stability inconsistency*: No field fortification samples were prepared, however, the researchers performed storage stability studies. The Registrant states that the long term storage stability study encompassed the duration of the actual field samples; however, the duration of storage for the field samples was not reported in the study. Only fipronil, (s)-methoprene and amitraz were studied for long term stability. Only fipronil, fipronil sulfone and (s)-methoprene were studied for the freeze/thaw cycle stability. The Registrant did not provide an explanation for the selection of chemicals for each stability test.

- *Pharmacokinetic discussion*: The Study Review does not contain a complete discussion of the pharmacokinetics of the active ingredients in the applied products. The degradation product MFN and metabolite fipronil sulfone are quantitated, however other potential metabolites are not discussed.

- *Application rate*: There is no product label for the test substances applied to the dogs. It cannot be determined whether or not the amount applied would be an efficacious application rate.

Tables

Table 1. Fipronil QC Concurrent Lab Recoveries						
Fortification Level (µg/g)	% Recovery Range	n	Average % Recovery	Overall Average % Recovery	Std. Dev	Geomean
0.2	86.0 to 106	33	97.2	99.2	4.91	99.1
1.0	90.8 to 114	34	99.4			
3.2	90.7 to 113	37	101			

Table 2. Fipronil Sulfone QC Concurrent Lab Recoveries						
Fortification Level (µg/g)	% Recovery Range	n	Average % Recovery	Overall Average % Recovery	Std. Dev	Geomean
0.2	86.0 to 106	24	93.7	97.0	4.74	96.9
1.0	90.8 to 114	23	98.0			
3.2	90.7 to 113	26	99.2			

Table 3. (s)-Methoprene QC Concurrent Lab Recoveries						
Fortification Level (µg/g)	% Recovery Range	n	Average % Recovery	Overall Average % Recovery	Std. Dev	Geomean
0.1	85.0 to 135	23	102	103	8.15	102
1.0	86.8 to 112	28	102			
3.2	85.5 to 124	26	104			

Table 4. Amitraz QC Concurrent Lab Recoveries						
Fortification Level (µg/g)	% Recovery Range	n	Average % Recovery	Overall Average % Recovery	Std. Dev	Geomean
0.3	85.3 to 114	25	97.0	96.5	5.81	96.4
1.0	85.8 to 105	24	94.7			
4.0	87.6 to 109	24	97.8			

Table 5. MFN QC Concurrent Lab Recoveries						
Fortification Level (µg/g)	% Recovery Range	n	Average % Recovery	Overall Average % Recovery	Std. Dev	Geomean
0.3	88.7 to 112	22	99.3	98.6	6.56	98.3
1.0	78.7 to 112	22	97.6			
4.0	88.9 to 109	22	98.7			

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 6. Fipronil –Concentration Found on Hair Samples in µg/g										
Time of Sampling	Sampled Zones	Residue (µg/g of hair weight)						Avg Level per Body Zone (µg/g of hair weight)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	2.79	0.709	6.04	0.47	8.26	15.0	5.54	5.54	2.98
	Right Side	19.9	1.73	13.0	4.54	3.97	15.3	9.74	7.34	7.06
	Left Side	1.14	0.565	3.69	2.80	10.2	7.61	4.33	3.80	2.83
	Middle Back	3.02	14.7	41.8	34.3	11.7	23.4	21.5	14.6	16.1
	Top of Neck	2.36	1.83	12.4	4.66	10.0	4.34	5.94	4.30	4.71
Day 3	Lumbar Zone	5.46	9.09	23.3	2.86	18.2	22.3	13.5	8.86	10.5
	Right Side	12.7	4.11	93.6	13.0	11.6	44.7	30.0	34.2	17.9
	Left Side	5.26	2.81	30.2	7.67	16.2	41.6	17.3	15.5	11.5
	Middle Back	16.4	25.4	71.2	49.4	42.2	69.4	45.7	22.4	40.3
	Top of Neck	4.18	10.4	14.6	19.7	22.6	18.0	14.9	6.75	13.1
Day 7	Lumbar Zone	28.0	23.1	39.2	6.22	34.3	49.4	30.1	14.8	25.4
	Right Side	25.4	16.1	102	22.3	24.3	37.0	37.9	32.3	30.7
	Left Side	19.2	18.5	70.2	14.6	21.3	33.4	29.5	20.9	25.3
	Middle Back	24.3	69.3	125	62.1	52.5	104	73.0	36.4	64.5
	Top of Neck	16.2	60.1	18.6	34.8	23.8	30.6	30.7	16.0	27.8
Day 14	Lumbar Zone	20.8	36.4	37.4	15.5	21.2	37.3	28.1	10.0	26.5
	Right Side	26.1	33.0	76.3	25.0	17.1	25.6	33.8	21.4	29.9
	Left Side	17.8	19.2	44.0	16.2	17.4	18.1	22.1	10.8	20.6
	Middle Back	30.4	75.1	107	70.8	42.4	46.0	62.0	28.1	56.9
	Top of Neck	10.9	31.8	8.26	13.2	11.5	6.11	13.6	9.25	11.8
Day 28	Lumbar Zone	21.1	21.9	17.4	8.46	4.48	6.51	13.3	7.75	11.2
	Right Side	8.61	12.4	15.4	7.80	2.95	3.07	8.38	4.98	6.99
	Left Side	4.87	9.61	12.7	8.95	3.12	3.74	7.16	3.82	6.29
	Middle Back	35.4	55.5	40.9	111	6.08	9.65	43.1	38.3	28.4
	Top of Neck	4.36	7.15	1.90	3.46	5.75	1.83	4.07	2.12	3.59
Day 42	Lumbar Zone	6.38	8.50	7.64	0.932	0.561	2.93	4.49	3.47	2.93
	Right Side	1.79	3.39	3.91	0.822	0.555	2.12	2.10	1.35	1.69
	Left Side	1.92	3.12	4.55	0.556	0.705	1.71	2.09	1.52	1.62
	Middle Back	16.9	62.7	16.3	2.13	0.613	30.3	21.5	23.0	9.38
	Top of Neck	0.513	0.948	0.886	0.208	0.216	0.644	0.569	0.319	0.482
Day 58	Lumbar Zone	0.994	4.52	3.02	0.572	0.149	0.299	1.59	1.78	0.838
	Right Side	0.855	1.49	2.02	0.388	0.135	0.299	0.864	0.748	0.585
	Left Side	1.18	1.15	3.23	0.762	0.181	0.283	1.13	1.11	0.744
	Middle Back	5.37	3.04	20.9	4.86	0.419	1.81	6.06	7.48	3.28
	Top of Neck	<LOQ	<LOQ	0.446	<LOQ	<LOQ	<LOQ	0.116	0.162	0.072

LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation and geomean.

Table 7. Fipronil Sulfone –Concentration Found on Hair Samples in µg/g										
Time of Sampling	Sampled Zones	Residue (µg/g of hair weight)						Avg Level per Body Zone (µg/g of hair weight)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	<LOQ	<LOQ	0.231	<LOQ	0.203	0.419	0.167	0.148	0.116
	Right Side	0.433	<LOQ	0.483	0.203	<LOQ	0.424	0.274	0.198	0.189
	Left Side	<LOQ	<LOQ	<LOQ	<LOQ	0.171	0.230	0.100	0.080	0.079
	Middle Back	<LOQ	0.404	1.26	0.459	0.376	0.598	0.524	0.402	0.371
	Top of Neck	<LOQ	<LOQ	0.483	<LOQ	0.236	<LOQ	0.153	0.178	0.095
Day 3	Lumbar Zone	0.323	0.250	0.729	0.103	0.511	0.719	0.439	0.257	0.361
	Right Side	0.467	0.114	2.62	0.493	0.372	1.46	0.920	0.950	0.578
	Left Side	0.166	<LOQ	0.821	0.345	0.480	1.35	0.535	0.480	0.339
	Middle Back	0.572	0.973	2.23	1.45	1.01	2.39	1.44	0.732	1.28
	Top of Neck	<LOQ	0.244	0.547	0.900	0.640	0.576	0.493	0.302	0.361
Day 7	Lumbar Zone	1.09	1.14	2.09	0.400	1.17	2.15	1.34	0.668	1.17
	Right Side	0.934	0.715	3.52	1.43	0.975	1.96	1.59	1.05	1.36
	Left Side	0.748	0.580	1.73	0.968	0.784	1.56	1.06	0.473	0.981
	Middle Back	0.804	2.72	3.74	2.87	1.85	4.31	2.72	1.27	2.39
	Top of Neck	1.19	2.13	0.692	1.52	0.794	1.18	1.25	0.526	1.16
Day 14	Lumbar Zone	1.19	1.99	2.00	1.39	1.24	2.43	1.71	0.504	1.65
	Right Side	1.55	1.76	3.77	2.41	1.61	2.48	2.26	0.840	2.15
	Left Side	1.06	1.07	2.23	1.58	1.04	1.63	1.43	0.471	1.38
	Middle Back	1.38	3.48	2.43	3.63	2.84	4.32	3.01	1.04	2.83
	Top of Neck	0.711	2.05	0.404	0.906	0.558	0.390	0.837	0.626	0.698
Day 28	Lumbar Zone	1.74	1.74	1.66	1.03	0.595	2.07	1.47	0.548	1.36
	Right Side	1.69	1.44	1.51	1.36	0.438	1.01	1.24	0.453	1.14
	Left Side	0.978	1.12	1.21	1.37	0.449	1.07	1.03	0.315	0.978
	Middle Back	2.13	3.75	2.91	8.52	0.917	3.71	3.66	2.61	2.96
	Top of Neck	0.740	0.588	<LOQ	0.570	0.484	0.410	0.474	0.235	0.367
Day 42	Lumbar Zone	1.34	1.24	1.07	0.468	0.171	0.597	0.814	0.470	0.663
	Right Side	0.664	1.13	0.568	0.386	0.140	0.776	0.611	0.339	0.511
	Left Side	0.497	0.579	0.697	0.233	0.166	0.629	0.467	0.218	0.412
	Middle Back	1.83	6.06	2.01	1.18	0.207	5.82	2.85	2.48	1.78
	Top of Neck	<LOQ	0.270	<LOQ	<LOQ	<LOQ	0.206	0.113	0.099	0.084
Day 58	Lumbar Zone	0.307	0.833	0.596	0.230	<LOQ	0.118	0.356	0.301	0.243
	Right Side	0.345	0.803	0.351	0.250	<LOQ	<LOQ	0.308	0.277	0.198
	Left Side	0.392	0.455	0.638	0.435	<LOQ	<LOQ	0.337	0.237	0.223
	Middle Back	1.26	1.34	3.83	2.03	0.222	0.567	1.54	1.29	1.09
	Top of Neck	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA

LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation and geomean.

