**EPA Reviewer:** _____ **Signature**: _____
**[Insert Branch], Health Effects Division (7509C)** **Date:** _____
Template version 02/06

# DATA EVALUATION RECORD

**STUDY TYPE:** Active Transfer; Animal Hair

**TEST MATERIAL:** The test material was Frontline® TopSpot™, a liquid pour-on insecticide for use on dogs. The product contains 100 mg/mL (9.7% w/v) of the active ingredient fipronil.

**SYNONYMS:** 1H-Pyrazole-3-carbonitrile, 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4 ((trifluoromethyl)sulfinyl)-; CAS No. 122068-37-3

**CITATION:**

| | |
|---|---|
| Study Authors: | G. de Fontenay, J.F. Campagna, S. Suberville, Ph. Birckel, and A. Weil |
| Title: | *Dislodgeable Residues of FipronilFollowing Topical Application of Frontline® Spot-on Treatment to Dogs* |
| Report Date: | December 1, 1997 |
| Performing Laboratories: | In-life phase - Merial, Toulouse, FRANCE<br>Analytical phase - Chrysalis, L'Arbresle, FRANCE |
| Identifying Codes: | Study No. MET416; Chrysalis Study No. 817/024B; MRID 445312-03 |

**SPONSOR:** Merial Limited (formally Rhone Merieux, Inc.)
115 Transtech Drive
Athens, Georgia 30601

**EXECUTIVE SUMMARY:**

This review analyzes the report "*Dislodgeable Residues of Fipronil Following Topical Application of Frontline® Spot-on Treatment to Dogs*" submitted by Merial Limited. The purpose of the study, which was conducted in France, was to measure the dislodgeability of the test substance, Frontline®, over time from the haircoat of dogs treated with a spot-on formulation containing fipronil as the active ingredient.

The test substance was administered to six Beagle dogs by topical application to the back (between the shoulders) using ready-to-use pipettes intended for commercial application. Each dog received a maximum label specified application dose of 1.34 mL (131,722 µg ai) of the test product on Day 0. The subsequent field sampling consisted of stroking the entire body surface of the dog by taking 5 strokes along the body of the dog using the palmar surface of one hand, while wearing cotton gloves to collect the residues. Glove samples were collected from each dog prior to treatment and at 10 intervals following treatment (1 hr to 28 days).

The cotton gloves were analyzed for fipronil and its metabolites RM1502, RM1602, and M&B46513. The results were reported by the Registrant as µg/glove for each metabolite and also for total fipronil (sum of fipronil plus 2 metabolites) per glove. The metabolite M&B46513 was not included in the total fipronil value because all M&B46513 residues were less than the limit of quantitation (LOQ). The Registrant did not correct any of the residues for laboratory fortification recoveries less than 90%. In

addition, the Registrant reported the percent of the applied dose that was dislodgeable at each sampling period after application.

Versar reported the results in terms of µg/glove and percentage of the applied dose for each analyte and for total fipronil (fipronil + RM1502 + RM1602). Versar corrected the RM1502 residues for an average laboratory fortification recovery of 88.4%. Versar did not correct any of the other analytes for laboratory recoveries because the average recoveries were greater than 90%. When residues were reported as less than the LOQ, Versar used a value of ½ LOQ.

The metabolite M&B46513 was not detected in any sample. For all other analytes, the maximum residues were detected 4 hours after application. The levels remained at a steady-state between 8 hours and 2 days after application. The residues then decreased through the end of the sampling period. Residues remained above the LOQ 28 days after application.

The average fipronil residue detected on the glove dosimeter increased from 0.8% of the applied dose at 1 hour after application of the test substance to a maximum of 1.03% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.453% of the applied dose at 8 hours after application and 0.481% of the applied dose at 1 day after application. At 2 days after application, the average residues were 0.445% of the applied dose. The average residues then declined to 0.0036% of the applied dose by 28 days after application.

The average RM1502 residues detected on the glove dosimeter increased from 0.00826% of the applied dose at 1 hour after application of the test substance to a maximum of 0.00898% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.00346% of the applied dose at 2 days after application. On day 4 after application all residues were <LOQ. On Day 7 after application all residues except one were <LOQ. Residues then remained <LOQ through 28 days after application.

The average RM1602 residues detected on the glove dosimeter increased from 0.0278% of the applied dose at 1 hour after application of the test substance to a maximum of 0.0389% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.0176% of the applied dose at 8 hours after application and 0.0214% of the applied dose at 1 day after application. At 2 days after application, the average residues were 0.0219% of the applied dose. The average residues then declined to 0.00199% of the applied dose by 28 days after application.

The average total fipronil residues detected on the glove dosimeter increased from 0.853% of the applied dose at 1 hour after application of the test substance to a maximum of 1.08% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.475% of the applied dose at 8 hours after application and 0.506% of the applied dose at 1 day after application. At 2 days after application, the average residues were 0.470% of the applied dose. The average residues then declined to 0.0067% of the applied dose by 28 days after application.

Versar performed a dissipation kinetics analysis for fipronil, RM1602 and total fipronil. Versar did not conduct an analysis for M&B46513 and RM1502 because all of the M&B46513 residues were less than the LOQ and the majority of the RM1502 residues were <LOQ after day 2. Due to the biphasic nature of the percent dislodgeable residue decline, Versar used the individual residue data (percentage of applied dose) collected from 2 days after application through day 28. The half-lives calculated by Versar were 3.86 days ($R^2$ = 0.942) for fipronil, 8.16 days ($R^2$ = 0.823) for RM1602 and 4.42 days ($R^2$ = 0.939) for total fipronil.

The following issues of concern are noted:

- The postapplication activity monitored in this study included stroking a dog five times with a hand. A typical exposure event likely involves more strokes with the hand and also hugging the dog.

- The Study Author has not identified a use for the data collected in this study. It is unclear how data presented as residue per glove could be used to estimate exposure in other scenarios.

- No information was provided on the fate of the product once it is applied.

- The strokes were collected from the same area of the dogs at each sampling interval (i.e., samples could not be collected from areas of the dog that had not already been wiped with a glove.) It is not known how this affects the percent dislodgeable residue of samples collected in subsequent sampling intervals.

- Cotton gloves were used to the collect the samples. No absorbency data were presented to quantify the difference between cotton gloves and bare hands, and residues of the metabolites in many of the cotton glove samples were less than the LOQ.

- The study took place in only one geographic location, France.

- The study was conducted with only one breed of dog.

- No field fortification samples were prepared or analyzed. Travel recovery, or storage stability samples were not prepared.

- Laboratory recovery samples were prepared; however, only one fortification level was used. For fipronil, the fortification level used (30 µg) was much lower than the majority of the residues detected in the field samples.

- The Study Report indicates that the method was validated; however, the results were not provided.

- The Report did not specify the length of time the samples were stored prior to analysis.

- The Study Report did not provide any details on instrument performance, calibration, or quantification of the analytical method.

**COMPLIANCE:** Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10(d) (1) (A), (B), or (C). The study sponsor and director stated that the study was conducted under EPA Good Laboratory Practice Standards (40 CFR part 160) with the following exception: Characterizations of the test substances and reference substances were not performed under GLP.

The study author stated that there were no influences, impacts or circumstances which might have impaired the integrity of the study.

**CONCURRENT EXPOSURE STUDY:** Yes

**WAS AIR SAMPLING CONDUCTED IN CONJUNCTION WITH SURFACE SAMPLING?** No

**GUIDELINE OR PROTOCOL FOLLOWED**: The study was reviewed using applicable parts of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2300 (indoor surface residue) and 875.2400 (dermal exposure). A compliance checklist is provided in Appendix A.

## I. MATERIALS AND METHODS

### A. MATERIALS

#### 1. Test Material:

| | |
|---|---|
| Active ingredient: | Fipronil |
| Formulation: | Frontline® TopSpot™, a 9.7% (w/v) liquid pour-on insecticide |
| Purity technical: | Not provided |
| Purity formulation: | 9.83 w/v |
| Lot # technical: | Not provided |
| Lot # formulation: | M02463AY |
| CAS #(s): | 122068-37-3 |
| Other Relevant Information: | EPA Reg. No. 65331-3. |

#### 2. Relevance of Test Material to Proposed Formulation(s):

The test material appears to be the same product as the proposed formulation based on review of the product label for EPA Registration No. 65331-3.

### B. STUDY DESIGN

#### 1. Site Description:

Test location: The study was conducted at Chrysalis Preclinical Services in L'Arbresle, France. The animals were housed in individual pens (approximately 1.44 $m^2$) in one room at the test facility.

Meteorological Data: In the experimental room, the temperature ranged from 19 to 25°C, relative humidity was >40% and the lighting cycle was 12 hours light (artificial) and 12 hours dark.

Ventilation/Air-Filtration: The test room was air conditioned. There were a minimum of 8 air changes per hour.

#### 2. Animal(s) Monitored:

Species/Breed: Beagle dogs

Number of animals in study: 6 (3 males and 3 females)

Age: 7 months at initiation of treatment

Body weight: 9.4 to 11.0 kg (20.7 to 24.3 lbs) at initiation of treatment

Feeding: The animals were fed a commercial diet (Diet A, Special Diet Services Ltd) that was analyzed for chemical and bacterial contaminants. Water was provided *ad libitum.* The water was analyzed at least once a year for chemical contaminants and at least twice a year for bacterial contaminants. No known contaminants were present in the diet or water at levels which might have interfered with the study.

Health: The animals received a standard canine vaccination and anti-parasite treatment by the supplier, a clinical examination for ill-health on arrival, and a full clinical examination during the 12-week acclimation period.

During the study no animals died, there were no treatment-related clinical signs, and there were no treatment-related changes in body weight.

Surface Characteristics: Characteristics of the dog surface were not provided; thus, it is assumed that the hair coat was typical of Beagle dogs.

Other products used: None

**3. Physical State of Formulation as Applied:**

The test substance was applied using a ready-to-use disposable, snap top, plastic backed, pipette which delivers an entire pre-measured unit dose to each dog.

