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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Bonaventure Akinlosotu

From: Clayton Myers, Entomologist **Date**: September 21, 2011 9-21-11

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD

DP barcode: 388571
Decision no.: 445857
Submission no: 891161
Action code: R310
Product Name: Hartz Ref #134
EPA Reg. No or File Symbol: 2596-RAO
Formulation Type: Pet Spot-on Product
Ingredients statement from the label with PC codes included: Etofenprox, 55%, PC: 128965; Piperonyl Butoxide, 10%, PC: 067501; MGK 264, 1%, PC: 057001; S-methoprene, 0.25%, PC: 105402
Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 as appropriate): Spot-on: 0.91 mL up to 14 lbs, 1.95 mL up to 30 lbs, 3.90 mL up to 60 lbs, 6.50 mL up to 150 lbs (0.065 mL/lb body weight).

I. Action Requested: Data was submitted to support pest claims for a new dog spot-on product

II. Background: The registrant seeks to register an etofenrpox/pbo/MGK 264 combo spot-on product for control of fleas and ticks on dogs. The registrant has submitted 4 studies to support efficacy claims.

III. MRID Summaries: (Primary Reviews attached)

a. MRID 48405806

(1) GLP with some exceptions
(2) A laboratory study was conducted with 35 mixed breed, mixed sex dogs from the test colony, reared under standard conditions. Dogs were pre-qualified for retention of fleas. Dogs were blocked by gender and ranked by flea count retention. 7 replicate blocks of 5 dogs were established and dogs were randomly assigned to the treatment groups (a control group and 4 different formulations of the test product). Parasites were applied one day prior to treatment, and reinfestations were conducted at 8, 15, 22, and 29 days after treatment (100 cat fleas and 50 brown dog ticks). At 24 hours after infestation, flea comb counts were conducted, with removal of fleas and determination of mortality. On test days 2, 9, 16, 23, and 30, each dog was infested with 100 cat fleas for the purpose of egg production. On days 5, 12, 19, 26, and 33, eggs were collected and fleas were removed afterword. Where possible, 50 flea eggs per dog were collected and incubated for 3 days to determine egg hatch and development of flea larvae for 32 days, with flea growth media. At 25 days after egg collection, adult emergence was determined. Flea and tick counts were transfomed and percent efficacy was calculated using Abbott's formula.
(3) Authors conclude that efficacy is supported for fleas and brown dog ticks. The primary reviewer correctly notes that efficacy against Brown dog ticks was not adequate on either days 2 or 16 of the evaluation. The primary reviewer concludes that 4 week control of adult fleas is

adequately supported. Efficacy against flea egg hatch and emergence is supported for up to 33 days (this is only applicable for products containing Nylar at 0.5%).
(4) The study is acceptable to support claims against flea adults for up to 30 days or one month. The study is not adequate to support any tick claims.

b. MRID 48405808

(1) GLP with some exceptions.
(2) A laboratory study was conducted with 14 mixed breed, mixed sex dogs from the test colony, reared under standard conditions. Dogs were pre-qualified for retention of ticks. Dogs were blocked by gender and ranked by flea count retention. The dogs were blocked by gender and ranked by tick retention, with 7 replicates of 2 dogs each randomly assigned to either the control or treatment group. Ticks were applied 7 days after treatment and reinfestations were conducted at 7, 14, 21, and 28 days after treatment (50 brown dog ticks). At 48 hours after infestation, flea comb counts were conducted, with removal of fleas and determination of mortality, on days 9, 16, 23, and 30. Tick counts were transfomed and percent efficacy was calculated using Abbott's formula.
(3) The test material provided >90% control of brown dog ticks throughout the study. The primary reviewer concludes that the study was adequate to support 30 day control claims against Brown dog ticks.
(4) The study is adequate to support a 30 day (one month) control claim against brown dog ticks.