Table 8. (s)-Methoprene –Concentration Found on Hair Samples in µg/g										
Time of Sampling	Sampled Zones	Residue (µg/g of hair weight)						Avg Level per Body Zone (µg/g of hair weight)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	2.91	0.714	7.83	0.804	8.73	24.7	7.62	9.07	3.76
	Right Side	21.1	1.19	19.4	8.43	4.47	23.9	13.1	9.58	8.72
	Left Side	1.49	1.09	2.65	4.60	7.03	12.0	4.81	4.14	3.44
	Middle Back	4.18	10.6	46.0	23.5	10.3	40.3	22.5	17.3	16.5
	Top of Neck	5.34	2.09	14.2	7.94	6.00	6.52	7.02	4.03	6.06
Day 3	Lumbar Zone	6.00	7.61	30.4	2.37	22.4	39.1	18.0	14.9	11.9
	Right Side	16.1	4.61	126	15.7	17.7	57.1	39.6	46.1	23.0
	Left Side	7.06	5.93	42.6	12.1	18.1	71.0	26.1	25.8	17.4
	Middle Back	20.6	20.0	93.1	54.6	42.7	100	55.2	34.8	45.6
	Top of Neck	5.31	21.5	16.0	25.7	17.4	28.6	19.1	8.27	16.9
Day 7	Lumbar Zone	35.2	34.7	57.8	11.4	43.5	60.4	40.5	18.0	35.8
	Right Side	32.8	32.7	162	37.6	32.5	51.2	58.1	51.4	47.1
	Left Side	25.9	27.6	104	21.6	30.7	48.3	43.0	31.2	36.5
	Middle Back	34.4	92.7	216	88.7	60.7	126	103	63.4	88.1
	Top of Neck	28.4	76.9	22.7	45.8	27.2	53.7	42.4	20.7	38.6
Day 14	Lumbar Zone	28.9	69.5	59.4	23.5	30.9	61.4	45.6	20.0	41.8
	Right Side	49.7	72.6	106	45.6	30.5	44.3	58.2	27.2	53.6
	Left Side	31.0	40.9	52.2	26.8	23.9	39.4	35.7	10.5	34.5
	Middle Back	54.9	120	112	118	NR	66.9	94.4	31.0	89.8
	Top of Neck	23.3	81.3	11.4	23.5	20.6	8.70	28.1	26.8	21.2
Day 28	Lumbar Zone	33.4	40.9	35.4	18.7	6.48	12.9	24.6	13.9	20.6
	Right Side	19.9	33.0	10.8	11.5	3.99	5.22	14.1	10.9	10.9
	Left Side	10.3	26.0	14.6	13.4	4.16	8.09	12.8	7.49	11.0
	Middle Back	77.9	104	59.5	225	8.85	18.7	82.3	78.4	51.2
	Top of Neck	8.80	11.9	3.83	6.86	2.41	2.36	6.03	3.85	5.00
Day 42	Lumbar Zone	14.3	19.1	13.1	5.35	2.88	0.738	9.23	7.27	5.86
	Right Side	5.80	9.48	2.41	5.47	0.317	0.844	4.05	3.50	2.41
	Left Side	4.90	13.6	3.91	3.53	0.282	3.73	5.00	4.52	3.15
	Middle Back	50.6	116	26.9	55.0	0.680	1.53	41.7	43.0	14.4
	Top of Neck	1.07	1.76	0.668	1.27	<LOQ	1.43	1.04	0.607	0.697
Day 58	Lumbar Zone	3.38	10.3	4.67	1.19	<LOQ	0.205	3.31	3.90	1.12
	Right Side	2.43	4.09	1.63	0.998	<LOQ	0.179	1.56	1.53	0.724
	Left Side	3.19	4.11	2.90	1.24	<LOQ	0.107	1.93	1.71	0.795
	Middle Back	19.0	18.0	11.5	7.71	0.110	0.351	9.45	8.26	3.25
	Top of Neck	0.206	0.200	0.174	<LOQ	<LOQ	<LOQ	0.122	0.079	0.098

LOQ = 0.05 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation and geomean.

Table 9. Amitraz –Concentration Found on Hair Samples in µg/g										
Time of Sampling	Sampled Zones	Residue (µg/g of hair weight)						Avg Level per Body Zone (µg/g of hair weight)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	6.13	2.21	10.0	0.886	24.8	18.3	10.4	9.44	6.15
	Right Side	34.1	2.6	39.2	7.8	13.1	32.7	21.6	15.6	15.0
	Left Side	2.42	5.58	8.04	5.75	22.2	16.1	10.0	7.56	7.79
	Middle Back	4.43	26.2	80.7	31.0	32.6	36.5	35.3	25.0	26.5
	Top of Neck	7.05	9.17	15.3	14.9	14.0	10.0	11.7	3.44	11.3
Day 3	Lumbar Zone	13.6	14.5	34.0	2.80	36.5	31.4	22.1	13.7	16.7
	Right Side	31.8	6.45	83.5	17.4	25.3	43.9	34.7	27.1	26.3
	Left Side	9.79	8.28	34.2	15.7	34.4	44.1	24.4	15.0	20.1
	Middle Back	36.1	43.6	83.1	44.8	65.4	72.7	57.6	18.8	55.1
	Top of Neck	8.24	72.2	15.4	38.3	28.6	48.9	35.3	23.4	28.1
Day 7	Lumbar Zone	27.0	35.7	30.2	11.9	29.0	38.6	28.7	9.31	27.0
	Right Side	30.2	26.8	50.8	26.6	31.6	43.6	35.0	10.0	33.9
	Left Side	23.5	28.4	35.2	21.6	25.3	34.7	28.1	5.75	27.6
	Middle Back	35.3	85.6	77.4	72.0	94.1	90.6	75.8	21.5	72.3
	Top of Neck	41.1	111	15.9	51.9	22.8	44.5	47.9	33.9	39.5
Day 14	Lumbar Zone	11.1	53.2	17.2	16.0	20.1	25.7	23.9	15.2	20.9
	Right Side	26.9	47.0	33.5	29.4	17.2	19.6	28.9	10.8	27.4
	Left Side	13.1	27.9	17.8	19.6	16.4	16.0	18.4	5.11	17.9
	Middle Back	25.5	95.6	67.5	46.3	46.0	51.6	55.4	23.8	51.2
	Top of Neck	25.4	37.6	5.28	19.6	7.83	8.88	17.4	12.6	13.8
Day 28	Lumbar Zone	8.94	15.1	8.11	6.98	1.69	5.74	7.76	4.40	6.48
	Right Side	7.30	14.7	5.67	11.6	1.48	1.95	7.12	5.26	5.23
	Left Side	4.69	8.92	2.51	8.86	1.38	2.33	4.78	3.36	3.79
	Middle Back	39.3	70.0	12.0	134	3.69	9.86	44.8	50.3	23.3
	Top of Neck	5.82	8.16	0.906	3.75	1.63	1.10	3.56	2.94	2.57
Day 42	Lumbar Zone	2.74	4.57	0.807	2.04	<LOQ	0.323	1.76	1.71	0.934
	Right Side	2.07	5.17	0.594	1.85	<LOQ	0.267	1.68	1.90	0.825
	Left Side	1.37	2.67	0.262	2.08	<LOQ	<LOQ	1.10	1.11	0.521
	Middle Back	14.0	47.0	2.66	35.8	<LOQ	0.634	16.7	20.1	3.98
	Top of Neck	0.481	0.663	<LOQ	0.680	<LOQ	<LOQ	0.354	0.287	0.245
Day 58	Lumbar Zone	0.521	1.46	<LOQ	0.251	<LOQ	<LOQ	0.422	0.534	0.240
	Right Side	0.363	0.696	<LOQ	0.240	<LOQ	<LOQ	0.267	0.236	0.198
	Left Side	0.437	0.859	<LOQ	0.388	<LOQ	<LOQ	0.331	0.301	0.229
	Middle Back	4.64	3.82	0.803	3.93	<LOQ	<LOQ	2.232	2.11	0.908
	Top of Neck	<LOQ	<LOQ	<LOQ	0.100	<LOQ	<LOQ	0.100	0.000	0.100

LOQ = 0.20 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation and geomean.

Table 10. MFN –Concentration Found on Hair Samples in µg/g										
Time of Sampling	Sampled Zones	Residue (µg/g of hair weight)						Avg Level per Body Zone (µg/g of hair weight)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No.148799	Dog No.152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	1.40	<LOQ	<LOQ	<LOQ	0.622	<LOQ	0.421	0.521	0.244
	Right Side	<LOQ	<LOQ	0.747	<LOQ	0.250	<LOQ	0.250	0.249	0.189
	Left Side	<LOQ	<LOQ	<LOQ	<LOQ	0.353	<LOQ	0.163	0.093	0.149
	Middle Back	<LOQ	0.347	1.05	0.563	0.661	<LOQ	0.479	0.357	0.358
	Top of Neck	<LOQ	<LOQ	<LOQ	<LOQ	0.559	<LOQ	0.197	0.177	0.160
Day 3	Lumbar Zone	0.624	0.373	1.95	<LOQ	0.939	1.13	0.857	0.649	0.626
	Right Side	0.359	<LOQ	5.01	0.282	0.678	0.340	1.13	1.91	0.495
	Left Side	<LOQ	<LOQ	2.55	<LOQ	0.537	<LOQ	0.598	0.971	0.263
	Middle Back	0.624	0.590	5.29	1.28	1.33	0.468	1.60	1.85	1.08
	Top of Neck	<LOQ	<LOQ	0.877	<LOQ	0.914	<LOQ	0.382	0.398	0.241
Day 7	Lumbar Zone	1.08	0.603	3.48	0.522	1.15	2.98	1.64	1.27	1.26
	Right Side	0.669	0.826	4.77	0.508	0.653	0.677	1.35	1.68	0.916
	Left Side	0.366	0.700	2.88	0.326	0.604	0.691	0.928	0.971	0.682
	Middle Back	0.803	1.36	5.08	1.44	1.69	1.24	1.93	1.57	1.60
	Top of Neck	<LOQ	0.772	1.14	0.443	1.08	1.36	0.819	0.465	0.644
Day 14	Lumbar Zone	1.03	1.39	2.35	0.676	0.392	2.97	1.47	1.00	1.18
	Right Side	0.539	0.937	2.75	0.522	0.359	0.887	0.999	0.887	0.783
	Left Side	0.306	0.714	2.44	0.478	0.301	0.525	0.793	0.819	0.585
	Middle Back	0.778	1.36	4.26	1.07	0.663	1.40	1.59	1.34	1.28
	Top of Neck	<LOQ	0.708	<LOQ	<LOQ	<LOQ	1.31	0.419	0.493	0.247
Day 28	Lumbar Zone	0.747	0.600	0.699	0.359	<LOQ	0.918	0.575	0.287	0.484
	Right Side	<LOQ	<LOQ	0.699	<LOQ	<LOQ	0.296	0.249	0.231	0.192
	Left Side	<LOQ	<LOQ	0.430	<LOQ	<LOQ	<LOQ	0.176	0.125	0.154
	Middle Back	1.08	0.513	0.941	1.24	<LOQ	0.611	0.751	0.411	0.605
	Top of Neck	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
Day 42	Lumbar Zone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Right Side	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Left Side	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Middle Back	0.310	0.596	0.403	0.260	<LOQ	<LOQ	0.303	0.180	0.259
	Top of Neck	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
Day 58	Lumbar Zone	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Right Side	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Left Side	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Middle Back	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA
	Top of Neck	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	NA	NA	NA

MFN = N-Methyl-N´-(2,4-xylyl) formamidine

LOQ = 0.25 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation and geomean.