**4. Application Rates and Regimes:**

Residential or Commercial Applicator: Not specified in the Study Report

Application rate(s): 1.34 mL (134 ai) of the test product was applied per animal. According to the product label for Frontline (EPA Reg. No.: 65331-3), this amount is for a dog weighing between 23 and 44 pounds. The dogs in this study weighed between 21 and 24 pounds, thus the maximum label application rate was used.

Based on the test product containing 9.83% ai, each dose contained 131,722 µg ai (0.00029 lb ai).

Application Regime: All animals were treated once on Day 0 (March 25, 1997). The test substance was applied topically to the dogs between the shoulders.

Application Equipment: The test substance was applied using pipettes and was applied directly from commercially packaged and available supplies (pipettes).

**5. Transferable Residue Sampling Procedures:**

Method and Equipment: Dye-free 100% cotton gloves were used to collect residues at each sample time point. Except on Day 21, the same person was used as the "sampler" at all time points for all animals.

Sampling Procedure(s): The sampler stroked with his dominant hand the whole body surface of the animal using motions that run with the lay of the hair coat, beginning from the head and ending at the base of the tail. Stroking motions were conducted using the palmar surface of the gloved hand, with fingers held in close opposition to one another.

Five strokes were necessary to cover the whole body surface:
-1 stroke on the back
-1 stroke on the right flank
-1 stroke on the left flank
-1 stroke on the right side of the ventral zone
-1 stroke on the left side of the ventral zone

Surface area(s) sampled: The palmar surface area was not provided.

Sampling Time: The length of time to complete a single stroke or the entire stroking procedure was not provided.

Replicates per surface:
- Replicates per sampling time: Six dogs were sampled at each interval
- Number of sampling times: There were a total of 11 sampling intervals, including one sampling event prior to application

Times of sampling: Samples were collected prior to treatment, at 1, 4, and 8 hours after treatment and at 1, 2, 4, 7, 14, 21 and 28 days after treatment.

## 6. Sample Handling:

After sampling, each glove was wrapped in aluminum foil and placed in a closed plastic bag and labeled with Chrysalis study number, the animal number, and the sample time point. All gloves were immediately frozen at about -20°C and then sent with dry ice to the Study Sponsor after day 7, day 21, and day 28. The time the samples were stored prior to analysis was not provided.

## 7. Analytical Methodology:

Extraction method(s): In the first step, a cotton glove was stirred for 3 minutes in 150 mL of acetonitrile. The solvent was then filtered medium fast paper filters. An aliquot (1 mL) of the extract was evaporated to dryness under a nitrogen stream.

In the second step, the dry residue was dissolved in 200 µl of a mixture of Acetonitrile – ultra pure water (50:50 v/v) and washed with 200 µl of n-hexan. After shake and configuration, n-hexan was discarded, 80 µL were injected into the chromatograph.

Detection method(s): A high performance liquid chromatograph (HPLC) method was used for the analysis of fipronil, RM1602, RM 1502, and M&B46513. A summary of the typical operating conditions is in Table 1.

| **Table 1. Summary of Chromatograhic Operating Conditions** | |
|---|---|
| Column | Symmetry C18, 5 µm, 250 x 4.6 mm internal diameter with guard column Adsorbosphere C18, 5 µm (ALLTECH), 7.5 x 4.6 mm internal diameter |
| Mobile phase with low pressure gradient | Solvent A: methanol/acetonitrile (80:20, v/v)…71%<br>Solvent B: Ultra pure water 29% |
| Pump flow rate | 1.2 mL/min |
| Injector volume | 80 µL |
| Injector type | Push loop |
| Detector wavelength | 278 nm |
| Detector rise time | 5 s |
| Detector data rate | 12 Hz |
| Detector run time | 30 min |
| Retention time | Fipronil = 11.04 min<br>RM1602 = 15.18 min<br>RM 1502 = 12.79 min<br>M&B46513 = 10.28 min |

Method validation: According to the Study Report, the HPLC method used was validated in terms of specificity, extraction recovery, linearity, precision, accuracy, and limit of quantification. The results are reported in Report MET406, Rhone Merieux, 7/18/97.

The limit of quantitation (LOQ) was 3 µg per glove for each of the analytes.

Instrument performance and calibration: Instrument performance and calibration was not discussed in the Study Report.

Quantification: Quantification was not discussed in the Study Report.

**8. <u>Quality Control</u>:**

Lab Recovery: Each set of samples was run with triplicate fortified controls at one spike level. The concentration levels were 30 µg per glove for fipronil, RM1602 and RM 1502 and 3 µg for M&B46513.

Average recoveries were 95.6±2.0% for fipronil (n=18), 96.2±3.3% for RM1602 (n=18), 88.4±2.7% for RM1502, and 90.1±5.0% for M&B46513.

The use of unfortified laboratory control samples was not discussed in the Study Report.

Field blanks: One control sample was collected from each dog prior to treatment. Residues were <LOQ in each sample.

Field recovery: Field fortification samples were not prepared.

Formulation: According to the Certificate of Analysis, the test product contained 9.83% w/v fipronil.

Tank mix: Not applicable.

Travel Recovery: Travel recovery samples were not prepared.

Storage Stability: Storage stability samples were not prepared.

## II. RESULTS AND CALCULATIONS

In this study, the test substance was administered to beagle dogs by topical application to the back using pipettes intended for commercial application. Residues were collected from treated dogs by stroking the dogs five times covering the entire body of the dog. Using cotton gloves, samples were collected from each dog at the following intervals: prior to treatment, at 1, 4, and 8 hours after treatment and at 1, 2, 4, 7, 14, 21, and 28 days after treatment. The samples were analyzed for fipronil and its metabolites (RM1502, RM1602, and M&B46513).

The results were reported by the Registrant in terms of µg/glove for each analyte and for total fipronil. Additionally, the Registrant reported the percentage of the applied dose for total fipronil. The Registrant calculated total fipronil as the sum of fipronil, RM1502 and RM1602. The metabolite M&B46513 was not included in the total fipronil value because all M&B46513 residues were less than the LOQ. The Registrant did not correct any of the residues for laboratory fortification recoveries less than 90%.

Versar reported the results in terms of µg/glove and percentage of the applied dose for each analyte and for total fipronil (fipronil + RM1502 + RM1602). Versar corrected the RM1502 residues for an average laboratory fortification recovery of 88.4%. Versar did not correct any of the other analytes for laboratory recoveries because the average recoveries were greater than 90%. When residues were reported as less than the LOQ, Versar used a finite value of ½ LOQ. The results, except for metabolite M&B46513 which was not detected in any sample, are shown in Table 2 through 5. Additionally, Figures 1 through 4 show the average percentage of the applied dose at each interval.

The metabolite M&B46513 was not detected in any sample. For all other analytes, the maximum residues were detected 4 hours after application. The levels remained at a steady-state between 8 hours and 2 days after application. The residues then decreased through the end of the sampling period. Residues remained above the LOQ 28 days after application.

The average fipronil residues detected on the glove dosimeter increased from 0.8% of the applied dose at 1 hour after application of the test substance to a maximum of 1.03% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.453% of the applied dose at 8 hours after application and 0.481% of the applied dose at 1 day after application. At 2 days after application, the average residues were 0.445% of the applied dose. The average residues then declined to 0.0036% of the applied dose by 28 days after application.

The average RM1502 residues detected on the glove dosimeter increased from 0.00826% of the applied dose at 1 hour after application of the test substance to a maximum of 0.00898% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.00346% of the applied dose at 2 days after application. On day 4 after application all residues were <LOQ. On Day 7 after application all residues except one were <LOQ. Residues then remained <LOQ through 28 days after application.

The average RM1602 residues detected on the glove dosimeter increased from 0.0278% of the applied dose at 1 hour after application of the test substance to a maximum of 0.0389% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.0176% of the applied dose at 8 hours after application and 0.0214% of the applied dose at 1 day after application. At 2

days after application, the average residues were 0.0219% of the applied dose. The average residues then declined to 0.00199% of the applied dose by 28 days after application.

The average total fipronil residues detected on the glove dosimeter increased from 0.853% of the applied dose at 1 hour after application of the test substance to a maximum of 1.08% of the applied dose at 4 hours after the application of the test substance. The average residues then decreased to 0.475% of the applied dose at 8 hours after application and 0.506% of the applied dose at 1 day after application. At 2 days after application, the average residues were 0.470% of the applied dose. The average residues then declined to 0.0067% of the applied dose by 28 days after application.

Residues of fipronil, RM1502, RM1602 and M&B46513 were not detected in any of the pre-application samples.

Versar performed a dissipation kinetics analysis for fipronil, RM1602, and total fipronil. Versar did not conduct an analysis for M&B46513 and RM1502 because all of the M&B46513 residues were less than the LOQ and the majority of the RM1502 residues were les than the LOQ after day 2. Due to the biphasic nature of the percent dislodgeable residue decline, Versar used the individual residue data (percentage of applied dose) collected from 2 days after application through day 28. The half-lives calculated by Versar were 3.86 days ($R^2 = 0.942$) for fipronil, 8.16 days ($R^2 = 0.823$) for RM1602 and 4.42 days ($R^2 = 0.939$) for total fipronil. The predicted values from the regression are shown in Tables 6, 7, and 8. It should be noted that the Day 0 predicted values were replaced with the worse-case value of all samples collected on Day 0 and the Day 1 predicted values were replaced with the actual average Day 1 value.

The Registrant did not perform a dissipation kinetics analysis.

## III. DISCUSSION

### A. LIMITATIONS OF THE STUDY:

The following issues of concern are noted:

- The postapplication activity monitored in this study included stroking a dog five times with a hand. A typical exposure event most likely involves more strokes with the hand and hugging the dog.
- The Study Author has not identified a use for the data collected in this study.
- No information was provided on the fate of the product once it is applied.
- The strokes were collected from the same area of the dogs at each sampling interval (i.e., samples could not be collected from areas of the dog that had not already been wiped with a glove.) It is not known how this affects the percent dislodgeable residue of samples collected in subsequent sampling intervals.
- Cotton gloves were used to the collect the samples. No absorbency data were presented to quantify the difference between cotton gloves and bare hands, and residues of the metabolites in many of the cotton glove samples were less than the LOQ.
- The study took place in only one geographic location, France.