c. MRID 48405809

(1) GLP with some exceptions.
(2) A laboratory study was conducted with 21 mixed breed, mixed sex dogs from the test colony, reared under standard conditions. Dogs were pre-qualified for retention of fleas. Dogs were blocked by gender and ranked by flea count retention. 7 replicate blocks of 3 dogs were established and dogs were randomly assigned to the treatment groups (a control group and 2 different formulations of the test product). Parasites were applied 6 and 1 days prior to treatment, and reinfestations were conducted at 4, 7, 14, 21, 28, and 32 days after treatment with 100 cat fleas. On days -1, 7, 14, 21, and 28, dogs were also infested with 50 brown dog ticks. On test days -13, 4, 11, 18, 25, and 32, each dog was infested with 100 cat fleas for the purpose of egg production. On days -10, 7, 14, 21, 28, and 35, eggs were collected and fleas were removed afterword. Where possible, 50 flea eggs per dog were collected and incubated for 3 days to determine egg hatch and development of flea larvae for 32 days, with flea growth media. At 25 days after egg collection, adult emergence was determined. Flea and tick counts were transfomed and percent efficacy was calculated using Abbott's formula. All dogs were shampooed weekly with shampoo, and the dog was rinsed with clean water for at least five minutes using a shower head with a flow rate of 2.8 gal/minute and towel dried.
(3) Both test materials provided adult flea efficacy through day 16, but efficacy was reduced after that point. Neither test material (2 variations of same product) was efficacious against Brown dog ticks. Both products were effective at preventing flea egg hatch and adult flea emergence through 35 days after treatment. The primary reviewer concludes that the product does not support 4 week claims for either adult fleas or ticks, but does support the claims against flea egg hatch and emergence. The lack of efficacy is likely due to the weekly shampooing of animals.
(4) This study is not adequate to support on month control claims against fleas or ticks, and a notation should be made on the label that the product is neither waterproof, nor wash proof. Any claims of waterproof efficacy must be removed from the label, except for flea eggs and larvae

d. MRID 48405811

(1) GLP with some exceptions
(2) A laboratory study was conducted with 12 mixed breed, mixed sex dogs from the test colony, reared under standard conditions. Dogs were pre-qualified for retention of fleas. Dogs were blocked by flea count retention. 6 blocks of 2 replicates each were establshed and randomly assigned to either the control or treatment group. On day 0, test material was applied according to

label directions. On day 2, each dog was infested with 100 cat fleas and a flea count was made at 8 hours using a comb. Each animal was then re-infested and a count made 15 minutes later. Animals were re-infested and evaluated at 12 hours, and then infested again for a 30 minute evaluation. Mortality was calculated using Abbott's formula.
(3) 90% treatment efficacy was observed at 15 minutes, with 95-99% efficacy observed through 12 hours. The primary reviewer concludes that the data are adequate to support a claim of killing fleas within 15 minutes of application.
(4) A 15 minute kills claim is problematic because it was not specified where the parasites were placed on the animal's body. Because animal spot-ons require some time to spread over the animal's hair and adequately cover the entire body, it cannot be concluded from this data that the product would be adequate to kill fleas within 15 minutes on every part of the dog's body. Therefore, this 15 minute claim is not adequately supported and must be removed from the label.

b. MRID 47518513 (cited)

This study was rated 'acceptable' by the Agency to support 30 day claims against Deer Ticks (*Ixodes scapularis*) and a general 30 day repellence and control claims against Mosquitoes at the proposed doses.

IV. RECOMMENDATIONS:

(1) Labeling:

(a) What pests and site/pest combinations may be added as follows to the label based on the submitted or cited data?

Fleas (adults), Fleas (eggs and larvae, only for products containing S-methoprene), Brown Dog Ticks, Deer Ticks, Mosquitoes

(b) What pests and site/pest combinations must be removed from the label?