Table 11. Weight of Hair Sample Collections (g)								
Time of Sampling	Sampled Zones	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Area Sampled (cm^2)
Day -6 (pre-application)	Lumbar Zone	1.13	0.732	0.749	0.677	0.780	0.776	8
	Right Side	0.768	0.730	0.654	0.723	0.722	0.722	4
	Left Side	0.827	0.849	0.673	0.696	0.711	0.709	4
	Middle Back	0.710	0.757	0.701	0.728	0.771	0.902	4
	Top of Neck	0.576	0.858	0.393	0.321	0.309	0.415	4
Day 1	Lumbar Zone	0.733	0.829	0.690	0.713	0.696	0.949	8
	Right Side	0.692	0.735	0.600	0.709	0.767	0.787	4
	Left Side	0.782	0.723	0.604	0.922	0.633	0.775	4
	Middle Back	0.754	0.749	0.667	0.730	0.754	0.712	4
	Top of Neck	0.375	0.479	0.426	0.651	0.434	0.720	4
Day 3	Lumbar Zone	0.748	0.801	0.776	0.751	0.765	0.718	8
	Right Side	0.749	0.701	0.603	0.858	0.787	0.762	4
	Left Side	0.775	0.717	0.876	0.735	0.702	0.811	4
	Middle Back	0.744	0.787	0.705	0.728	0.739	0.718	4
	Top of Neck	0.328	0.361	0.303	0.323	0.289	0.353	4
Day 7	Lumbar Zone	0.745	0.902	0.746	0.720	0.793	0.837	8
	Right Side	0.715	0.825	0.545	0.740	0.781	0.722	4
	Left Side	0.724	0.747	0.562	0.836	0.731	0.793	4
	Middle Back	0.901	0.816	0.686	0.825	0.814	0.846	4
	Top of Neck	0.332	0.308	0.321	0.390	0.318	0.382	4
Day 14	Lumbar Zone	0.884	0.714	0.643	0.778	0.629	0.700	8
	Right Side	0.829	0.705	0.517	0.724	0.610	0.712	4
	Left Side	0.812	0.688	0.548	0.738	0.593	0.588	4
	Middle Back	0.787	0.945	0.532	0.883	0.511	0.687	4
	Top of Neck	0.376	0.377	0.495	0.537	0.327	0.447	4
Day 28	Lumbar Zone	0.915	0.811	0.784	0.758	0.668	0.948	8
	Right Side	0.871	0.771	0.758	0.624	0.739	0.810	4
	Left Side	0.759	0.781	0.630	0.625	0.776	0.842	4
	Middle Back	0.872	0.890	0.629	0.839	0.953	0.836	4
	Top of Neck	0.454	0.465	0.457	0.511	0.324	0.453	4
Day 42	Lumbar Zone	1.01	1.01	0.728	0.934	1.83	1.17	8
	Right Side	0.822	0.873	0.794	0.792	0.793	0.866	4
	Left Side	0.881	0.931	0.849	0.750	0.794	0.731	4
	Middle Back	1.37	0.879	0.714	1.12	1.14	0.873	4
	Top of Neck	0.589	0.480	0.421	0.482	0.424	0.715	4
Day 58	Lumbar Zone	0.706	1.02	0.702	0.802	0.727	0.779	8
	Right Side	0.887	0.854	0.717	0.737	0.828	0.923	4
	Left Side	0.739	0.737	0.751	0.821	0.762	0.835	4
	Middle Back	0.826	0.877	1.06	0.788	0.793	0.996	4
	Top of Neck	0.452	0.433	0.312	0.462	0.323	0.471	4

Table 12. Fipronil - Concentration Found on Hair Samples in µg/cm^2										
Time of Sampling	Sampled Zones	Residue Level[1] (µg/cm^2)						Avg Level Per Body Zone (µg/cm^2)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	0.256	0.073	0.521	0.042	0.719	1.78	0.565	0.649	0.284
	Right Side	3.45	0.318	1.95	0.805	0.761	3.00	1.71	1.30	1.26
	Left Side	0.223	0.102	0.557	0.646	1.61	1.47	0.769	0.634	0.519
	Middle Back	0.569	2.75	6.97	6.25	2.21	4.17	3.82	2.46	2.93
	Top of Neck	0.221	0.219	1.32	0.759	1.09	0.782	0.732	0.447	0.588
Day 3	Lumbar Zone	0.511	0.910	2.26	0.269	1.74	2.00	1.28	0.830	0.997
	Right Side	2.38	0.719	14.1	2.79	2.28	8.51	5.13	5.15	3.31
	Left Side	1.02	0.503	6.61	1.41	2.85	8.44	3.47	3.29	2.20
	Middle Back	3.06	4.99	12.5	8.99	7.80	12.4	8.31	3.86	7.42
	Top of Neck	0.343	0.934	1.10	1.59	1.63	1.59	1.20	0.512	1.06
Day 7	Lumbar Zone	2.61	2.60	3.66	0.559	3.40	5.17	3.00	1.52	2.50
	Right Side	4.54	3.32	13.9	4.12	4.74	6.67	6.22	3.94	5.49
	Left Side	3.48	3.46	9.86	3.05	3.90	6.61	5.06	2.68	4.59
	Middle Back	5.48	14.1	21.5	12.8	10.7	22.1	14.4	6.40	13.1
	Top of Neck	1.34	4.63	1.49	3.40	1.89	2.92	2.61	1.28	2.36
Day 14	Lumbar Zone	2.30	3.25	3.01	1.51	1.67	3.26	2.50	0.79	2.38
	Right Side	5.41	5.81	9.86	4.52	2.60	4.55	5.46	2.42	5.05
	Left Side	3.62	3.29	6.03	2.99	2.58	2.66	3.53	1.29	3.38
	Middle Back	5.98	17.7	14.3	15.6	5.42	7.90	11.2	5.35	10.0
	Top of Neck	1.02	3.00	1.02	1.78	0.938	0.682	1.41	0.861	1.24
Day 28	Lumbar Zone	2.42	2.22	1.71	0.802	0.374	0.771	1.38	0.850	1.13
	Right Side	1.88	2.39	2.93	1.22	0.545	0.622	1.60	0.967	1.33
	Left Side	0.924	1.88	2.00	1.40	0.605	0.788	1.27	0.585	1.15
	Middle Back	7.73	12.3	6.44	23.3	1.45	2.02	8.88	8.12	5.89
	Top of Neck	0.494	0.831	0.217	0.442	0.466	0.207	0.443	0.228	0.395
Day 42	Lumbar Zone	0.809	1.07	0.695	0.109	0.128	0.428	0.540	0.386	0.392
	Right Side	0.368	0.740	0.776	0.163	0.110	0.459	0.436	0.281	0.347
	Left Side	0.424	0.726	0.966	0.104	0.140	0.313	0.446	0.340	0.333
	Middle Back	5.78	13.8	2.91	0.598	0.174	6.62	4.98	5.04	2.33
	Top of Neck	0.076	0.114	0.093	0.025	0.023	0.115	0.074	0.042	0.061
Day 58	Lumbar Zone	0.088	0.577	0.265	0.057	0.014	0.029	0.172	0.219	0.082
	Right Side	0.190	0.317	0.362	0.071	0.028	0.069	0.173	0.141	0.120
	Left Side	0.217	0.212	0.606	0.156	0.034	0.059	0.214	0.206	0.144
	Middle Back	1.11	0.667	5.51	0.957	0.083	0.451	1.46	2.01	0.726
	Top of Neck	0.006	0.005	0.035	0.006	0.004	0.006	0.010	0.012	0.007

Residue Level (µg/cm^2) = Level (µg/g) x weight of hair sample (g) / area sampled (8 cm^2 for lumbar zone or 4 cm^2 for the other zones)