- The study was conducted with only one breed of dog.

- No field fortification samples were prepared or analyzed. Travel recovery, or storage stability samples were not prepared.

- Laboratory recovery samples were prepared; however, only one fortification level was used. For fipronil, the fortification level used (30 µg) was much lower than the majority of the residues detected in the field samples.

- The Study Report indicates that the method was validated; however, the results were not provided.

- The Report did not specify the length of time the samples were stored prior to analysis.

- The Study Report did not provide any details on instrument performance, calibration, or quantification of the analytical method.

## B. CONCLUSIONS:

The Registrant and Versar calculated similar percentages of the applied dose dislodgeable for total fipronil. Slight differences are due to Versar's correction of the RM1502 data for the average laboratory recovery.

| **Table 2. Summary of Fipronil Residue and Percent of Applied Fipronil Dose Dislodged After Five Strokes** | | | | | | |
|---|---|---|---|---|---|---|
| Interval (day) | Fipronil Residue | | | Percent of Applied Fipronil Dose Dislodged After 5 Strokes | | |
| | Fipronil Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose dislodged[2] | Average (%) | Standard Deviation (%) |
| 0.042 (1 hour) | 230 | 1053 | 1552 | 0.175 | 0.80 | 1.18 |
| | 276 | | | 0.210 | | |
| | 72.2 | | | 0.0548 | | |
| | 4,115 | | | 3.12 | | |
| | 1,208 | | | 0.917 | | |
| | 415 | | | 0.315 | | |
| 0.17 (4 hours) | 893 | 1359 | 809 | 0.678 | 1.03 | 0.61 |
| | 805 | | | 0.611 | | |
| | 512 | | | 0.390 | | |
| | 2,733 | | | 2.07 | | |
| | 1,506 | | | 1.14 | | |
| | 1,703 | | | 1.29 | | |
| 0.33 (8 hours) | 578 | 597 | 198 | 0.439 | 0.453 | 0.150 |
| | 622 | | | 0.472 | | |
| | 290 | | | 0.220 | | |
| | 913 | | | 0.693 | | |
| | 610 | | | 0.463 | | |
| | 568 | | | 0.431 | | |
| 1 | 698 | 633 | 152 | 0.530 | 0.481 | 0.115 |
| | 559 | | | 0.424 | | |
| | 368 | | | 0.279 | | |
| | 652 | | | 0.495 | | |
| | 790 | | | 0.600 | | |
| | 733 | | | 0.557 | | |
| 2 | 917 | 586 | 248 | 0.696 | 0.445 | 0.188 |
| | 321 | | | 0.244 | | |
| | 806 | | | 0.612 | | |
| | 495 | | | 0.376 | | |
| | 649 | | | 0.493 | | |
| | 326 | | | 0.248 | | |
| 4 | 398 | 289 | 91.7 | 0.302 | 0.220 | 0.070 |
| | 211 | | | 0.160 | | |
| | 297 | | | 0.226 | | |
| | 228 | | | 0.173 | | |
| | 201 | | | 0.153 | | |
| | 401 | | | 0.304 | | |
| 7 | 319 | 213 | 65.7 | 0.242 | 0.161 | 0.050 |
| | 206 | | | 0.156 | | |
| | 225 | | | 0.171 | | |
| | 160 | | | 0.122 | | |
| | 235 | | | 0.178 | | |
| | 130 | | | 0.0987 | | |

**Table 2. Summary of Fipronil Residue and Percent of Applied Fipronil Dose Dislodged After Five Strokes**

| Interval (day) | Fipronil Residue | | | Percent of Applied Fipronil Dose Dislodged After 5 Strokes | | |
|---|---|---|---|---|---|---|
| | Fipronil Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose dislodged[2] | Average (%) | Standard Deviation (%) |
| 14 | 59.5 | 47.2 | 18.5 | 0.0452 | 0.0358 | 0.0141 |
| | 57.8 | | | 0.0439 | | |
| | 72.7 | | | 0.0552 | | |
| | 28.4 | | | 0.0216 | | |
| | 31.1 | | | 0.0236 | | |
| | 33.5 | | | 0.0254 | | |
| 21 | 32.1 | 20.6 | 8.71 | 0.0244 | 0.0156 | 0.00661 |
| | 18.3 | | | 0.0139 | | |
| | 30.7 | | | 0.0233 | | |
| | 16 | | | 0.0121 | | |
| | 15.3 | | | 0.0116 | | |
| | 11.1 | | | 0.0084 | | |
| 28 | 7.91 | 4.68 | 2.45 | 0.0060 | 0.00355 | 0.00186 |
| | 4.08 | | | 0.0031 | | |
| | 7.32 | | | 0.0056 | | |
| | 3.7 | | | 0.0028 | | |
| | 3.58 | | | 0.0027 | | |
| | 1.5 | | | 0.0011 | | |

1. The LOQ = 3.0 µg/glove. When residues were reported as less than the LOQ, Versar used a value of ½ LOQ (1.5 µg/glove) in the calculations.
2. % of applied dose dislodged = fipronil residue (µg/glove) / applied dose (131,722 µg) *100

| Table 3. Summary of RM-1502 Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | | |
|---|---|---|---|---|---|---|---|
| Interval (day) | RM-1502 Residue (µg/glove) | | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | RM1502 Residue[1] (µg/glove) | Corrected RM1502 Residue[2] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[3] | Average (%) | Standard Deviation (%) |
| 0.042 (1 hour) | 1.5 | 1.5 | 10.9 | 18.1 | 0.0011 | 0.00826 | 0.01373 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 41.7 | 47.17 | | | 0.0358 | | |
| | 8.93 | 10.10 | | | 0.0077 | | |
| | 3.09 | 3.50 | | | 0.0027 | | |
| 0.17 (4 hours) | 7.89 | 8.93 | 11.8 | 6.1 | 0.0068 | 0.00898 | 0.00464 |
| | 6.84 | 7.74 | | | 0.0059 | | |
| | 4.42 | 5.00 | | | 0.0038 | | |
| | 19.6 | 22.17 | | | 0.0168 | | |
| | 11.2 | 12.67 | | | 0.0096 | | |
| | 12.8 | 14.48 | | | 0.0110 | | |
| 0.33 (8 hours) | 5.53 | 6.26 | 5.5 | 2.1 | 0.0047 | 0.00418 | 0.00158 |
| | 4.98 | 5.63 | | | 0.0043 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 6.71 | 7.59 | | | 0.0058 | | |
| | 5.01 | 5.67 | | | 0.0043 | | |
| | 5.65 | 6.39 | | | 0.0049 | | |
| 1 | 5.22 | 5.90 | 5.0 | 1.8 | 0.0045 | 0.00378 | 0.00137 |
| | 4.14 | 4.68 | | | 0.0036 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 4.71 | 5.33 | | | 0.0040 | | |
| | 5.72 | 6.47 | | | 0.0049 | | |
| | 5.26 | 5.95 | | | 0.0045 | | |
| 2 | 6.91 | 7.82 | 4.6 | 2.7 | 0.0059 | 0.00346 | 0.00202 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 6 | 6.79 | | | 0.0052 | | |
| | 3.67 | 4.15 | | | 0.0032 | | |
| | 4.91 | 5.55 | | | 0.0042 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| 4 | 1.5 | 1.5 | 1.5 | 0.0 | 0.0011 | 0.00114 | 0.00000 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| 7 | 3.81 | 4.31 | 2.0 | 1.1 | 0.0033 | 0.00149 | 0.00087 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |

| Table 3. Summary of RM-1502 Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | | |
|---|---|---|---|---|---|---|---|
| Interval (day) | RM-1502 Residue (µg/glove) | | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | RM1502 Residue[1] (µg/glove) | Corrected RM1502 Residue[2] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[3] | Average (%) | Standard Deviation (%) |
| 14 | 1.5 | 1.5 | 1.5 | 0.0 | 0.0011 | 0.00114 | 0.00000 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| 21 | 1.5 | 1.5 | 1.5 | 0.0 | 0.0011 | 0.00114 | 0.00000 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| 28 | 1.5 | 1.5 | 1.5 | 0.0 | 0.0011 | 0.00114 | 0.00000 |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |
| | 1.5 | 1.5 | | | 0.0011 | | |