General Tick claims (not supported because no American Dog Tick data were submitted or cited). Claims must either be species specific or qualified to exclude American Dog Ticks, unless additional data is submitted or cited. Claims against killing within 15 minutes of treatment must be removed from the label, or alternatively revised to say "starts killing within 15 minutes." Claims of specific percentages of control are not acceptable and all such claims must be removed from the label.

(c) List changes to the directions for use:

(d) List changes to the optional marketing claims:

All general 'tick' claims must be revised to exclude American Dog Ticks.
Claims against killing within 15 minutes of treatment must be removed from the label, or alternatively revised to say "starts killing within 15 minutes."
Claims of specific percentages of control are not acceptable and all such claims must be removed from the label.

<u>The following marketing claims must be deleted from the label (line by line, pages 6-7)</u>:

~~"Kills fleas in as little as 15 minutes"~~
~~"Kills fleas in 15 minutes"~~
~~"Kills fleas in 15 minutes and lasts for 30 days (1 month)(4 weeks)"~~
~~"Kills fleas within 15 minutes"~~
~~"Stops fleas from biting in as little as 15 minutes"~~
~~"Stops fleas from biting in as little as 15 minutes and lasts for 30 days (1 month)(4 weeks)"~~
~~"Stops fleas from biting in 15 minutes"~~

~~"Stops fleas from biting in 15 minutes and lasts for 30 days (1 month)(4 weeks)"~~
~~"Stops fleas from biting within 15 minutes"~~
~~"Stops fleas from biting within 15 minutes and lasts for 30 days (1 month)(4 weeks)"~~
~~"Rapidly eliminates fleas"~~
~~"Fast acting"~~
~~"Kills 95% of fleas in 8 hours (of initial application)"~~
~~"Kills 99% of fleas in 12 hours (of initial application)"~~

The claims "starts killing fleas within 15 minutes" are acceptable and may be retained.

TASK 2 DATA EVALUATION RECORD

STUDY TYPE: Product Performance

MRID 484058-06. Young, D.R. In Vivo Ovicidal (and Adulticidal) Activity of Flea and Tick Dermal Treatments Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. March 9, 2010.

MRID 484058-08. Young, D.R. *In Vivo* Acaracidal Activity of a Flea and Tick Dermal Treatment Against the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. June 21, 2010.

MRID 484058-09. Fourie, J.J. The Effect of Weekly Shampooing and Water Rinsing on the Persistent Efficacy of Two Stripe-On Formulations Against Ticks (*Rhipicephalus sanguineus*) and Fleas (*Ctenocepyalides felis*) on Dogs. April 7, 2010.

MRID 484058-11. Everett, W.R. Speed of Kill Efficacy of a Dermal Treatment Applied to Dogs Against Cat Fleas (*Ctenocephalides felis*). July 28, 2010.

Treatments to Control Pests of Humans and Pets (810.3300)
Product Name: Hartz Reference No. 132; Hartz Reference No. 134; Hartz Reference No. 135
EPA Reg. No. or File Symbol: 2596-RAT; 2596-RAO; 2596-RAI
Decision number: 445859; 445857; 445858
DP number: 388561; 388571; 388567

Prepared for
Registration Division (7505P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Washington, DC 20460

Prepared by
Summitec Corporation
Task Order Nos.: 2-10; 2-11; 2-12

Primary Reviewer:
Eric B. Lewis, M.S.

Signature: Eric B. Lewis
Date: AUG 26 2011

Secondary Reviewers:
Gene Burgess, Ph.D.

Signature: Gene Burgess AB
Date: AUG 26 2011

Robert Ross, M.S., Program Manager

Signature: Robert H. Ross
Date: AUG 26 2011

Quality Assurance:
Angela M. Edmonds, B.S.