Table 13. Fipronil Sulfone - Concentration Found on Hair Samples in µg/cm^2										
Time of Sampling	Sampled Zones	Residue Level[1] (µg/cm^2)						Avg Level Per Body Zone (µg/cm^2)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	0.005	0.005	0.020	0.004	0.018	0.050	0.017	0.017	0.011
	Right Side	0.075	0.009	0.072	0.036	0.010	0.083	0.048	0.034	0.034
	Left Side	0.010	0.009	0.008	0.012	0.027	0.045	0.018	0.015	0.014
	Middle Back	0.009	0.076	0.209	0.084	0.071	0.106	0.093	0.066	0.067
	Top of Neck	0.005	0.006	0.051	0.008	0.026	0.009	0.017	0.018	0.012
Day 3	Lumbar Zone	0.030	0.025	0.071	0.010	0.049	0.065	0.042	0.024	0.034
	Right Side	0.087	0.020	0.395	0.106	0.073	0.277	0.160	0.144	0.107
	Left Side	0.032	0.009	0.180	0.063	0.084	0.273	0.107	0.100	0.065
	Middle Back	0.106	0.191	0.393	0.264	0.187	0.429	0.262	0.126	0.235
	Top of Neck	0.004	0.022	0.041	0.073	0.046	0.051	0.040	0.024	0.029
Day 7	Lumbar Zone	0.102	0.128	0.195	0.036	0.115	0.225	0.134	0.068	0.116
	Right Side	0.167	0.147	0.480	0.264	0.190	0.354	0.267	0.129	0.244
	Left Side	0.135	0.108	0.243	0.202	0.143	0.310	0.190	0.076	0.178
	Middle Back	0.181	0.555	0.641	0.592	0.376	0.912	0.543	0.248	0.485
	Top of Neck	0.098	0.164	0.056	0.148	0.063	0.112	0.107	0.044	0.099
Day 14	Lumbar Zone	0.132	0.178	0.160	0.136	0.098	0.213	0.153	0.040	0.148
	Right Side	0.322	0.311	0.488	0.436	0.246	0.441	0.374	0.094	0.363
	Left Side	0.216	0.184	0.305	0.291	0.155	0.239	0.232	0.059	0.225
	Middle Back	0.271	0.822	0.323	0.801	0.363	0.742	0.554	0.260	0.499
	Top of Neck	0.067	0.193	0.050	0.122	0.046	0.044	0.087	0.060	0.073
Day 28	Lumbar Zone	0.199	0.176	0.163	0.098	0.050	0.246	0.155	0.071	0.138
	Right Side	0.369	0.277	0.285	0.212	0.081	0.204	0.238	0.097	0.216
	Left Side	0.186	0.219	0.191	0.213	0.087	0.226	0.187	0.051	0.179
	Middle Back	0.465	0.834	0.457	1.79	0.218	0.775	0.756	0.553	0.614
	Top of Neck	0.084	0.068	0.006	0.073	0.039	0.046	0.053	0.028	0.040
Day 42	Lumbar Zone	0.170	0.156	0.097	0.055	0.039	0.087	0.101	0.053	0.089
	Right Side	0.136	0.247	0.113	0.076	0.028	0.168	0.128	0.076	0.105
	Left Side	0.109	0.135	0.148	0.044	0.033	0.115	0.097	0.048	0.084
	Middle Back	0.629	1.33	0.359	0.332	0.059	1.27	0.664	0.526	0.442
	Top of Neck	0.007	0.032	0.005	0.006	0.005	0.037	0.016	0.015	0.011
Day 58	Lumbar Zone	0.027	0.106	0.052	0.023	0.005	0.011	0.037	0.038	0.024
	Right Side	0.077	0.171	0.063	0.046	0.010	0.012	0.063	0.059	0.041
	Left Side	0.072	0.084	0.120	0.089	0.010	0.010	0.064	0.045	0.043
	Middle Back	0.260	0.294	1.01	0.400	0.044	0.141	0.358	0.343	0.240
	Top of Neck	0.006	0.005	0.004	0.006	0.004	0.006	0.005	0.001	0.005

Residue Level (µg/cm^2) = Level (µg/g) x weight of hair sample (g) / area sampled (8 cm^2 for lumbar zone or 4 cm^2 for the other zones)

Table 14. (s)-Methoprene - Concentration Found on Hair Samples in µg/cm^2										
Time of Sampling	Sampled Zones	Residue Level[1] (µg/cm^2)						Avg Level Per Body Zone (µg/cm^2)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	0.266	0.074	0.675	0.072	0.759	2.94	0.797	1.09	0.359
	Right Side	3.65	0.218	2.91	1.49	0.858	4.70	2.31	1.73	1.55
	Left Side	0.292	0.197	0.400	1.06	1.11	2.32	0.897	0.801	0.631
	Middle Back	0.788	1.99	7.68	4.29	1.93	7.17	3.97	2.91	2.99
	Top of Neck	0.501	0.251	1.52	1.29	0.651	1.17	0.897	0.500	0.757
Day 3	Lumbar Zone	0.561	0.761	2.95	0.223	2.14	3.51	1.69	1.37	1.13
	Right Side	3.02	0.809	19.0	3.38	3.49	10.9	6.76	6.91	4.26
	Left Side	1.37	1.06	9.32	2.22	3.18	14.4	5.26	5.41	3.34
	Middle Back	3.83	3.94	16.4	9.94	7.90	18.0	10.0	6.07	8.39
	Top of Neck	0.436	1.94	1.21	2.07	1.26	2.53	1.57	0.750	1.37
Day 7	Lumbar Zone	3.28	3.91	5.39	1.03	4.31	6.31	4.04	1.83	3.53
	Right Side	5.85	6.74	22.1	6.96	6.35	9.25	9.54	6.26	8.42
	Left Side	4.69	5.14	14.6	4.52	5.61	9.58	7.35	4.01	6.64
	Middle Back	7.75	18.9	37.0	18.3	12.3	26.7	20.2	10.5	17.9
	Top of Neck	2.35	5.92	1.82	4.47	2.16	5.13	3.64	1.75	3.28
Day 14	Lumbar Zone	3.19	6.20	4.78	2.29	2.43	5.37	4.04	1.63	3.76
	Right Side	10.3	12.8	13.7	8.26	4.65	7.89	9.60	3.38	9.05
	Left Side	6.29	7.03	7.15	4.95	3.55	5.79	5.79	1.37	5.64
	Middle Back	10.8	28.4	14.9	26.0	NR	11.5	18.3	8.30	16.9
	Top of Neck	2.19	7.66	1.41	3.16	1.69	0.972	2.85	2.47	2.23
Day 28	Lumbar Zone	3.82	4.15	3.47	1.77	0.541	1.53	2.55	1.46	2.08
	Right Side	4.34	6.37	2.04	1.79	0.737	1.06	2.72	2.19	2.07
	Left Side	1.96	5.08	2.30	2.10	0.806	1.70	2.32	1.45	2.01
	Middle Back	17.0	23.2	9.35	47.1	2.11	3.92	17.1	16.7	10.6
	Top of Neck	0.998	1.38	0.437	0.876	0.196	0.268	0.693	0.468	0.550
Day 42	Lumbar Zone	1.82	2.40	1.19	0.625	0.659	0.108	1.13	0.850	0.783
	Right Side	1.19	2.07	0.479	1.08	0.063	0.183	0.845	0.756	0.495
	Left Side	1.08	3.18	0.830	0.66	0.056	0.682	1.08	1.08	0.645
	Middle Back	17.4	25.4	4.79	15.5	0.193	0.334	10.6	10.4	3.58
	Top of Neck	0.157	0.211	0.070	0.154	0.005	0.256	0.142	0.092	0.089
Day 58	Lumbar Zone	0.298	1.32	0.410	0.119	0.005	0.020	0.362	0.495	0.110
	Right Side	0.538	0.873	0.292	0.184	0.010	0.041	0.323	0.331	0.149
	Left Side	0.590	0.757	0.545	0.255	0.010	0.022	0.363	0.314	0.154
	Middle Back	3.92	3.95	3.05	1.52	0.022	0.087	2.09	1.81	0.718
	Top of Neck	0.023	0.022	0.014	0.006	0.004	0.006	0.012	0.009	0.010

Residue Level ($\mu g/cm^2$) = Level ($\mu g/g$) x weight of hair sample (g) / area sampled (8 cm^2 for lumbar zone or 4 cm^2 for the other zones)

Table 15. Amitraz - Concentration Found on Hair Samples in µg/cm^2										
Time of Sampling	Sampled Zones	Residue Level[1] (µg/cm^2)						Avg Level Per Body Zone (µg/cm^2)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	0.562	0.229	0.860	0.079	2.16	2.17	1.01	0.934	0.587
	Right Side	5.90	0.470	5.88	1.37	2.51	6.44	3.76	2.62	2.67
	Left Side	0.473	1.008	1.21	1.32	3.52	3.12	1.78	1.24	1.43
	Middle Back	0.835	4.904	13.5	5.66	6.15	6.50	6.25	4.09	4.82
	Top of Neck	0.660	1.098	1.63	2.42	1.52	1.80	1.52	0.602	1.41
Day 3	Lumbar Zone	1.27	1.46	3.30	0.262	3.49	2.82	2.10	1.29	1.58
	Right Side	5.95	1.13	12.6	3.73	4.98	8.36	6.12	3.97	4.86
	Left Side	1.90	1.48	7.49	2.89	6.03	8.93	4.79	3.13	3.86
	Middle Back	6.72	8.58	14.7	8.15	12.1	13.0	10.5	3.15	10.1
	Top of Neck	0.676	6.51	1.16	3.09	2.07	4.32	2.97	2.18	2.28
Day 7	Lumbar Zone	2.52	4.02	2.81	1.07	2.87	4.04	2.89	1.10	2.66
	Right Side	5.40	5.52	6.92	4.93	6.18	7.88	6.14	1.10	6.06
	Left Side	4.25	5.30	4.95	4.52	4.62	6.88	5.09	0.949	5.02
	Middle Back	7.94	17.5	13.27	14.8	19.1	19.2	15.3	4.31	14.7
	Top of Neck	3.41	8.57	1.27	5.06	1.81	4.24	4.06	2.63	3.36
Day 14	Lumbar Zone	1.23	4.75	1.38	1.55	1.58	2.25	2.12	1.33	1.88
	Right Side	5.57	8.29	4.34	5.32	2.62	3.48	4.94	1.98	4.62
	Left Side	2.66	4.80	2.44	3.61	2.43	2.35	3.05	0.979	2.94
	Middle Back	5.02	22.6	8.97	10.2	5.88	8.86	10.3	6.36	9.03
	Top of Neck	2.39	3.54	0.653	2.63	0.640	0.993	1.81	1.22	1.45
Day 28	Lumbar Zone	1.02	1.53	0.794	0.661	0.141	0.681	0.805	0.458	0.655
	Right Side	1.59	2.83	1.07	1.81	0.274	0.394	1.33	0.961	0.991
	Left Side	0.890	1.74	0.395	1.38	0.267	0.489	0.861	0.593	0.693
	Middle Back	8.56	15.6	1.89	28.1	0.880	2.06	9.52	10.7	4.84
	Top of Neck	0.661	0.949	0.104	0.479	0.132	0.124	0.408	0.350	0.283
Day 42	Lumbar Zone	0.347	0.576	0.073	0.238	0.023	0.047	0.217	0.216	0.125
	Right Side	0.425	1.13	0.118	0.367	0.020	0.058	0.353	0.415	0.170
	Left Side	0.302	0.621	0.056	0.390	0.020	0.018	0.234	0.246	0.107
	Middle Back	4.81	10.3	0.475	10.1	0.028	0.138	4.31	4.90	0.989
	Top of Neck	0.071	0.080	0.011	0.082	0.011	0.018	0.045	0.036	0.031
Day 58	Lumbar Zone	0.046	0.186	0.009	0.025	0.009	0.010	0.048	0.070	0.023
	Right Side	0.080	0.149	0.018	0.044	0.021	0.023	0.056	0.051	0.041
	Left Side	0.081	0.158	0.019	0.080	0.019	0.021	0.063	0.055	0.044
	Middle Back	0.957	0.838	0.212	0.775	0.020	0.025	0.471	0.432	0.201
	Top of Neck	0.011	0.011	0.008	0.012	0.008	0.012	0.010	0.002	0.010

Residue Level ($\mu g/cm^2$) = Level ($\mu g/g$) x weight of hair sample (g) / area sampled (8 cm^2 for lumbar zone or 4 cm^2 for the other zones)