1. The LOQ = 3.0 µg/glove. When residues were reported as less than the LOQ, Versar used a value of ½ LOQ (1.5 µg/glove) in the calculations.
2. The RM1502 residues were corrected for an average laboratory recovery of 88.4%.
3. % of applied dose dislodged = Corrected RM1502 residue (µg/glove) / applied dose (131,722 µg) *100

| Table 4. Summary of RM-1602 Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | |
|---|---|---|---|---|---|---|
| Interval (day) | RM-1602 Residue (µg/glove) | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | RM1602 Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[2] | Average (%) | Standard Deviation (%) |
| 0.042 (1 hour) | 10.4 | 36.7 | 52.7 | 0.0079 | 0.0278 | 0.0400 |
| | 9.56 | | | 0.0073 | | |
| | 1.5 | | | 0.0011 | | |
| | 140 | | | 0.1063 | | |
| | 44.1 | | | 0.0335 | | |
| | 14.5 | | | 0.0110 | | |
| 0.17 (4 hours) | 33.4 | 51.3 | 28.3 | 0.0254 | 0.0389 | 0.0215 |
| | 29.8 | | | 0.0226 | | |
| | 20.5 | | | 0.0156 | | |
| | 94.8 | | | 0.0720 | | |
| | 61.4 | | | 0.0466 | | |
| | 67.8 | | | 0.0515 | | |
| 0.33 (8 hours) | 22.3 | 23.2 | 6.5 | 0.0169 | 0.0176 | 0.00491 |
| | 24.6 | | | 0.0187 | | |
| | 12.7 | | | 0.0096 | | |
| | 33 | | | 0.0251 | | |
| | 23.2 | | | 0.0176 | | |
| | 23.4 | | | 0.0178 | | |
| 1 | 30.8 | 28.3 | 5.8 | 0.0234 | 0.0214 | 0.00444 |
| | 24.7 | | | 0.0188 | | |
| | 20 | | | 0.0152 | | |
| | 25.3 | | | 0.0192 | | |
| | 33.8 | | | 0.0257 | | |
| | 34.9 | | | 0.0265 | | |
| 2 | 43.2 | 28.8 | 10.9 | 0.0328 | 0.0219 | 0.00826 |
| | 17.4 | | | 0.0132 | | |
| | 41 | | | 0.0311 | | |
| | 21.7 | | | 0.0165 | | |
| | 28.3 | | | 0.0215 | | |
| | 21.4 | | | 0.0162 | | |
| 4 | 20.5 | 16.6 | 3.6 | 0.0156 | 0.0126 | 0.00274 |
| | 13.5 | | | 0.0102 | | |
| | 16.5 | | | 0.0125 | | |
| | 11.3 | | | 0.0086 | | |
| | 17.5 | | | 0.0133 | | |
| | 20 | | | 0.0152 | | |
| 7 | 21.5 | 17.0 | 3.7 | 0.0163 | 0.0129 | 0.00284 |
| | 16.6 | | | 0.0126 | | |
| | 17.7 | | | 0.0134 | | |
| | 10.2 | | | 0.0077 | | |
| | 17.1 | | | 0.0130 | | |
| | 18.7 | | | 0.0142 | | |

| Table 4. Summary of RM-1602 Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | |
|---|---|---|---|---|---|---|
| Interval (day) | RM-1602 Residue (µg/glove) | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | RM1602 Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[2] | Average (%) | Standard Deviation (%) |
| 14 | 8.97 | 8.32 | 3.2 | 0.0068 | 0.0063 | 0.00243 |
| | 9.91 | | | 0.0075 | | |
| | 11 | | | 0.0084 | | |
| | 3.67 | | | 0.0028 | | |
| | 5.05 | | | 0.0038 | | |
| | 11.3 | | | 0.0086 | | |
| 21 | 7.65 | 6.04 | 1.7 | 0.0058 | 0.00458 | 0.00127 |
| | 5.47 | | | 0.0042 | | |
| | 8.15 | | | 0.0062 | | |
| | 3.59 | | | 0.0027 | | |
| | 5.28 | | | 0.0040 | | |
| | 6.08 | | | 0.0046 | | |
| 28 | 4.62 | 2.62 | 1.3 | 0.0035 | 0.00199 | 0.00101 |
| | 1.5 | | | 0.0011 | | |
| | 3.57 | | | 0.0027 | | |
| | 3.02 | | | 0.0023 | | |
| | 1.5 | | | 0.0011 | | |
| | 1.5 | | | 0.0011 | | |

1. The LOQ = 3.0 µg/glove. When residues were reported as less than the LOQ, Versar used a value of ½ LOQ (1.5 µg/glove) in the calculations.
2. % of applied dose dislodged = RM1602 residue (µg/glove) / applied dose (131,722 µg) *100

| Table 5. Summary of Total Fipronil Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | |
|---|---|---|---|---|---|---|
| Interval (days) | Total Fipronil Residue (µg/glove) | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | Total Fipronil Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[2] | Average (%) | Standard Deviation (%) |
| 0.042 (1 hour) | 242 | 1100 | 1623 | 0.184 | 0.835 | 1.2322 |
| | 287 | | | 0.218 | | |
| | 75.2 | | | 0.0571 | | |
| | 4302 | | | 3.27 | | |
| | 1262 | | | 0.958 | | |
| | 433 | | | 0.329 | | |
| 0.17 (4 hours) | 935 | 1422 | 843 | 0.710 | 1.079 | 0.6398 |
| | 843 | | | 0.640 | | |
| | 538 | | | 0.408 | | |
| | 2850 | | | 2.16 | | |
| | 1580 | | | 1.20 | | |
| | 1785 | | | 1.36 | | |
| 0.33 (8 hours) | 607 | 626 | 206 | 0.460 | 0.475 | 0.15665 |
| | 652 | | | 0.495 | | |
| | 304 | | | 0.231 | | |
| | 954 | | | 0.724 | | |
| | 639 | | | 0.485 | | |
| | 598 | | | 0.454 | | |
| 1 | 735 | 667 | 159 | 0.558 | 0.506 | 0.12056 |
| | 588 | | | 0.447 | | |
| | 390 | | | 0.296 | | |
| | 683 | | | 0.518 | | |
| | 830 | | | 0.630 | | |
| | 774 | | | 0.587 | | |
| 2 | 968 | 619 | 261 | 0.735 | 0.470 | 0.19840 |
| | 340 | | | 0.258 | | |
| | 854 | | | 0.648 | | |
| | 521 | | | 0.395 | | |
| | 683 | | | 0.518 | | |
| | 349 | | | 0.265 | | |
| 4 | 420 | 307 | 95 | 0.319 | 0.233 | 0.07177 |
| | 226 | | | 0.172 | | |
| | 315 | | | 0.239 | | |
| | 241 | | | 0.183 | | |
| | 220 | | | 0.167 | | |
| | 423 | | | 0.321 | | |
| 7 | 345 | 231 | 69 | 0.262 | 0.176 | 0.05230 |
| | 224 | | | 0.170 | | |
| | 244 | | | 0.185 | | |
| | 172 | | | 0.130 | | |
| | 254 | | | 0.193 | | |
| | 150 | | | 0.114 | | |

| Table 5. Summary of Total Fipronil Residue and Percent of Applied Dose Dislodged After 5 Strokes | | | | | | |
|---|---|---|---|---|---|---|
| Interval (days) | Total Fipronil Residue (µg/glove) | | | % of Applied Dose Dislodged After 5 Strokes | | |
| | Total Fipronil Residue[1] (µg/glove) | Average (µg/glove) | Standard Deviation (µg/glove) | % of applied dose[2] | Average (%) | Standard Deviation (%) |
| 14 | 70.0 | 57.0 | 20.7 | 0.0531 | 0.0433 | 0.01574 |
| | 69.2 | | | 0.0525 | | |
| | 85.2 | | | 0.0647 | | |
| | 33.6 | | | 0.0255 | | |
| | 37.7 | | | 0.0286 | | |
| | 46.3 | | | 0.0351 | | |
| 21 | 41.3 | 28.1 | 10.1 | 0.0313 | 0.0214 | 0.00763 |
| | 25.3 | | | 0.0192 | | |
| | 40.4 | | | 0.0306 | | |
| | 21.1 | | | 0.0160 | | |
| | 22.1 | | | 0.0168 | | |
| | 18.7 | | | 0.0142 | | |
| 28 | 14.0 | 8.80 | 3.66 | 0.0107 | 0.00668 | 0.00278 |
| | 7.1 | | | 0.00537 | | |
| | 12.4 | | | 0.00941 | | |
| | 8.2 | | | 0.00624 | | |
| | 6.6 | | | 0.00500 | | |
| | 4.5 | | | 0.00342 | | |

1. Total Fipronil Residue (µg/glove) = Fipronil residue (µg/glove) + Corrected RM1502 residue (µg/glove) + RM1602 residue (µg/glove).
2. % of applied dose dislodged = Total Fipronil residue (µg/glove) / applied dose (131,722 µg) *100

| Table 6. Fipronil - Predicted Percent of Applied Dose Dislodgeable (derived from regression curve – Appendix A) | |
|---|---|
| Days After Application | % of Applied Dose Dislodgeable |
| 0 | 1.03[a] |
| 1 | 0.481 [b] |
| 2 | 0.355 |
| 3 | 0.297 |
| 4 | 0.248 |
| 5 | 0.207 |
| 6 | 0.173 |
| 7 | 0.145 |
| 8 | 0.121 |
| 9 | 0.101 |
| 10 | 0.0843 |
| 11 | 0.070 |
| 12 | 0.0589 |
| 13 | 0.0492 |
| 14 | 0.0411 |
| 15 | 0.0343 |
| 16 | 0.0287 |
| 17 | 0.0240 |
| 18 | 0.0200 |
| 19 | 0.0167 |
| 20 | 0.0140 |

a Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0
b Day 1 Predicted Value = Actual Average Day 1 Value

| Table 7. RM-1602 - Predicted Percent of Applied Dose Dislodgeable (derived from regression curve – Appendix A) | |
|---|---|
| Days After Application | % of Applied Dose Dislodgeable |
| 0 | 0.0389[a] |
| 1 | 0.0214[b] |
| 2 | 0.0180 |
| 3 | 0.0165 |
| 4 | 0.0152 |
| 5 | 0.0139 |
| 6 | 0.0128 |
| 7 | 0.0118 |
| 8 | 0.0108 |
| 9 | 0.00992 |
| 10 | 0.00911 |
| 11 | 0.00837 |
| 12 | 0.00769 |
| 13 | 0.00706 |
| 14 | 0.00649 |
| 15 | 0.00596 |
| 16 | 0.00547 |
| 17 | 0.00503 |
| 18 | 0.00462 |
| 19 | 0.00424 |
| 20 | 0.00390 |

a Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0
b Day 1 Predicted Value = Actual Average Day 1 Value

| Table 8. Total Fipronil - Predicted Percent of Applied Dose Dislodgeable (derived from regression curve – Appendix A) | |
|---|---|
| Days After Application | % of Applied Dose Dislodgeable |
| 0 | 1.079[a] |
| 1 | 0.506[b] |
| 2 | 0.354 |
| 3 | 0.302 |
| 4 | 0.258 |
| 5 | 0.221 |
| 6 | 0.189 |
| 7 | 0.161 |
| 8 | 0.138 |
| 9 | 0.118 |
| 10 | 0.101 |
| 11 | 0.0861 |
| 12 | 0.0736 |
| 13 | 0.0629 |
| 14 | 0.0538 |
| 15 | 0.0460 |
| 16 | 0.0393 |
| 17 | 0.0336 |
| 18 | 0.0287 |
| 19 | 0.0245 |
| 20 | 0.0210 |

a Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0
b Day 1 Predicted Value = Actual Average Day 1 Value