Signature: Angela M. Edmonds
Date: AUG 26 2011

RECOMMENDED CLASSIFICATION: **Partially Acceptable**

Disclaimer

This review may have been altered subsequent to the contractors' signatures above.
Summitec Corporation for the U.S. Environmental Protection Agency under Contract No. EP-W-11-014

DATA EVALUATION RECORD

[Primary Reviewer's Name]

STUDY TYPE:	PRODUCT PERFORMANCE (810.3300)
MRIDS:	MRID 484058-06. Young, D.R. In Vivo Ovicidal (and Adulticidal) Activity of Flea and Tick Dermal Treatments Against the Cat Flea (*Ctenocephalides felis*) and the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. March 9, 2010. MRID 484058-08. Young, D.R. *In Vivo* Acaracidal Activity of a Flea and Tick Dermal Treatment Against the Brown Dog Tick (*Rhipicephalus sanguineus*) on Dogs. June 21, 2010. MRID 484058-09. Fourie, J.J. The Effect of Weekly Shampooing and Water Rinsing on the Persistent Efficacy of Two Stripe-On Formulations Against Ticks (*Rhipicephalus sanguineus*) and Fleas (*Ctenocepyalides felis*) on Dogs. April 7, 2010. MRID 484058-11. Everett, W.R. Speed of Kill Efficacy of a Dermal Treatment Applied to Dogs Against Cat Fleas (*Ctenocephalides felis*). July 28, 2010.
DP BARCODE:	388561; 388571; 388567
DECISION NO:	445859; 445857; 445858
SUBMISSION NO:	891159; 891161; 891160
SPONSOR:	The Hartz Mountain Corporation, 400 Plaza Drive, Secaucus, NJ 07094
TESTING FACILITY:	MRIDs 484058-06, 484058-08: Young Veterinary Research Services, 7243 East Avenue, Turlock, CA 95380 MRID 484058-09: ClinVet International (Pty) Ltd., P.O. Box 11186, Universitas 9321, South Africa MRID 484058-11: BerTek, Inc. 104 Wilson Bottom Road, Greenbrier, AR 72058
STUDY DIRECTOR:	MRIDs 484058-06, 484058-08: David R. Young, D.V.M. MRID 484058-09: J.J. Fourie, Investigator MRID 484058-11: William R. Everett,

President/Laboratory Director

SUBMITTER:

MRIDs 484058-06, 484058-08, 484058-11: Robert Rossenwasser, Director, Regulatory Affairs

MRID 484058-09: K. Goldman, Sponsor Representative

STUDY COMPLETED:

MRID 484058-06: March 9, 2010

MRID 484058-08: June 21, 2010

MRID 484058-09: April 7, 2010

MRID 484058-11: June 23, 2010

CONFIDENTIALITY CLAIMS:

MRIDs 484058-06, 484058-08: Confidential information is contained in a confidential appendix

MRIDs 484058-09, 484058-11: None

GOOD LABORATORY PRACTICE:

MRIDs 484058-06, 484058-08: The studies were in compliance with 40 CFR Part 160, with the following exceptions: validation of the computer systems used to generate the statistical analyses was not verified by the study director or contract laboratory QAU. The statistical analysis report appended to the amended final report was audited by the contract laboratory QAU. However, internal data processing systems were not verified; therefore the data presented and discussions incorporating conclusions based on statistical analysis referred to in these reports are unverified.

MRID 484058-09: The study was conducted in compliance with 40 CFR Part 160.

MRID 484058-11: The study was conducted in compliance with 40 CFR Part 160 with the following exceptions: the commercial animal ration and drinking water used in the study were not analyzed for specific contaminants, because none were expected. The drinking water was potable water from the local public supply and is routinely analyzed by the local water authority.