Table 16. MFN - Concentration Found on Hair Samples in µg/cm^2										
Time of Sampling	Sampled Zones	Residue Level[1] (µg/cm^2)						Avg Level Per Body Zone (µg/cm^2)		
		Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.	Geomean
Day -6 (pre-application)	Lumbar Zone	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Right Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Left Side	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Middle Back	ND	ND	ND	ND	ND	ND	NA	NA	NA
	Top of Neck	ND	ND	ND	ND	ND	ND	NA	NA	NA
Day 1	Lumbar Zone	0.129	0.013	0.011	0.011	0.054	0.015	0.039	0.047	0.023
	Right Side	0.022	0.023	0.112	0.022	0.048	0.025	0.042	0.036	0.034
	Left Side	0.024	0.023	0.019	0.029	0.056	0.024	0.029	0.013	0.027
	Middle Back	0.024	0.065	0.175	0.103	0.125	0.022	0.086	0.060	0.065
	Top of Neck	0.012	0.015	0.013	0.020	0.061	0.023	0.024	0.018	0.020
Day 3	Lumbar Zone	0.058	0.037	0.189	0.012	0.090	0.101	0.081	0.062	0.059
	Right Side	0.067	0.022	0.756	0.060	0.133	0.065	0.184	0.282	0.091
	Left Side	0.024	0.022	0.559	0.023	0.094	0.025	0.125	0.214	0.051
	Middle Back	0.116	0.116	0.933	0.232	0.246	0.084	0.288	0.323	0.198
	Top of Neck	0.010	0.011	0.066	0.010	0.066	0.011	0.029	0.029	0.020
Day 7	Lumbar Zone	0.100	0.068	0.325	0.047	0.114	0.312	0.161	0.124	0.124
	Right Side	0.120	0.170	0.650	0.094	0.127	0.122	0.214	0.215	0.164
	Left Side	0.066	0.131	0.405	0.068	0.110	0.137	0.153	0.127	0.124
	Middle Back	0.181	0.277	0.871	0.296	0.344	0.262	0.372	0.250	0.324
	Top of Neck	0.010	0.059	0.092	0.043	0.085	0.129	0.070	0.042	0.055
Day 14	Lumbar Zone	0.114	0.124	0.189	0.066	0.031	0.260	0.131	0.083	0.106
	Right Side	0.112	0.165	0.356	0.094	0.055	0.158	0.157	0.106	0.132
	Left Side	0.062	0.123	0.334	0.088	0.045	0.077	0.121	0.107	0.096
	Middle Back	0.153	0.320	0.566	0.236	0.085	0.240	0.267	0.168	0.226
	Top of Neck	0.012	0.067	0.015	0.017	0.010	0.146	0.044	0.054	0.026
Day 28	Lumbar Zone	0.085	0.061	0.069	0.034	0.010	0.109	0.061	0.035	0.049
	Right Side	0.027	0.024	0.132	0.020	0.023	0.060	0.048	0.044	0.036
	Left Side	0.024	0.024	0.068	0.020	0.024	0.026	0.031	0.018	0.028
	Middle Back	0.235	0.114	0.148	0.259	0.030	0.128	0.152	0.084	0.126
	Top of Neck	0.014	0.015	0.014	0.016	0.010	0.014	0.014	0.002	0.014
Day 42	Lumbar Zone	0.016	0.016	0.011	0.015	0.029	0.018	0.017	0.006	0.017
	Right Side	0.026	0.027	0.025	0.025	0.025	0.027	0.026	0.001	0.026
	Left Side	0.028	0.029	0.027	0.023	0.025	0.023	0.026	0.002	0.026
	Middle Back	0.106	0.131	0.072	0.073	0.036	0.027	0.074	0.040	0.064
	Top of Neck	0.018	0.015	0.013	0.015	0.013	0.022	0.016	0.004	0.016
Day 58	Lumbar Zone	0.011	0.016	0.011	0.013	0.011	0.012	0.012	0.002	0.012
	Right Side	0.028	0.027	0.022	0.023	0.026	0.029	0.026	0.003	0.026
	Left Side	0.023	0.023	0.023	0.026	0.024	0.026	0.024	0.001	0.024
	Middle Back	0.026	0.027	0.033	0.025	0.025	0.031	0.028	0.004	0.028
	Top of Neck	0.014	0.014	0.010	0.014	0.010	0.015	0.013	0.002	0.013

Residue Level ($\mu g/cm^2$) = Level ($\mu g/g$) x weight of hair sample (g) / area sampled (8 cm^2 for lumbar zone or 4 cm^2 for the other zones)
MFN = N-Methyl-N´-(2,4-xylyl) formamidine
LOQ = 0.25 $\mu g/g$

Table 17. Average Fipronil Concentration on Lumbar Zone				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Lumbar Zone	0.565	0.649	0.284
Day 3	Lumbar Zone	1.28	0.830	0.997
Day 7	Lumbar Zone	3.00	1.52	2.50
Day 14	Lumbar Zone	2.50	0.789	2.38
Day 28	Lumbar Zone	1.38	0.850	1.13
Day 42	Lumbar Zone	0.540	0.386	0.392
Day 58	Lumbar Zone	0.172	0.219	0.082

Table 18. Average Fipronil Concentration on Left Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Right Side	1.71	1.30	1.26
Day 3	Right Side	5.13	5.15	3.31
Day 7	Right Side	6.22	3.94	5.49
Day 14	Right Side	5.46	2.42	5.05
Day 28	Right Side	1.60	0.967	1.33
Day 42	Right Side	0.436	0.281	0.347
Day 58	Right Side	0.173	0.141	0.120

Table 19. Average Fipronil Concentration on Right Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Left Side	0.769	0.634	0.519
Day 3	Left Side	3.47	3.29	2.20
Day 7	Left Side	5.06	2.68	4.59
Day 14	Left Side	3.53	1.29	3.38
Day 28	Left Side	1.27	0.585	1.15
Day 42	Left Side	0.446	0.340	0.333
Day 58	Left Side	0.214	0.206	0.144

Table 20. Average Fipronil Concentration on Middle Back				
Time of Sampling	Sampled Zones	Arithmetic Average ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Middle Back	3.82	2.46	2.93
Day 3	Middle Back	8.31	3.86	7.42
Day 7	Middle Back	14.4	6.40	13.1
Day 14	Middle Back	11.2	5.35	10.0
Day 28	Middle Back	8.88	8.12	5.89
Day 42	Middle Back	4.98	5.04	2.33
Day 58	Middle Back	1.46	2.01	0.726

Table 21. Average Fipronil Concentration on Top of Neck				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Top of Neck	0.732	0.447	0.588
Day 3	Top of Neck	1.20	0.512	1.06
Day 7	Top of Neck	2.61	1.28	2.36
Day 14	Top of Neck	1.41	0.861	1.24
Day 28	Top of Neck	0.443	0.228	0.395
Day 42	Top of Neck	0.074	0.042	0.061
Day 58	Top of Neck	0.010	0.012	0.007

Table 22. Average Fipronil Sulfone Concentration on Lumbar Zone				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Lumbar Zone	0.017	0.017	0.011
Day 3	Lumbar Zone	0.042	0.024	0.034
Day 7	Lumbar Zone	0.134	0.068	0.116
Day 14	Lumbar Zone	0.153	0.040	0.148
Day 28	Lumbar Zone	0.155	0.071	0.138
Day 42	Lumbar Zone	0.101	0.053	0.089
Day 58	Lumbar Zone	0.037	0.038	0.024

Table 23. Average Fipronil Sulfone Concentration on Left Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Right Side	0.048	0.034	0.034
Day 3	Right Side	0.160	0.144	0.107
Day 7	Right Side	0.267	0.129	0.244
Day 14	Right Side	0.374	0.094	0.363
Day 28	Right Side	0.238	0.097	0.216
Day 42	Right Side	0.128	0.076	0.105
Day 58	Right Side	0.063	0.059	0.041

Table 24. Average Fipronil Sulfone Concentration on Right Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Left Side	0.018	0.015	0.014
Day 3	Left Side	0.107	0.100	0.065
Day 7	Left Side	0.190	0.076	0.178
Day 14	Left Side	0.232	0.059	0.225
Day 28	Left Side	0.187	0.051	0.179
Day 42	Left Side	0.097	0.048	0.084
Day 58	Left Side	0.064	0.045	0.043

Table 25. Average Fipronil Sulfone Concentration on Middle Back				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Middle Back	0.093	0.066	0.067
Day 3	Middle Back	0.262	0.126	0.235
Day 7	Middle Back	0.543	0.248	0.485
Day 14	Middle Back	0.554	0.260	0.499
Day 28	Middle Back	0.756	0.553	0.614
Day 42	Middle Back	0.664	0.526	0.442
Day 58	Middle Back	0.358	0.343	0.240

Table 26. Average Fipronil Sulfone Concentration on Top of Neck				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Top of Neck	0.017	0.018	0.012
Day 3	Top of Neck	0.040	0.024	0.029
Day 7	Top of Neck	0.107	0.044	0.099
Day 14	Top of Neck	0.087	0.060	0.073
Day 28	Top of Neck	0.053	0.028	0.040
Day 42	Top of Neck	0.016	0.015	0.011
Day 58	Top of Neck	0.005	0.001	0.005

Table 27. Average (s)-Methoprene Concentration on Lumbar Zone				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Lumbar Zone	0.797	1.09	0.359
Day 3	Lumbar Zone	1.69	1.37	1.13
Day 7	Lumbar Zone	4.04	1.83	3.53
Day 14	Lumbar Zone	4.04	1.63	3.76
Day 28	Lumbar Zone	2.55	1.46	2.08
Day 42	Lumbar Zone	1.13	0.850	0.783
Day 58	Lumbar Zone	0.362	0.495	0.110

Table 28. Average (s)-Methoprene Concentration on Left Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Right Side	2.31	1.73	1.55
Day 3	Right Side	6.76	6.91	4.26
Day 7	Right Side	9.54	6.26	8.42
Day 14	Right Side	9.60	3.38	9.05
Day 28	Right Side	2.72	2.19	2.07
Day 42	Right Side	0.845	0.756	0.495
Day 58	Right Side	0.323	0.331	0.149

Table 29. Average (s)-Methoprene Concentration on Right Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Left Side	0.897	0.801	0.631
Day 3	Left Side	5.26	5.41	3.34
Day 7	Left Side	7.35	4.01	6.64
Day 14	Left Side	5.79	1.37	5.64
Day 28	Left Side	2.32	1.45	2.01
Day 42	Left Side	1.08	1.08	0.645
Day 58	Left Side	0.363	0.314	0.154