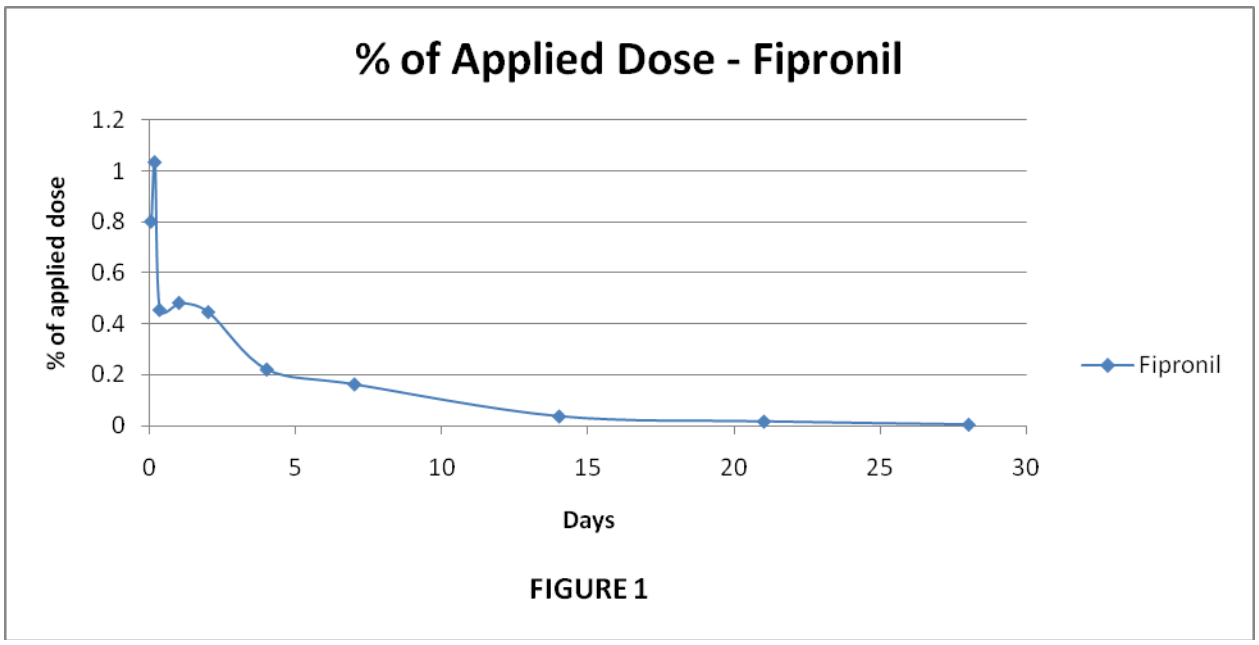



**FIGURE 1**

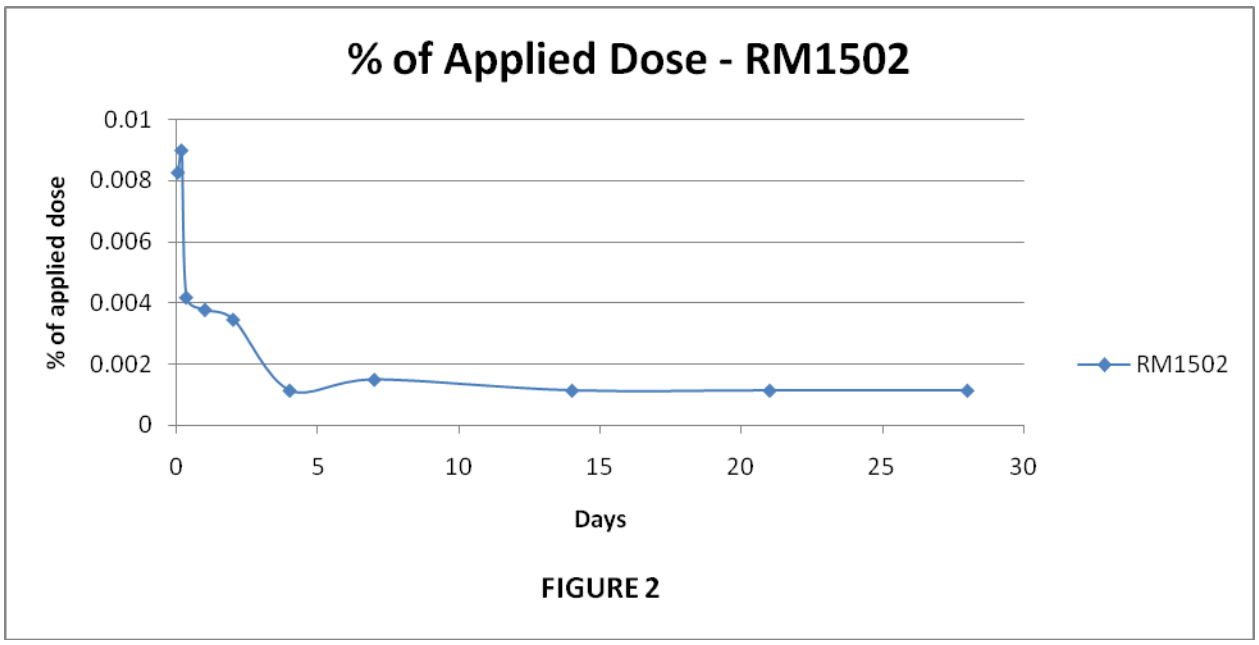



**FIGURE 2**

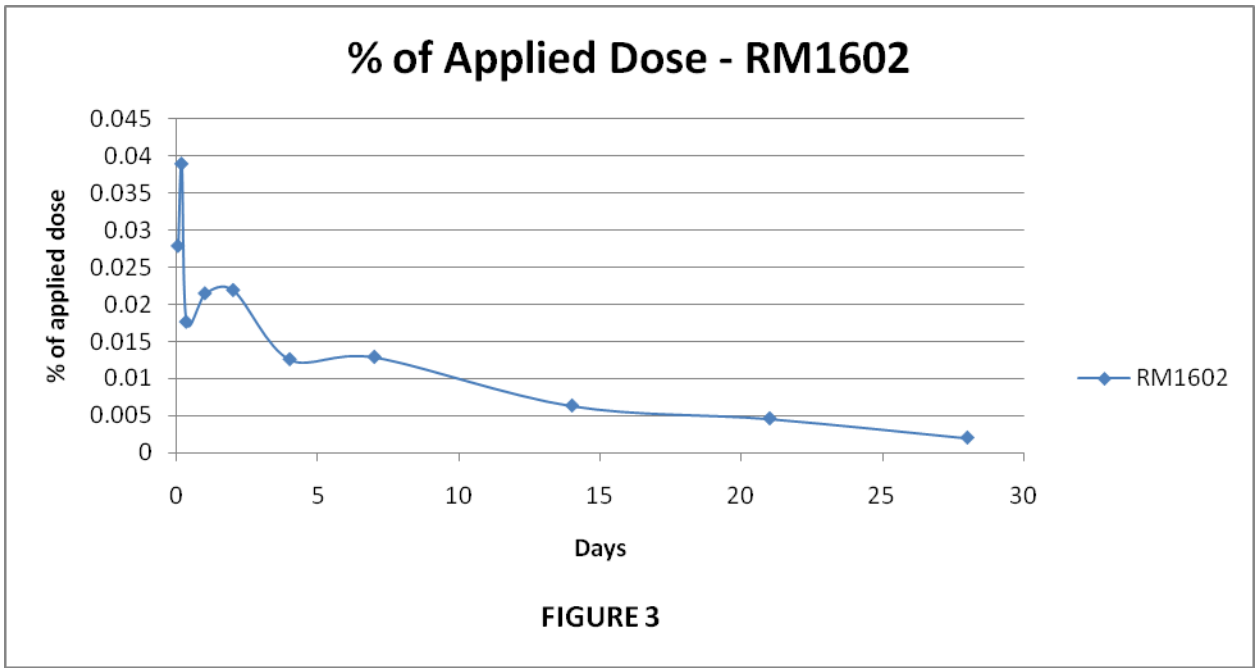



**FIGURE 3**

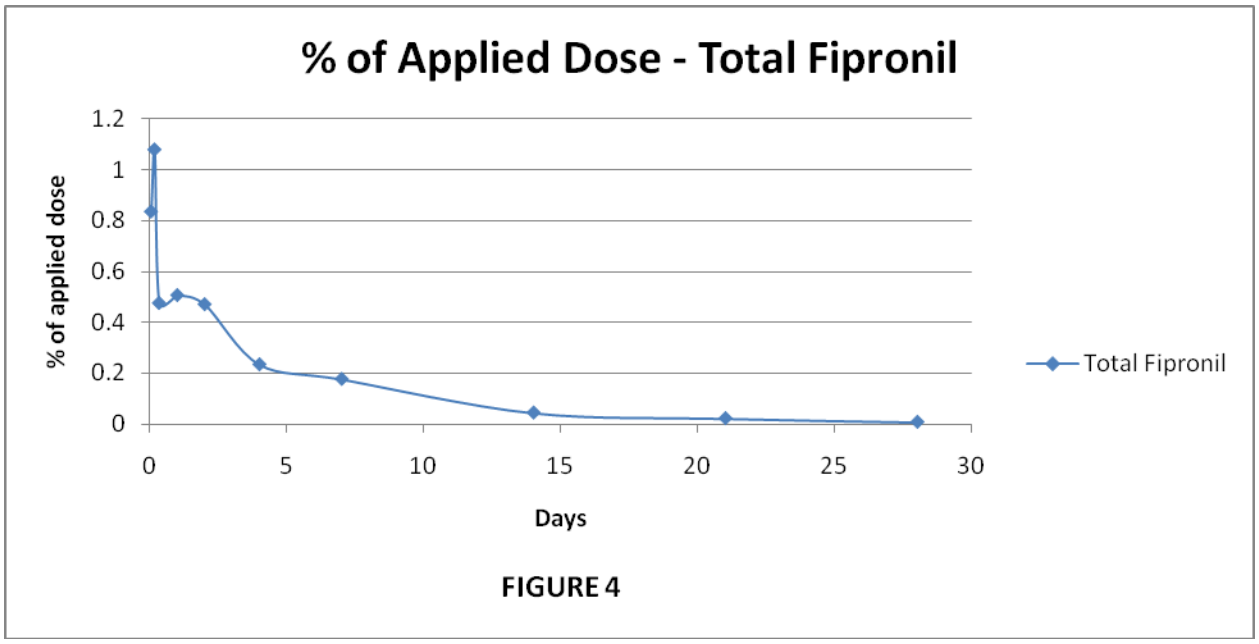



**FIGURE 4**

# Appendix A

# Compliance Checklist

## COMPLIANCE CHECKLIST

This compliance checklist is based on applicable parts of the OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2300 (indoor surface residue) and OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group B: 875.2400 (dermal exposure).