TEST MATERIALS:

PRODUCT NAME: Hartz Reference No. 132

EPA FILE SYMBOL: 2596-RAT

ACTIVE INGREDIENT NAMES: Etofenprox Technical; PBO Technical; MGK-264 Technical

CHEMICAL NAMES: [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether]; piperonyl butoxide; N-octyl bicycloheptene dicarboximide

A.I. %: 55.0%; 10.0%; 1.0%

PC CODE: 128965; 067501; 057001

CAS NO.: 80844-07-1; 51-03-6; 113-48-4

FORMULATION TYPE: Topical solution

PRODUCT APPLICATION RATE(S): 0.91 to 6.50 mL/dog, depending on weight

ACTIVE INGREDIENT APPLICATION RATE(S): Etofenprox Technical, 0.50 to 3.58 mL/dog; PBO Technical, 0.09 to 0.65 mL/dog, MGK-264 Technical: 0.001 to 0.065 mL/dog

PRODUCT NAME: Hartz Reference No. 134

EPA FILE SYMBOL: 2596-RAO

ACTIVE INGREDIENT NAME: Etofenprox Technical; Nylar Technical; S-Methoprene Technical; PBO Technical; MGK-264 Technical

CHEMICAL NAME: [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether]; pyriproxifen; [isopropyl (2E,4E,7S)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate]; piperonyl butoxide; N-octyl bicycloheptene dicarboximide

A.I. %: 55.0%; 0.5%; 0.25%; 10.0%; 1.0%

PC CODE: 128965; 129032; 105402; 067501; 057001

CAS NO.: 80844-07-1; 95737-68-1; 65733-16-6; 51-03-6; 113-48-4

FORMULATION TYPE: Topical solution

PRODUCT APPLICATION RATE(S): 0.91 to 6.50 mL/dog, depending on weight

ACTIVE INGREDIENT APPLICATION RATE(S): Etofenprox Technical, 0.50 to 3.58 mL/dog; PBO Technical, 0.09 to 0.65 mL/dog; MGK-264 Technical, 0.001 to 0.065 mL/dog; Nylar Technical, 0.005 to 0.033 mL/dog, s-Methoprene Technical, 0.002 to 0.016 mL/dog

PRODUCT NAME: Hartz Reference No. 135

EPA FILE SYMBOL: 2596-RAI

ACTIVE INGREDIENT NAME: Etofenprox Technical; Nylar Technical; PBO Technical; MGK-264 Technical

CHEMICAL NAME: [2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether]; pyriproxifen; piperonyl butoxide; N-octyl bicycloheptene dicarboximide

A.I. %: 55.0%; 0.5%; 10.0%; 1.0%

PC CODE: 128965; 129032; 067501; 057001

CAS NO.: 80844-07-1; 95737-68-1; 51-03-6; 113-48-4

FORMULATION TYPE: Topical solution

PRODUCT APPLICATION RATE(S): 0.91 to 6.50 mL/dog, depending on weight

ACTIVE INGREDIENT APPLICATION RATE(S): Etofenprox Technical, 0.50 to 3.58 mL/dog; PBO Technical, 0.09 to 0.65 mL/dog; MGK-264 Technical, 0.001 to 0.065 mL/dog; Nylar Technical, 0.005 to 0.033 mL/dog

PROPOSED LABEL MARKETING CLAIMS:

Hartz Reference No. 132: Kills fleas, ticks for four weeks. Starts killing fleas within 15 minutes. Kills 95% of fleas in 8 hours, 99% in 12 hours.

Hartz Reference No. 134: Kills fleas, ticks for four weeks. Starts killing fleas within 15 minutes. Kills 95% of fleas in 8 hours, 99% in 12 hours. Kills all stages of the flea life cycle. Waterproof control of flea eggs (and larvae).

Hartz Reference No. 135: Kills fleas, ticks, flea eggs for four weeks. Starts killing fleas within 15 minutes. Kills 95% of fleas in 8 hours, 99% in 12 hours. Kills all stages of the flea life cycle. Waterproof control of flea eggs (and larvae).