Table 30. Average (s)-Methoprene Concentration on Middle Back				
Time of Sampling	Sampled Zones	Arithmetic Average ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Middle Back	3.97	2.91	2.99
Day 3	Middle Back	10.0	6.07	8.39
Day 7	Middle Back	20.2	10.5	17.9
Day 14	Middle Back	18.3	8.30	16.9
Day 28	Middle Back	17.1	16.7	10.6
Day 42	Middle Back	10.6	10.4	3.58
Day 58	Middle Back	2.09	1.81	0.718

Table 31. Average (s)-Methoprene Concentration on Top of Neck				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Top of Neck	0.897	0.500	0.757
Day 3	Top of Neck	1.57	0.750	1.37
Day 7	Top of Neck	3.64	1.75	3.28
Day 14	Top of Neck	2.85	2.47	2.23
Day 28	Top of Neck	0.693	0.468	0.550
Day 42	Top of Neck	0.142	0.092	0.089
Day 58	Top of Neck	0.012	0.009	0.010

Table 32. Average Amitraz Concentration on Lumbar Zone				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Lumbar Zone	1.01	0.934	0.587
Day 3	Lumbar Zone	2.10	1.29	1.58
Day 7	Lumbar Zone	2.89	1.10	2.66
Day 14	Lumbar Zone	2.12	1.33	1.88
Day 28	Lumbar Zone	0.805	0.458	0.655
Day 42	Lumbar Zone	0.217	0.216	0.125
Day 58	Lumbar Zone	0.048	0.070	0.023

Table 33. Average Amitraz Concentration on Left Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Right Side	3.76	2.62	2.67
Day 3	Right Side	6.12	3.97	4.86
Day 7	Right Side	6.14	1.10	6.06
Day 14	Right Side	4.94	1.98	4.62
Day 28	Right Side	1.33	0.961	0.991
Day 42	Right Side	0.353	0.415	0.170
Day 58	Right Side	0.056	0.051	0.041

Table 34. Average Amitraz Concentration on Right Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Left Side	1.78	1.24	1.43
Day 3	Left Side	4.79	3.13	3.86
Day 7	Left Side	5.09	0.949	5.02
Day 14	Left Side	3.05	0.979	2.94
Day 28	Left Side	0.861	0.593	0.693
Day 42	Left Side	0.234	0.246	0.107
Day 58	Left Side	0.063	0.055	0.044

Table 35. Average Amitraz Concentration on Middle Back				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Middle Back	6.25	4.09	4.82
Day 3	Middle Back	10.5	3.15	10.1
Day 7	Middle Back	15.3	4.31	14.7
Day 14	Middle Back	10.3	6.36	9.03
Day 28	Middle Back	9.52	10.7	4.84
Day 42	Middle Back	4.31	4.90	0.989
Day 58	Middle Back	0.471	0.432	0.201

Table 36. Average Amitraz Concentration on Top of Neck				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Top of Neck	1.52	0.602	1.41
Day 3	Top of Neck	2.97	2.18	2.28
Day 7	Top of Neck	4.06	2.63	3.36
Day 14	Top of Neck	1.81	1.22	1.45
Day 28	Top of Neck	0.408	0.350	0.283
Day 42	Top of Neck	0.045	0.036	0.031
Day 58	Top of Neck	0.010	0.002	0.010

Table 37. Average MFN Concentration on Lumbar Zone				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Lumbar Zone	0.039	0.047	0.023
Day 3	Lumbar Zone	0.081	0.062	0.059
Day 7	Lumbar Zone	0.161	0.124	0.124
Day 14	Lumbar Zone	0.131	0.083	0.106
Day 28	Lumbar Zone	0.061	0.035	0.049
Day 42	Lumbar Zone	0.017	0.006	0.017
Day 58	Lumbar Zone	0.012	0.002	0.012

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 38. Average MFN Concentration on Left Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Right Side	0.042	0.036	0.034
Day 3	Right Side	0.184	0.282	0.091
Day 7	Right Side	0.214	0.215	0.164
Day 14	Right Side	0.157	0.106	0.132
Day 28	Right Side	0.048	0.044	0.036
Day 42	Right Side	0.026	0.001	0.026
Day 58	Right Side	0.026	0.003	0.026

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 39. Average MFN Concentration on Right Side				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Left Side	0.029	0.013	0.027
Day 3	Left Side	0.125	0.214	0.051
Day 7	Left Side	0.153	0.127	0.124
Day 14	Left Side	0.121	0.107	0.096
Day 28	Left Side	0.031	0.018	0.028
Day 42	Left Side	0.026	0.002	0.026
Day 58	Left Side	0.024	0.001	0.024

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 40. Average MFN Concentration on Middle Back				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Middle Back	0.086	0.060	0.065
Day 3	Middle Back	0.288	0.323	0.198
Day 7	Middle Back	0.372	0.250	0.324
Day 14	Middle Back	0.267	0.168	0.226
Day 28	Middle Back	0.152	0.084	0.126
Day 42	Middle Back	0.074	0.040	0.064
Day 58	Middle Back	0.028	0.004	0.028

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 41. Average MFN Concentration on Top of Neck				
Time of Sampling	Sampled Zones	Arithmetic Mean ($\mu g/cm^2$)	Std Dev. ($\mu g/cm^2$)	Geomean ($\mu g/cm^2$)
Day 1	Top of Neck	0.024	0.018	0.020
Day 3	Top of Neck	0.029	0.029	0.020
Day 7	Top of Neck	0.070	0.042	0.055
Day 14	Top of Neck	0.044	0.054	0.026
Day 28	Top of Neck	0.014	0.002	0.014
Day 42	Top of Neck	0.016	0.004	0.016
Day 58	Top of Neck	0.013	0.002	0.013

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Table 42. Storage Stability Summary Table																				
Stability Test	Fipronil				Fipronil Sulfone				(s)-Methoprene				Amitraz				MFN			
Long Term Stability at -80°C																				
Theoretical concentrations (µg/g)	0.2		3		NA				0.10		3.00		0.30		4.00		NA			
Days in storage	183		183						183		183		172		172					
Average % recovery	86.0		93.8						115		108		106		104					
Short Term Temperature Stability at Room Temperature																				
Theoretical concentrations (µg/g)	0.2		3.2		0.2		3.2		0.1		3.2		0.3		4		0.3		4	
Hours in storage	0	4	0	4	0	4	0	4	0	4	0	4	0	4	0	4	0	4	0	4
Average % recovery	102	103	97.8	101	94.4	89.0	103	95.7	97.0	105	94.9	102	102	100	103	102	95.5	96.4	99.5	96.9
Freeze and Thaw Cycle Stability at -80°C																				
Theoretical concentrations (µg/g)	0.2		3.2		0.2		3.2		0.1		3.2		NA				NA			
Number of freeze/thaw cycles	2		2		2		2		2		2									
Average % recovery	88.4		95.1		107		93.5		102		98.0									