1. *The test substance must be the typical end use product of the active ingredient.* This criterion was met.

2. *The production of metabolites, breakdown products, or the presence of contaminants of potential toxicologic concern, should be considered on a case-by-case basis.* This criterion was met.

3. *Indoor surface residue studies should be conducted under ambient conditions similar to those encountered during the intended use season, and should represent reasonable worst case conditions.* This criterion was met.

4. *Ambient conditions (i.e., temperature, barometric pressure, ventilation) should be monitored.* This criterion was met.

5. The *end use product should be applied by the application method recommended on the label. Information that verifies that the application equipment (e.g., sprayer) was properly calibrated should be included.* This criterion was met.

6. *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate is more appropriate in certain cases.* This criterion was met.

7. *If multiple applications are made, the minimum allowable interval between applications should be used.* This criterion does not apply. Only one application was made.

8. *Indoor surface residue (ISR) data should be collected from several different types of media (e.g., carpeting, hard surface flooring, counter tops, or other relevant materials).* This criterion was not met. Only one breed of dog was monitored.

9. *Sampling should be sufficient to characterize the dissipation mechanisms of the compound (e.g., three half-lives or 72 hours after application, unless the compound has been found to fully dissipate in less time; for more persistent pesticides, longer sampling periods may be necessary). Sampling intervals may be relatively short in the beginning and lengthen as the study progresses. Background samples should be collected before application of the test substance occurs.* This criterion was met.

10. *Triplicate, randomly collected samples should be collected at each sampling interval for each surface type.* This criterion was met. Six replicates were collected.

11. *Samples should be collected using a suitable methodology (e.g., California Cloth Roller, Polyurethane Roller, Drag Sled, Coupons, Wipe Samples, Hand Press, vacuum cleaners for dust and debris, etc.) for indoor surfaces.* It is uncertain if this criterion was met. Samples were collected using cotton gloves and five strokes.

12. *Samples should be stored in a manner that will minimize deterioration and loss of analytes*

*between collection and analysis. Information on storage stability should be provided.* This criterion was not met. Information on storage stability was not provided.

13. *Validated analytical methods of sufficient sensitivity are needed. Information on method efficiency (residue recovery), and limit of quantitation (LOQ) should be provided.* This criterion was partially met. An LOQ was provided; however, the method validation results were not reported.

14. *Information on recovery samples must be included in the study report. A complete set of field recoveries should consist of at least one blank control sample and three or more each of a low-level and high-level fortification. These fortifications should be in the range of anticipated residue levels in the field study.* This criterion was not met. Field fortification samples were not prepared.

15. *Raw residue data must be corrected if appropriate recovery values are less than 90 percent.* This criterion was not met. Samples were not corrected for recoveries. There were no field fortification samples collected.

16. *The monitoring period should be of sufficient duration to result in reasonable detectability on dosimeters. Monitoring should be conducted before residues have dissipated beyond the limit of quantification. Baseline samples should be collected before the exposure activity commences.* These criteria were partially met. Background samples were collected from each dog prior to application and analyzed. These residues were <LOQ. Residues from samples collected after application of the test substance were above the LOQ in most of the samples analyzed for fipronil, RM1602 and RM1502. No residues of M&B46513 were detected any samples.

17. *Activities monitored must be clearly defined and representative of typical practice.* This criterion was partially met. The activity of stroking a dog is a typical post-application activity; however, only five strokes per replicate were conducted in this study. Additionally, postapplication activity also typically includes hugging.

18. *Sufficient control samples should be collected.* This criterion was met. A control sample was collected from each dog prior to the application event.

# Appendix B

# Regressions

**Regression Analysis: Summary Output for Fipronil**

| *Regression Statistics* | |
|---|---|
| Multiple R | 0.970341 |
| R Square | 0.941562 |
| Adjusted $R^2$ | 0.939843 |
| Standard Error | 0.431889 |
| Observations | 36 |

ANOVA

| | *df* | *SS* | *MS* | *F* | *Signif. F* |
|---|---|---|---|---|---|
| Regression | 1 | 102.1829 | 102.1829 | 547.81364 | 1.51061E-22 |
| Residual | 34 | 6.34197 | 0.186529 | | |
| Total | 35 | 108.5248 | | | |

| | *Coeff.* | *Std. Error* | *t Stat* | *P-value* | *Lower 95%* | *Upper 95%* |
|---|---|---|---|---|---|---|
| Intercept | -0.6762 | 0.120996 | -5.58857 | 2.951E-06 | -0.922089793 | -0.430302185 |
| Slope | -0.17971 | 0.007678 | -23.4054 | 1.511E-22 | -0.195313201 | -0.164105623 |

Half Life = 3.857044 Days

**Predicted DFR Levels**

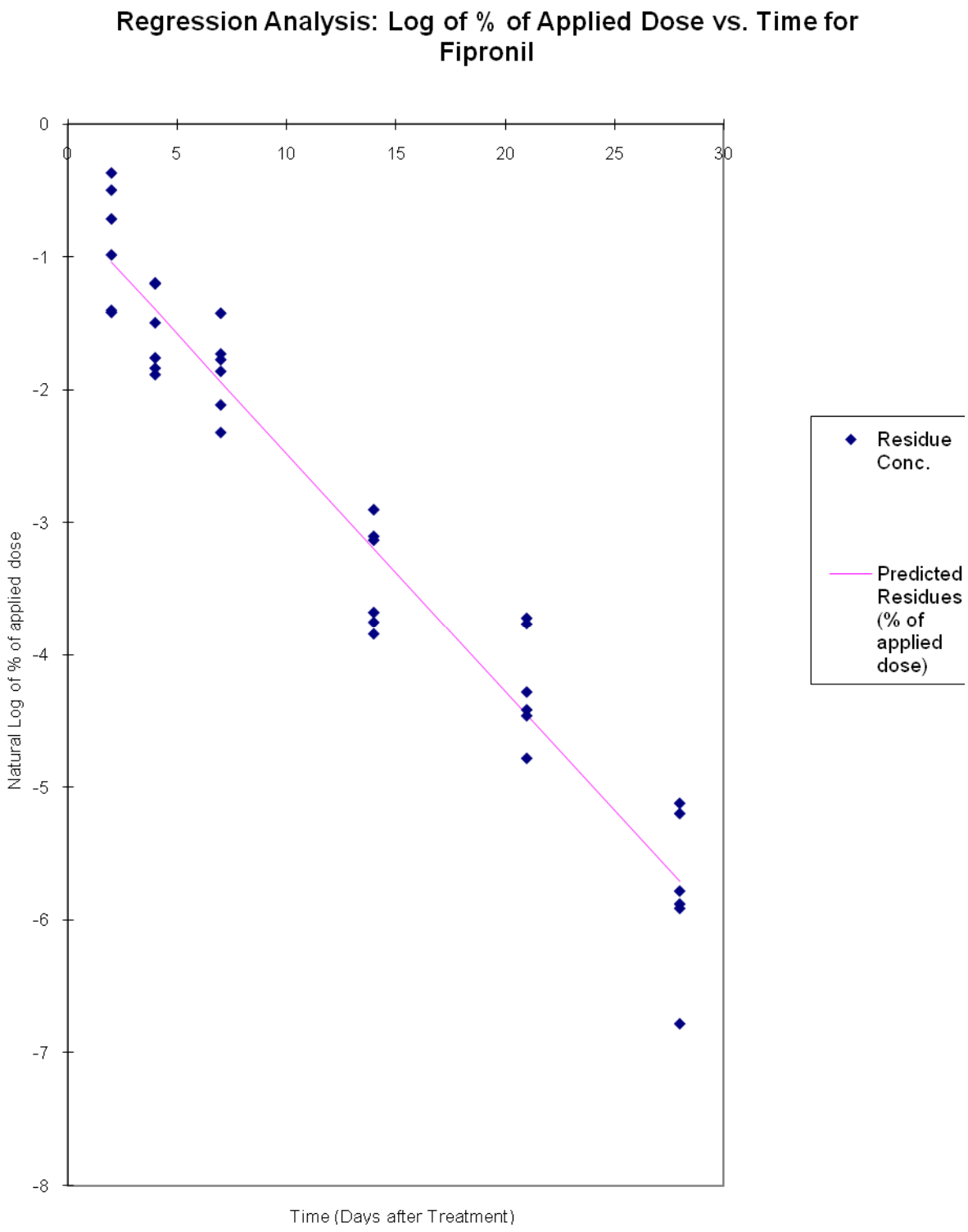
| Time (Days) | Residue (% of applied dose) |
|---|---|
| 0 | 1.03* |
| 1 | 0.481** |
| 2 | 0.355008 |
| 3 | 0.296614 |
| 4 | 0.247825 |
| 5 | 0.207061 |
| 6 | 0.173002 |
| 7 | 0.144545 |
| 8 | 0.12077 |
| 9 | 0.100905 |
| 10 | 0.084307 |
| 11 | 0.07044 |
| 12 | 0.058853 |
| 13 | 0.049173 |
| 14 | 0.041084 |
| 15 | 0.034327 |
| 16 | 0.02868 |
| 17 | 0.023963 |
| 18 | 0.020021 |
| 19 | 0.016728 |
| 20 | 0.013976 |

| Time (Days) | Residue (% of applied dose) |
|---|---|
| 21 | 0.0116775 |
| 22 | 0.0097567 |
| 23 | 0.0081518 |
| 24 | 0.006811 |
| 25 | 0.0056906 |
| 26 | 0.0047546 |
| 27 | 0.0039725 |
| 28 | 0.0033191 |
| 29 | 0.0027732 |
| 30 | 0.002317 |
| 31 | 0.0019359 |
| 32 | 0.0016175 |
| 33 | 0.0013514 |
| 34 | 0.0011291 |
| 35 | 0.0009434 |