EPA REQUESTS: [EPA WILL ADD DIRECTIVES HERE]

STUDY REVIEW

Study Number/Title: (if more than one study is provided in the MRID)

Purpose:

The registrant is using the same group of studies (MRIDs 484058-06, 484058-08, 484058-09, and 484058-11) to support registration of three different products (Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135) to control fleas and ticks on dogs (*Canis familiaris*).

MATERIALS AND METHODS

Test Location:

MRIDs 4844058-06 and 484058-08: Turlock, CA; MRID 484058-09: Bloemfontein, South Africa; MRID 484058-11: Greenbrier, AR

Test Material(s):

All the test materials contain Etofenprox, piperonyl butoxide, and MGK-264 in approximately the same concentrations as those in Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135. Some of the test materials contain, in addition to the three active ingredients above, the insect growth regulator Nylar (found in Hartz Reference #134 and Hartz Reference #135).

The test material dose used in MRIDs 484058-06, 484058-08, 484058-09, and 484058-11 was 0.065 mL/lb body weight. The labels for Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 recommend an application rate of 0.91 mL for dogs weighing 5 to 14 lbs, 1.95 mL for dogs weighing 15 to 30 lbs, 3.90 mL for dogs weighing 31 to 60 lbs, and 6.50 mL for dogs weighing more than 60 lbs. The registrant explains in MRID 484058-00 that the recommended application rates are based on the ratio of dog surface area to weight.

MRID 484058-06:

Stripe On TS# 13321 [a.i., Etofenprox (54.61%); piperonyl butoxide (9.54%); MGK-264 (0.93%); Nylar (0.46%)]. Stripe On TS# 13321 contains the same active ingredients, in the same proportions (when rounded), as Hartz Reference #135.

Stripe On TS# 13322 [a.i., Etofenprox (54.86%); piperonyl butoxide (9.55%); MGK-264 (0.96%); Nylar (0.93%)] . Stripe On TS# 13322 contains the same active ingredients, in the same proportions (when rounded) as Hartz Reference #135, with the exception that the concentration of Nylar is approximately double that in Hartz Reference #135.

Stripe On TS#13323 [a.i., etofenprox (53.48%); piperonyl butoxide (9.55%); MGK-264 (0.92%); Nylar (0.50%)]. Stripe On TS# 13323 contains the same active ingredients, in the same proportions (when rounded), as Hartz Reference #135, with the exception that the concentration of Etofenprox is approximately two percent lower than in Hartz Reference #135.

Stripe On TS#13324 [a.i., etofenprox (53.82%); piperonyl butoxide (9.60%); MGK-264 (0.97%); Nylar (0.98)]. Stripe On TS# 13324 contains the same active ingredients, in the same proportions (when rounded), as Hartz Reference #135, with the exception that the concentration of Etofenprox is approximately one percent lower than in Hartz Reference #135, and the concentration of Nylar is approximately double that in Hartz Reference #135.

MRID 484058-08:

Stripe On TS# 13377 [a.i., etofenprox (54.71%); piperonyl butoxide (9.91%); MGK-264 (0.95%)]. Stripe On TS# 13377 has the same active ingredients, in the same proportions (when rounded), as Hartz Reference #132.

MRID 484058-09:

TS# 13337 [a.i., etofenprox (54.92%); piperonyl butoxide (9.78%); N-octyl-bicycloheptene dicarboximide (0.94%); Nylar (0.96%). Stripe On TS# 13337 contains the same active ingredients, in the same proportions (when rounded) as Hartz Reference #135, with the exception that the concentration of Nylar is approximately double that in Hartz Reference #135.

TS# 13338 [a.i., etofenprox (54.21%); piperonyl butoxide (9.67%); N-octyl bicycloheptene dicarboximide (0.97%); Nylar (0.96%). Stripe On TS# 13338 contains the same active ingredients, in the same proportions (when rounded), as Hartz Reference #135, with the exception that the concentration of etofenprox is approximately one percent lower than in Hartz Reference #135, and the concentration of Nylar is approximately double that in Hartz Reference #135.