MFN = N-Methyl-N′-(2,4-xylyl) formamidine

Figure 1. Average Fipronil Concentration Per Body Zone

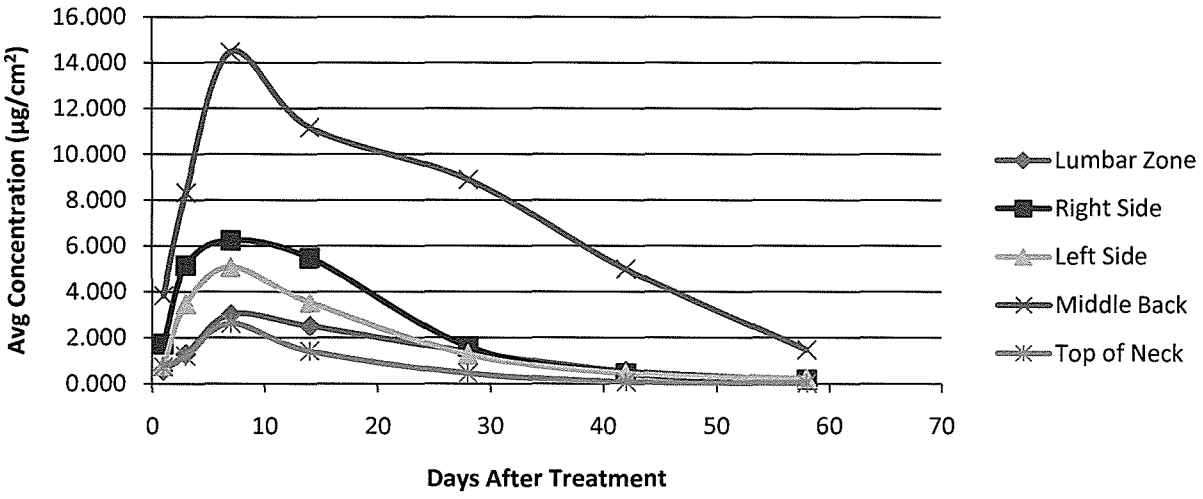


Figure 2. Average Fipronil Sulfone Concentration Per Body Zone

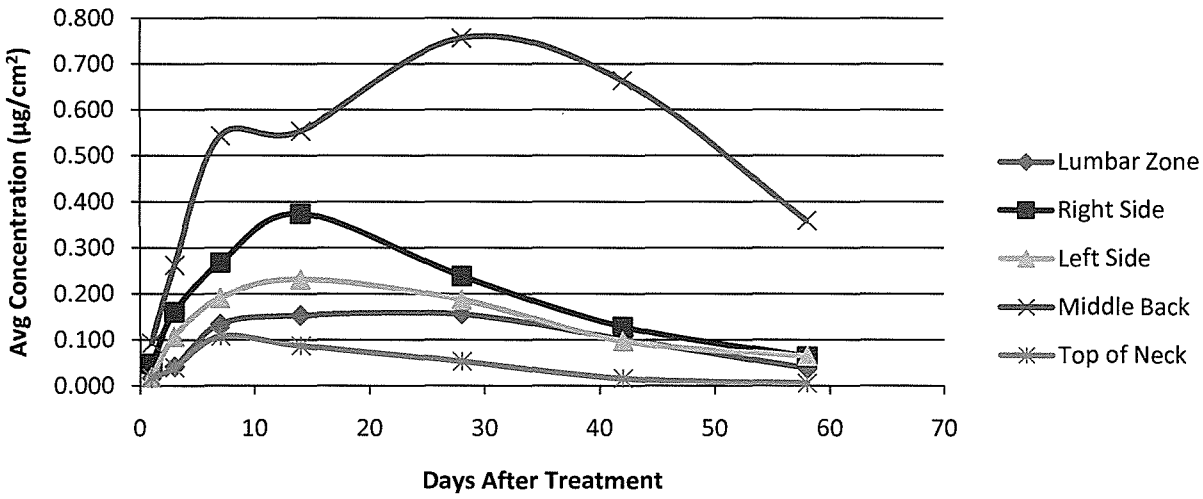


Figure 3. Average (s)-Methoprene Concentration Per Body Zone

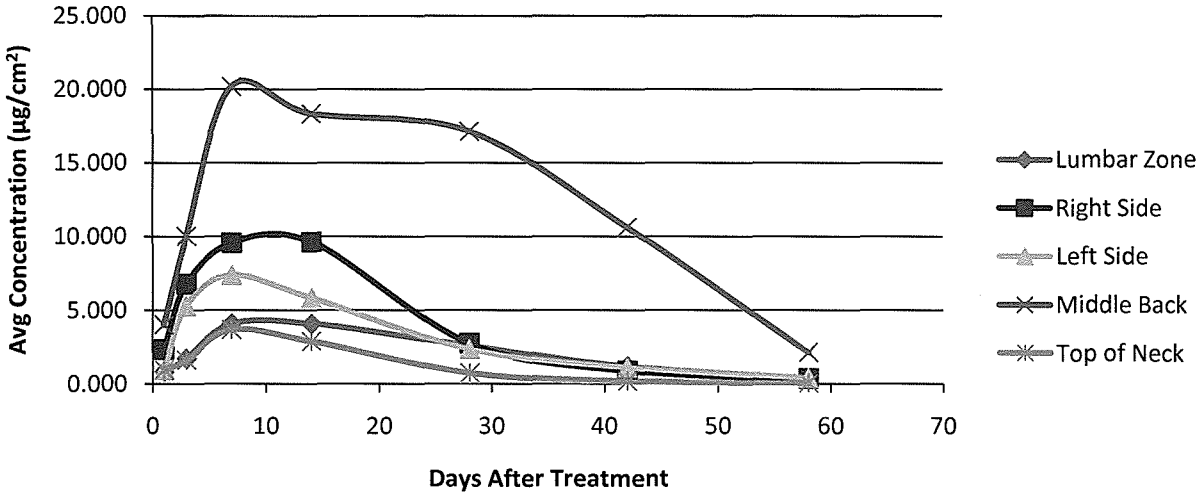
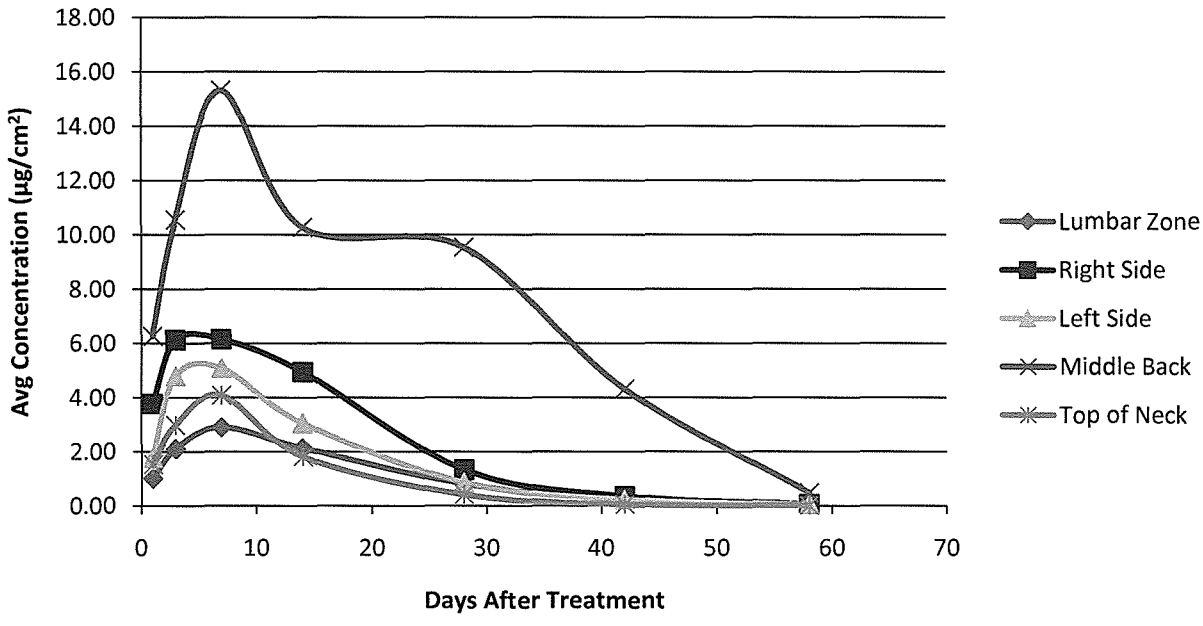
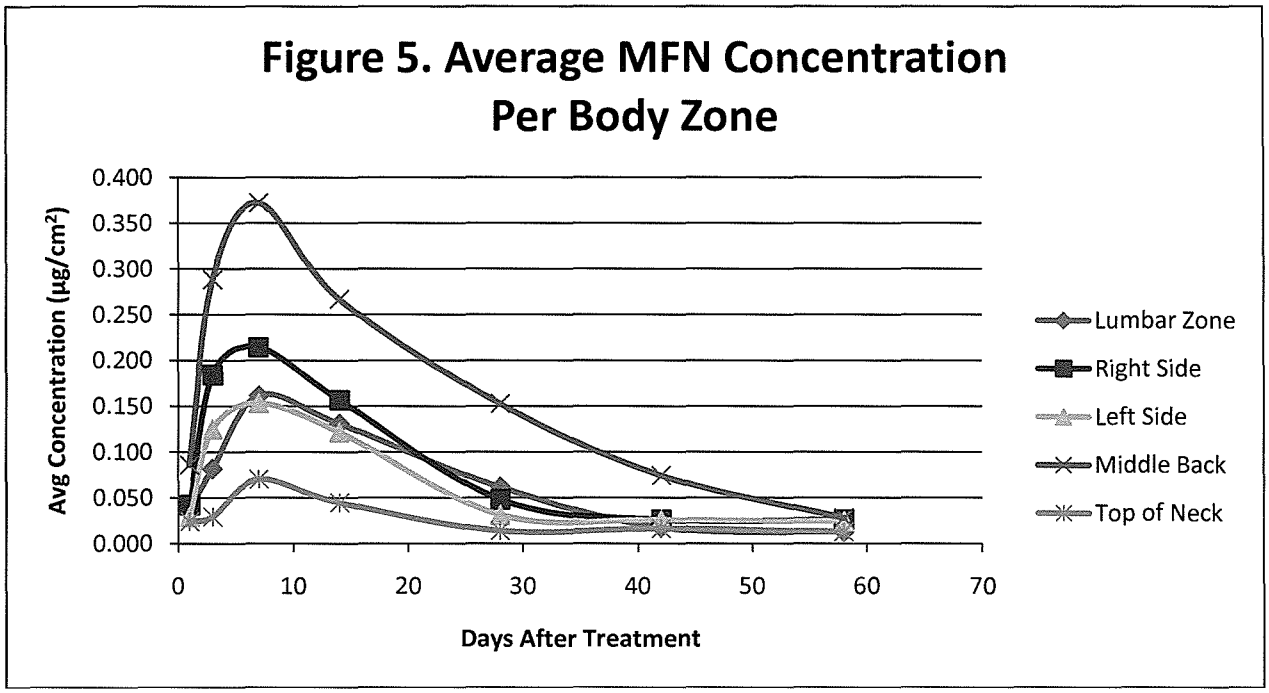


Figure 4. Average Amitraz Concentration Per Body Zone





Additional Tables (Addendum Tables for the Study Review of "*A Study to Determine the Haircoat Distribution of a Single Topical Treatment with a Combination of ML-2,095,988 509T and ML-3,948,906 in Dogs*" (MRID 479142-40, TAF 5-279)

Table A. Average Amitraz Found in 4cm² Patch of Dog Hair (µg/sample)

Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	6.75	6.17	18.4	8.69	12.7	16.0	**11.5**	5.08
Day 3	13.2	15.3	31.4	14.5	22.9	30.0	**21.2**	8.08
Day 7	18.8	32.7	23.4	24.3	27.7	33.8	**26.8**	5.76
Day 14	13.5	35.2	14.2	18.7	10.5	14.3	**17.7**	8.93
Day 28	10.2	18.1	3.41	26.0	1.36	3.00	**10.3**	9.87
Day 42	4.77	10.2	0.586	8.90	0.081	0.224	**4.12**	4.56
Day 58	0.941	1.07	0.212	0.748	0.061	0.072	**0.518**	0.456

Notes:
1. Lumbar zone samples represent an 8 cm² surface area while all the other zone samples represent a 4 cm² surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. When residues were <LOQ = 0.20 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table B. Average Amitraz Detected in/on Dog Hair ($\mu g/cm^2$)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	1.69	1.54	4.61	2.17	3.17	4.00	**2.86**	1.27
Day 3	3.30	3.83	7.84	3.63	5.73	7.49	**5.30**	2.02
Day 7	4.70	8.17	5.85	6.09	6.92	8.44	**6.70**	1.44
Day 14	3.37	8.79	3.56	4.67	2.63	3.59	**4.43**	2.23
Day 28	2.54	4.53	0.852	6.49	0.339	0.750	**2.58**	2.47
Day 42	1.19	2.55	0.146	2.23	0.020	0.056	**1.03**	1.14
Day 58	0.235	0.268	0.053	0.187	0.015	0.018	**0.130**	0.11

Notes:
1. Lumbar zone residues represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area.
2. When residues were <LOQ = 0.20 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table C. Amitraz: % of Original Application Rate Detected in/on a 4 cm^2 Patch of Hair[3]								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	6.03E-03	6.43E-03	2.30E-02	9.05E-03	1.58E-02	1.82E-02	**1.31E-02**	6.98E-03
Day 3	1.18E-02	1.60E-02	**3.92E-02**	1.51E-02	2.86E-02	3.41E-02	**2.41E-02**	1.14E-02
Day 7	1.68E-02	3.41E-02	2.92E-02	2.54E-02	3.46E-02	3.84E-02	**2.97E-02**	7.79E-03
Day 14	1.21E-02	3.66E-02	1.78E-02	1.94E-02	1.31E-02	1.63E-02	**1.92E-02**	8.97E-03
Day 28	9.09E-03	1.89E-02	4.26E-03	2.71E-02	1.69E-03	3.41E-03	**1.07E-02**	1.01E-02
Day 42	4.26E-03	1.06E-02	7.32E-04	9.28E-03	1.02E-04	2.54E-04	**4.21E-03**	4.72E-03
Day 58	8.40E-04	1.12E-03	2.65E-04	7.79E-04	7.67E-05	8.21E-05	**5.27E-04**	4.43E-04