* **Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0 (4 hr Value)**
****Day 1 Predicted Value = Actual Average Day 1 Value**

**Regression Analysis: Means and CVs for Fipronil**

| Days after Last Treatment | Residues (% of applied dose) | Mean (% of applied dose) | Standard Deviation (% of applied dose) | Coefficient of Variation (%) |
|---|---|---|---|---|
| 2 | 0.696163 | 0.445 | 0.188 | 42.3 |
| | 0.243695 | | | |
| | 0.611895 | | | |
| | 0.375791 | | | |
| | 0.492704 | | | |
| | 0.247491 | | | |
| 4 | 0.302152 | 0.22 | 0.0696 | 31.6 |
| | 0.160186 | | | |
| | 0.225475 | | | |
| | 0.173092 | | | |
| | 0.152594 | | | |
| | 0.304429 | | | |
| 7 | 0.242177 | 0.161 | 0.0499 | 31 |
| | 0.15639 | | | |
| | 0.170814 | | | |
| | 0.121468 | | | |
| | 0.178406 | | | |
| | 0.098693 | | | |
| 14 | 0.045171 | 0.0358 | 0.0141 | 39.3 |
| | 0.04388 | | | |
| | 0.055192 | | | |
| | 0.021561 | | | |
| | 0.02361 | | | |
| | 0.025432 | | | |
| 21 | 0.02437 | 0.0156 | 0.00661 | 42.4 |
| | 0.013893 | | | |
| | 0.023307 | | | |
| | 0.012147 | | | |
| | 0.011615 | | | |
| | 0.008427 | | | |
| 28 | 0.006005 | 0.00355 | 0.00186 | 52.4 |
| | 0.003097 | | | |
| | 0.005557 | | | |
| | 0.002809 | | | |
| | 0.002718 | | | |
| | 0.00114 | | | |


Regression Analysis: Log of % of Applied Dose vs. Time for Fipronil
0
-1
-2
-3
-4
-5
-6
-7
-8
0
5
10
15
20
25
30
Natural Log of % of applied dose
Time (Days after Treatment)
Residue Conc.
Predicted Residues (% of applied dose)

**Regression Analysis: Summary Output for RM1602**

| *Regression Statistics* | |
|---|---|
| Multiple R | 0.90698 |
| R Square | 0.822612 |
| Adjusted $R^2$ | 0.817395 |
| Standard Error | 0.380302 |
| Observations | 36 |

ANOVA

| | *df* | *SS* | *MS* | *F* | *Signif. F* |
|---|---|---|---|---|---|
| Regression | 1 | 22.80388 | 22.80388 | 157.67071 | 2.53827E-14 |
| Residual | 34 | 4.917413 | 0.14463 | | |
| Total | 35 | 27.7213 | | | |

| | *Coeff.* | *Std. Error* | *t Stat* | *P-value* | *Lower 95%* | *Upper 95%* |
|---|---|---|---|---|---|---|
| Intercept | -3.84951 | 0.106544 | -36.1308 | 1.037E-28 | -4.066036221 | -3.632990431 |
| Slope | -0.0849 | 0.006761 | -12.5567 | 2.538E-14 | -0.098635777 | -0.071155804 |

Half Life = 8.164683 Days

**Predicted DFR Levels**

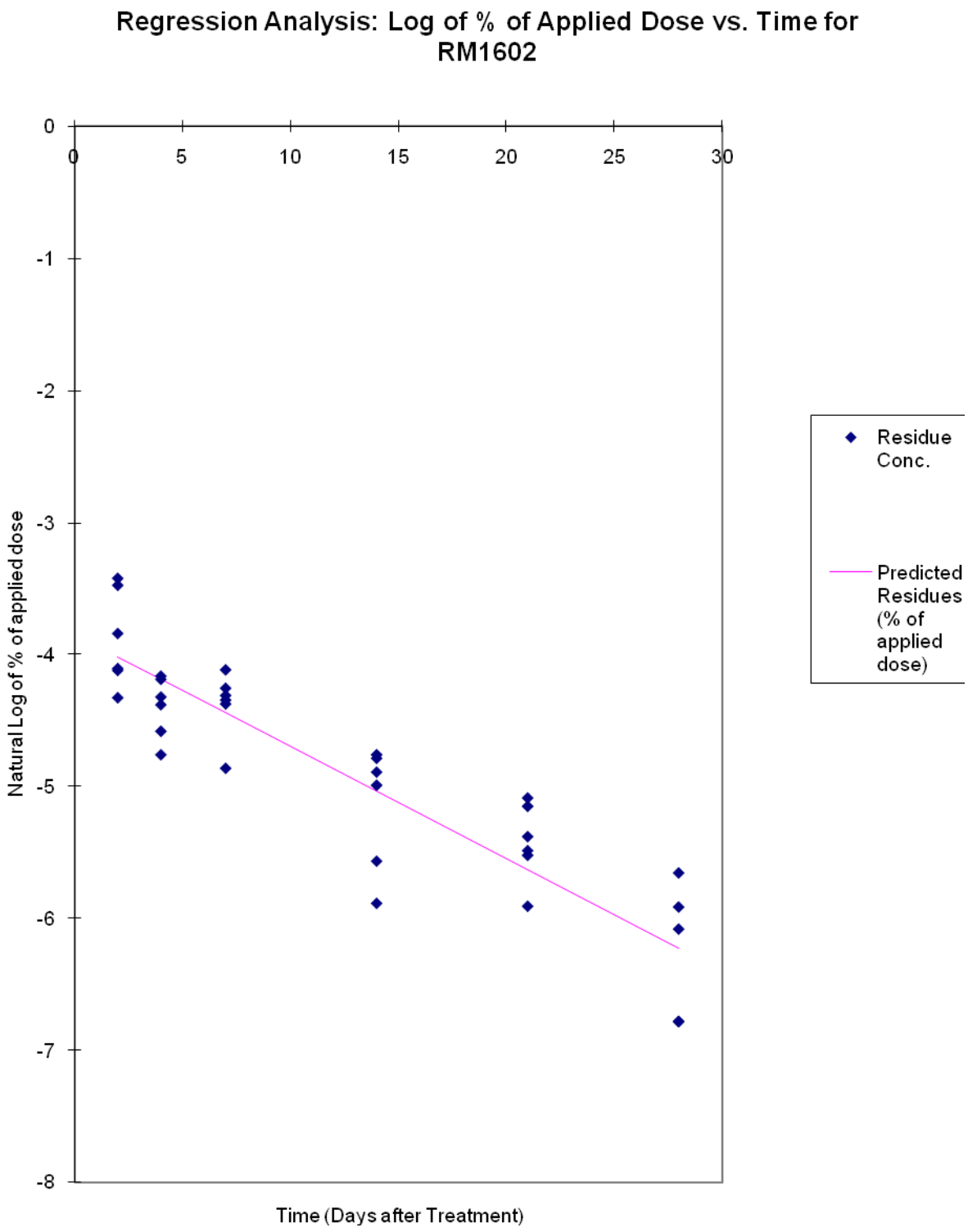
| Time (Days) | Residue (% of applied dose) |
|---|---|
| 0 | 0.0389* |
| 1 | 0.0214** |
| 2 | 0.017965 |
| 3 | 0.016503 |
| 4 | 0.01516 |
| 5 | 0.013926 |
| 6 | 0.012793 |
| 7 | 0.011751 |
| 8 | 0.010795 |
| 9 | 0.009916 |
| 10 | 0.009109 |
| 11 | 0.008368 |
| 12 | 0.007687 |
| 13 | 0.007061 |
| 14 | 0.006486 |
| 15 | 0.005958 |
| 16 | 0.005473 |
| 17 | 0.005028 |
| 18 | 0.004619 |
| 19 | 0.004243 |
| 20 | 0.003897 |

| Time (Days) | Residue (% of applied dose) |
|---|---|
| 21 | 0.0035802 |
| 22 | 0.0032888 |
| 23 | 0.0030212 |
| 24 | 0.0027753 |
| 25 | 0.0025494 |
| 26 | 0.0023419 |
| 27 | 0.0021513 |
| 28 | 0.0019762 |
| 29 | 0.0018153 |
| 30 | 0.0016676 |
| 31 | 0.0015318 |
| 32 | 0.0014072 |
| 33 | 0.0012926 |
| 34 | 0.0011874 |
| 35 | 0.0010908 |

* **Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0 (4 hr Value)**
****Day 1 Predicted Value = Actual Average Day 1 Value**