MRID 484058-11:

TS# 13396 [a.i., etofenprox (~55%); piperonyl butoxide (~10%); MGK-264 (~1%)]. TS# 13396 contains the same active ingredients, in the same proportions, as Hartz Reference #132.

Test Species Name, Life Stage, Sex and Age:

MRIDs 484058-06 and 484058-09: Cat flea (*Ctenocephalides felis*) eggs and adults, mixed sexes; Brown dog tick (*Rhipicephalus sanguineus*) adults, mixed sexes.

MRID 484058-08: Brown dog tick (*Rhipicephalus sanguineus*) adults, mixed sexes.

MRID 484058-11: Cat flea (*Ctenocephalides felis*) adults, mixed sexes.

Describe test containers, chambers and/or apparatusand how experiment was conducted:

MRID 484058-06:

Thirty-five adult, mixed breed dogs of both sexes from the test facility colony were housed individually in 4 x 6 ft runs of galvanized wire with a sloping concrete floor. Solid metal panels separated the runs. The dogs were acclimated to the test facility and were healthy at test start. The dogs were fed Nutrena River Run Meat Based Dog Food (No Soy) during the test. Well water was available *ad libitum*. Prior to assignment to treatment groups, the ability of each dog to hold a viable population of adult fleas and provide viable flea egg counts was determined. The dogs were blocked by gender and ranked by flea count. Seven replicate blocks of five dogs each were established, and within each replicate, dogs were randomly assigned to the treatment groups. Body weight of the dogs ranged from 19.2 to 91.9 lbs.

On test day -8, hair coat description and length were recorded, and on day -2 body weight was recorded. On day 0, the appropriate test material was applied to the test material groups using a needleless syringe placed on the back between the shoulder blades. The tip of the syringe was used to part the hair so that the test material was applied at skin level. The test material was applied so as to form a stripe down the back to the base of the tail. Any parasites applied to the test animals after treatment were applied away from the treatment site.

On test days -1, 8, 15, 22, and 29, each dog in treatment groups 1, 4, and 5 was infested with ~100 unfed cat fleas (in house colony). On days 2, 9, 16, 23, and 30, a flea count was performed by systematically using a single-sided, fine-tooth flea comb to comb the entire body of each dog for five minutes, or until fleas were no longer found.

On test days -2, 7, 14, 21, and 28, each dog in treatment groups 1, 4, and 5 was infested with 50 brown dog ticks (El Labs). On days 2, 9, 16, 23, and 30, a tick count was performed along with the flea count.

On test days 2, 9, 16, 23, and 30, each dog was infested with ~100 cat fleas for the purpose of egg production. On days 5, 12, 19, 26, and 33, eggs were collected, and the fleas were removed afterward. When possible, 50 eggs were collected from each dog and incubated for three days in a petri dish. The larval hatch was then counted, after which flea growth media was added to the dish and the eggs/larvae were incubated for an additional 32 days. At 25 days after egg collection, adult emergence was determined.

List the treatments including untreated control:

TABLE 1. Treatments used in MRID 484058-06

Group	N	
1	7	Untreated control
2	7	Stripe On TS# 13321, 0.065 mL/lb body weight
3	7	Stripe On TS# 13322, 0.065 mL/lb body weight
4	7	Stripe On TS# 13323, 0.065 mL/lb body weight
5	7	Stripe On TS# 13324, 0.065 mL/lb body weight

Data from p. 11, MRID 484058-06

Number of replicates per treatment: 7

Number of individuals per replicate: 5

Length of exposure to treatment: Fleas, 1 to 3 days; ticks, 2 to 4 days.

Were tested specimens transferred to clean containers? Not applicable.

Experimental conditions: Temperature was stated to be thermostatically controlled as necessary.

Data or endpoints that were to be collected/recorded: Flea counts, tick counts, percent flea egg hatch, percent of flea eggs developing to adults.