Notes:
1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. Percent ai applied was calculated using the µg/sample divided by the application rate as µg/dog and then multiplied by 100. This calculation yields the same results as when the dog's surface area is estimated by using the Wildlife Exposure Factors equation and the dog's weight.
3. HED selected the result of all measured samples from the dog with the highest percent residue transfer, due to the uncertainty in using data collected from a study using the pet fur clipping method. Using this approach, **0.0392%** of total amitraz residue applied is assumed to be available for dermal transfer to humans. This value was derived from the highest residue obtained of 6 dogs sampled on Day 3 after application

Table D. Average Fipronil Found in/on a 4cm^2 Patch of Dog Hair (µg/sample)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	3.77	2.77	9.06	6.80	5.11	8.97	**6.08**	2.64
Day 3	5.85	6.45	29.3	12.0	13.0	26.4	**15.5**	10.0
Day 7	14.0	22.5	40.4	19.1	19.7	34.7	**25.1**	10.2
Day 14	14.7	26.5	27.4	21.1	10.6	15.2	**19.2**	6.84
Day 28	10.8	15.7	10.6	21.7	2.75	3.52	**10.9**	7.23
Day 42	5.97	13.1	4.36	0.799	0.460	6.35	**5.18**	4.64
Day 58	1.29	1.42	5.42	1.00	0.130	0.491	**1.63**	1.92

Notes:
1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table E. Average Fipronil Detected in/on Dog Hair (µg/cm^2)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	0.943	0.692	2.26	1.70	1.28	2.24	**1.52**	0.661
Day 3	1.46	1.61	7.33	3.01	3.26	6.60	**3.88**	2.51
Day 7	3.49	5.63	10.1	4.79	4.92	8.69	**6.27**	2.55
Day 14	3.67	6.62	6.84	5.28	2.64	3.81	**4.81**	1.71
Day 28	2.69	3.93	2.66	5.43	0.687	0.881	**2.71**	1.81
Day 42	1.49	3.29	1.09	0.200	0.115	1.59	**1.29**	1.16
Day 58	0.322	0.356	1.35	0.250	0.033	0.123	**0.406**	0.480

Notes:
1. Lumbar zone residues represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table F. Fipronil: % of Original Application Rate Detected in/on a 4 cm^2 Patch of Hair								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	4.02E-03	3.46E-03	1.35E-02	8.51E-03	7.63E-03	6.52E-03	**7.27E-03**	3.64E-03
Day 3	6.22E-03	8.06E-03	4.37E-02	1.51E-02	1.95E-02	1.67E-02	**1.82E-02**	1.35E-02
Day 7	1.49E-02	2.81E-02	6.02E-02	2.39E-02	2.94E-02	2.48E-02	**3.02E-02**	1.56E-02
Day 14	1.56E-02	3.31E-02	4.08E-02	2.64E-02	1.58E-02	1.34E-02	**2.42E-02**	1.11E-02
Day 28	1.14E-02	1.97E-02	1.59E-02	2.72E-02	4.11E-03	3.51E-03	**1.36E-02**	9.19E-03
Day 42	6.35E-03	1.64E-02	6.50E-03	9.99E-04	6.87E-04	5.53E-04	**5.25E-03**	6.14E-03
Day 58	1.37E-03	1.78E-03	8.08E-03	1.25E-03	1.95E-04	1.69E-04	**2.14E-03**	2.98E-03

Notes:
1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. Percent ai applied was calculated using the µg/sample divided by the application rate as µg/dog and then multiplied by 100. This calculation yields the same results as when the dog's surface area is estimated by using the Wildlife Exposure Factors equation and the dog's weight.

Table G. Average (s)-Methoprene Found in/on a 4cm^2 Patch of Dog Hair (µg/sample)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	4.40	2.18	10.5	6.57	4.25	14.6	**7.10**	4.66
Day 3	7.37	6.81	39.1	14.3	14.4	39.4	**20.2**	15.1
Day 7	19.1	32.5	64.7	28.2	24.6	45.6	**35.8**	16.8
Day 14	26.2	49.7	33.6	35.7	12.3	25.2	**30.5**	12.5
Day 28	22.5	32.2	14.1	42.9	3.51	6.78	**20.3**	15.2
Day 42	17.3	26.6	5.89	14.4	0.781	1.25	**11.0**	10.2
Day 58	4.29	5.54	3.45	1.67	0.040	0.14	**2.52**	2.26

Notes: 1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table H. Average (s)-Methoprene Detected in/on Dog Hair (µg/cm^2)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	1.10	0.546	2.64	1.64	1.06	3.66	**1.77**	1.16
Day 3	1.84	1.70	9.78	3.57	3.59	9.86	**5.06**	3.78
Day 7	4.78	8.13	16.2	7.05	6.15	11.4	**8.95**	4.19
Day 14	6.56	12.4	8.39	8.93	3.08	6.30	**7.61**	3.13
Day 28	5.62	8.04	3.52	10.7	0.878	1.70	**5.08**	3.81
Day 42	4.32	6.66	1.47	3.60	0.195	0.313	**2.76**	2.55
Day 58	1.07	1.38	0.862	0.417	0.010	0.035	**0.630**	0.566

Notes: 1. Lumbar zone residues represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table I: (s)-Methoprene: % of Original Application Rate Detected in/on a 4 cm^2 Patch of Hair								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	5.20E-03	3.03E-03	1.75E-02	9.13E-03	7.05E-03	2.20E-02	**1.06E-02**	7.45E-03
Day 3	8.71E-03	9.46E-03	6.49E-02	1.98E-02	2.38E-02	5.92E-02	**3.10E-02**	2.48E-02
Day 7	2.26E-02	4.52E-02	1.07E-01	3.92E-02	4.08E-02	6.84E-02	**5.39E-02**	3.00E-02
Day 14	3.10E-02	6.90E-02	5.57E-02	4.96E-02	2.04E-02	3.79E-02	**4.39E-02**	1.76E-02
Day 28	2.66E-02	4.47E-02	2.33E-02	5.96E-02	5.82E-03	1.02E-02	**2.84E-02**	2.05E-02
Day 42	2.04E-02	3.70E-02	9.76E-03	2.00E-02	1.30E-03	1.88E-03	**1.51E-02**	1.36E-02
Day 58	5.08E-03	7.69E-03	5.71E-03	2.32E-03	6.67E-05	2.12E-04	**3.51E-03**	3.13E-03

Notes: 1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. Percent ai applied was calculated using the µg/sample divided by the application rate as µg/dog and then multiplied by 100. This calculation yields the same results as when the dog's surface area is estimated by using the Wildlife Exposure Factors equation and the dog's weight.

Table J. Average MFN Found in 4cm^2 Patch of Dog Hair (µg/sample)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	0.168	0.111	0.264	0.148	0.275	0.087	**0.175**	0.078
Day 3	0.221	0.167	2.00	0.270	0.504	0.229	**0.566**	0.714
Day 7	0.382	0.564	1.87	0.439	0.625	0.770	**0.776**	0.555
Day 14	0.362	0.639	1.17	0.401	0.180	0.704	**0.576**	0.348
Day 28	0.308	0.190	0.345	0.279	0.078	0.270	**0.245**	0.096
Day 42	0.155	0.174	0.118	0.121	0.102	0.094	**0.127**	0.031
Day 58	0.081	0.085	0.080	0.080	0.077	0.090	**0.082**	0.005

Notes: 1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. When residue was <LOQ = 0.25 µg/g; ½ LOQ was used for calculating the arithmetic mean and standard deviation.

Table K. Average MFN Detected in/on Dog Hair (µg/cm^2)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Overall Average	Std Dev.
Day 1	0.042	0.028	0.066	0.037	0.069	0.022	**0.044**	0.020
Day 3	0.055	0.042	0.501	0.067	0.126	0.057	**0.141**	0.178
Day 7	0.095	0.141	0.468	0.110	0.156	0.192	**0.194**	0.139
Day 14	0.090	0.160	0.292	0.100	0.045	0.176	**0.144**	0.087
Day 28	0.077	0.048	0.086	0.070	0.020	0.067	**0.061**	0.024
Day 42	0.039	0.044	0.030	0.030	0.025	0.024	**0.032**	0.008
Day 58	0.020	0.021	0.020	0.020	0.019	0.023	**0.021**	0.001

Notes: 1. Lumbar zone residues represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area.
2. When residue was <LOQ = 0.25 µg/g; ½ LOQ was used for calculating the arithmetic mean and standard deviation.

Table L. Average Fipronil Sulfone Found in/on a 4cm^2 Patch of Dog Hair (µg/sample)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.
Day 1	0.083	0.084	0.289	0.115	0.121	0.235	**0.154**	0.086
Day 3	0.208	0.214	0.864	0.413	0.352	0.875	**0.488**	0.306
Day 7	0.547	0.883	1.29	0.993	0.710	1.53	**0.993**	0.366
Day 14	0.806	1.35	1.06	1.43	0.725	1.34	**1.12**	0.302
Day 28	1.04	1.26	0.882	1.91	0.380	1.20	**1.11**	0.501
Day 42	0.842	1.52	0.578	0.411	0.131	1.34	**0.804**	0.541
Day 58	0.353	0.529	1.00	0.451	0.058	0.144	**0.423**	0.335

Notes: 1. Lumbar zone samples represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area; therefore, the residues for lumbar zone were divided by 2 before the average across all zones was calculated.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation

Table M. Average Fipronil Sulfone Detected in/on Dog Hair (µg/cm^2)								
Time of Sampling	Dog No. 149079	Dog No. 147812	Dog No. 149543	Dog No. 147840	Dog No. 148799	Dog No. 152759	Arithmetic Mean	Std Dev.
Day 1	0.021	0.021	0.072	0.029	0.030	0.059	**0.039**	0.022
Day 3	0.052	0.053	0.216	0.103	0.088	0.219	**0.122**	0.077
Day 7	0.137	0.221	0.323	0.248	0.178	0.383	**0.248**	0.091
Day 14	0.201	0.338	0.265	0.357	0.181	0.336	**0.280**	0.075
Day 28	0.260	0.315	0.220	0.477	0.095	0.299	**0.278**	0.125
Day 42	0.210	0.380	0.144	0.103	0.033	0.336	**0.201**	0.135
Day 58	0.088	0.132	0.250	0.113	0.014	0.036	**0.106**	0.084

Notes: 1. Lumbar zone residues represent an 8 cm^2 surface area while all the other zone samples represent a 4 cm^2 surface area.
2. When residues were <LOQ = 0.10 µg/g; ½ LOQ was used for calculating the arithmetic mean, standard deviation