**Regression Analysis: Means and CVs for RM1602**

| Days after Last Treatment | Residues (% of applied dose) | Mean (% of applied dose) | Standard Deviation (% of applied dose) | Coefficient of Variation (%) |
|---|---|---|---|---|
| 2 | 0.032796 | 0.0219 | 0.00826 | 37.7 |
| | 0.01321 | | | |
| | 0.031126 | | | |
| | 0.016474 | | | |
| | 0.021485 | | | |
| | 0.016246 | | | |
| 4 | 0.015563 | 0.0126 | 0.00274 | 21.8 |
| | 0.010249 | | | |
| | 0.012526 | | | |
| | 0.008579 | | | |
| | 0.013286 | | | |
| | 0.015183 | | | |
| 7 | 0.016322 | 0.0129 | 0.00284 | 22 |
| | 0.012602 | | | |
| | 0.013437 | | | |
| | 0.007744 | | | |
| | 0.012982 | | | |
| | 0.014197 | | | |
| 14 | 0.00681 | 0.00631 | 0.00243 | 38.5 |
| | 0.007523 | | | |
| | 0.008351 | | | |
| | 0.002786 | | | |
| | 0.003834 | | | |
| | 0.008579 | | | |
| 21 | 0.005808 | 0.00458 | 0.00127 | 27.7 |
| | 0.004153 | | | |
| | 0.006187 | | | |
| | 0.002725 | | | |
| | 0.004008 | | | |
| | 0.004616 | | | |
| 28 | 0.003507 | 0.00199 | 0.00101 | 50.7 |
| | 0.0 | | | |
| | 0.00271 | | | |
| | 0.002293 | | | |
| | 0.0 | | | |
| | 0.0 | | | |


Regression Analysis: Log of % of Applied Dose vs. Time for RM1602
0
5
10
15
20
25
30
-1
-2
-3
-4
-5
-6
-7
-8
Natural Log of % of applied dose
Time (Days after Treatment)
Residue Conc.
Predicted Residues (% of applied dose)

**Regression Analysis: Summary Output for Total Fipronil**

| *Regression Statistics* | |
|---|---|
| Multiple R | 0.969272 |
| R Square | 0.939489 |
| Adjusted $R^2$ | 0.937709 |
| Standard Error | 0.384154 |
| Observations | 36 |

ANOVA

| | *df* | *SS* | *MS* | *F* | *Signif. F* |
|---|---|---|---|---|---|
| Regression | 1 | 77.90163 | 77.90163 | 527.88127 | 2.73509E-22 |
| Residual | 34 | 5.017521 | 0.147574 | | |
| Total | 35 | 82.91915 | | | |

| | *Coeff.* | *Std. Error* | *t Stat* | *P-value* | *Lower 95%* | *Upper 95%* |
|---|---|---|---|---|---|---|
| Intercept | -0.72604 | 0.107623 | -6.74614 | 9.408E-08 | -0.944754316 | -0.507322779 |
| Slope | -0.15691 | 0.006829 | -22.9757 | 2.735E-22 | -0.170790737 | -0.143032455 |

Half Life = 4.417438 Days

**Predicted DFR Levels**

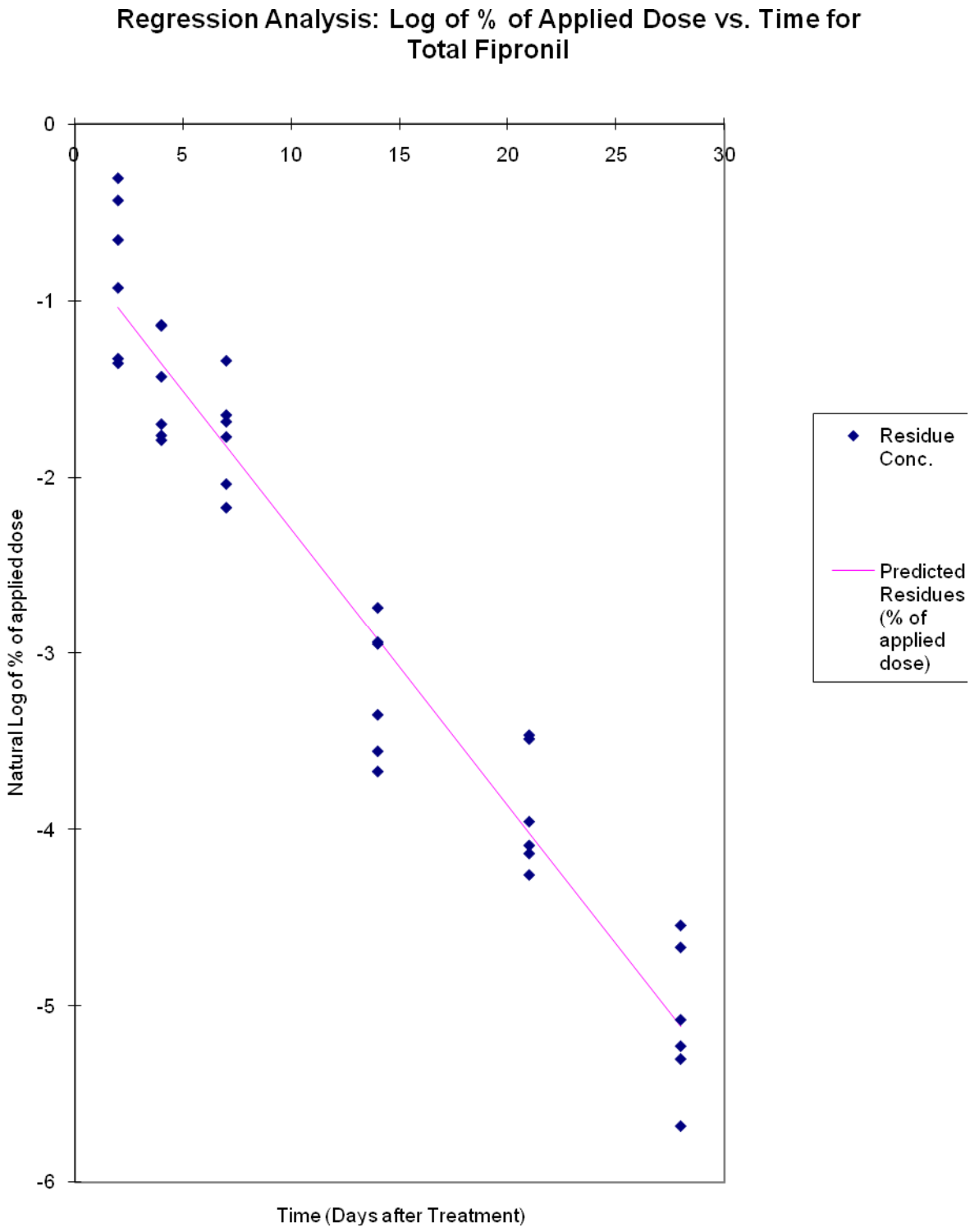
| Time (Days) | Residue (% of applied dose) |
|---|---|
| 0 | 1.0794* |
| 1 | 0.506** |
| 2 | 0.353504 |
| 3 | 0.302168 |
| 4 | 0.258287 |
| 5 | 0.220778 |
| 6 | 0.188717 |
| 7 | 0.161311 |
| 8 | 0.137886 |
| 9 | 0.117862 |
| 10 | 0.100746 |
| 11 | 0.086115 |
| 12 | 0.07361 |
| 13 | 0.06292 |
| 14 | 0.053783 |
| 15 | 0.045972 |
| 16 | 0.039296 |
| 17 | 0.03359 |
| 18 | 0.028712 |
| 19 | 0.024542 |
| 20 | 0.020978 |

| Time (Days) | Residue (% of applied dose) |
|---|---|
| 21 | 0.0179318 |
| 22 | 0.0153277 |
| 23 | 0.0131018 |
| 24 | 0.0111992 |
| 25 | 0.0095728 |
| 26 | 0.0081826 |
| 27 | 0.0069944 |
| 28 | 0.0059786 |
| 29 | 0.0051104 |
| 30 | 0.0043683 |
| 31 | 0.0037339 |
| 32 | 0.0031917 |
| 33 | 0.0027282 |
| 34 | 0.002332 |
| 35 | 0.0019933 |

* **Day 0 Predicted Value = Worse Case Value Of All Samples Collected on Day 0 (4 hr Value)**
****Day 1 Predicted Value = Actual Average Day 1 Value**

**Regression Analysis: Means and CVs for Total Fipronil**

| Days after Last Treatment | Residues (% of applied dose) | Mean (% of applied dose) | Standard Deviation (% of applied dose) | Coefficient of Variation (%) |
|---|---|---|---|---|
| 2 | 0.734894 | 0.47 | 0.198 | 42.2 |
| | 0.258043 | | | |
| | 0.648174 | | | |
| | 0.395417 | | | |
| | 0.518406 | | | |
| | 0.264876 | | | |
| 4 | 0.318853 | 0.233 | 0.0718 | 30.8 |
| | 0.171573 | | | |
| | 0.23914 | | | |
| | 0.182809 | | | |
| | 0.167018 | | | |
| | 0.320751 | | | |
| 7 | 0.261771 | 0.176 | 0.0523 | 29.7 |
| | 0.170131 | | | |
| | 0.18539 | | | |
| | 0.13035 | | | |
| | 0.192527 | | | |
| | 0.114028 | | | |
| 14 | 0.053119 | 0.0433 | 0.0157 | 36.4 |
| | 0.052542 | | | |
| | 0.064682 | | | |
| | 0.025485 | | | |
| | 0.028583 | | | |
| | 0.03515 | | | |
| 21 | 0.031316 | 0.0213 | 0.00763 | 35.8 |
| | 0.019184 | | | |
| | 0.030633 | | | |
| | 0.016011 | | | |
| | 0.016763 | | | |
| | 0.014181 | | | |
| 28 | 0.010651 | 0.00668 | 0.00278 | 41.6 |
| | 0.0 | | | |
| | 0.009406 | | | |
| | 0.00624 | | | |
| | 0.0 | | | |
| | 0.0 | | | |


Regression Analysis: Log of % of Applied Dose vs. Time for Total Fipronil
0
5
10
15
20
25
30
-1
-2
-3
-4
-5
-6
Natural Log of % of applied dose
Time (Days after Treatment)
Residue Conc.
Predicted Residues (% of applied dose)