MRID 484058-08:

Fourteen adult, mixed breed dogs of both sexes from the test facility colony were housed individually in 4 x 6 ft runs of galvanized wire with a sloping concrete floor. Solid metal panels separated the runs. The dogs were acclimated to the test facility and were healthy at test start. The dogs were fed Nutrena River Run Meat Based Dog Food (No Soy) during the test. Well water was available *ad libitum*. Prior to assignment to treatment groups, the ability of each dog to maintain a tick infestation was determined. The dogs were blocked by gender and ranked by tick count. Seven replicate blocks of two dogs each were established, and within each replicate, dogs were randomly assigned to the treatment groups. Body weight of the dogs ranged from 19.9 to 71.2 lbs.

On test day -8, hair coat description and length were recorded, and on day -2 body weight was recorded. On day 0, the test material was applied to the test material groups using a needleless syringe placed on the back between the shoulder blades. The tip of the syringe was used to part the hair so that the test material was applied at skin level. The test material was applied so as to form a

stripe down the back to the base of the tail. Any parasites applied to the test animals after treatment were applied away from the treatment site.

On test days 7, 14, 21, and 28, each dog was infested with 50 unfed brown dog ticks (El Labs). On days 9, 16, 23, and 30, a tick count was performed by systematically using a single-sided, fine-tooth flea comb to comb the entire body of each dog for five minutes or until ticks were no longer found.

List the treatments including untreated control:

TABLE 2. Treatments used in MRID 484058-08		
Group	N	
1	7	Untreated control
2	7	Stripe On TS# 13377, 0.065 mL/lb body weight

Data from p. 8, MRID 484058-08

Number of replicates per treatment: 7

Number of individuals per replicate: 2

Length of exposure to treatment: 2 days

Were tested specimens transferred to clean containers? Not applicable.

Experimental conditions: Temperature was stated to be thermostatically controlled as necessary.

Data or endpoints that were to be collected/recorded: Tick counts.

MRID 484058-09:

Twenty-one sub-adult and adult, mixed breed dogs of both sexes from the test facility colony were housed individually in 1.9 x 2.97 m pens with concrete floors. No contact between dogs was possible. The dogs were acclimated to the test facility and were healthy at test start. The dogs were fed Ultradog Superwoof Adult Maintenance commercial dog diet once daily during the test. Local municipal water was provided *ad libitum*. Prior to assignment to treatment groups, each dog received a flea count. The dogs were blocked by gender and ranked by flea count. Seven replicate blocks of three dogs each were established, and within each replicate, dogs were randomly assigned to the treatment groups. Body weight of the dogs ranged from 26.0 to 37.9 lbs, and hair length from 12.75 to 36.25 mm (0.5 to 1.4 in).

On day 0, the appropriate test material was applied to the test material groups using a needleless syringe placed on the back between the shoulder blades. The tip of the syringe was used to part the hair so that the test material was applied at skin level. The test material was applied so as to form a stripe down the back to the base of the tail. Any parasites applied to the test animals after treatment were applied away from the treatment site.

On test days -6, -1, 4, 7, 14, 21, 28, and 32 each dog was infested with ~100 unfed cat fleas (in house colony). On days 2, 9, 16, 23, and 30, a flea count was performed by systematically using a fine-tooth flea comb to comb the entire body of each dog.

On test days -1, 7, 14, 21, and 28, each dog was sedated and infested with 50 unfed laboratory-bred brown dog ticks. On days 2, 9, 16, 23, and 30, a tick count was performed along with the flea count.

On test days -13, 4, 11, 18, 25, and 32, each dog was infested with ~100 cat fleas for the purpose of egg production. On days -10, 7, 14, 21, 28, and 35, eggs were collected, and the fleas were removed from the dogs afterward. When possible, 50 eggs were collected from each dog and incubated for three days in a petri dish. The larval hatch was then counted, after which flea growth media was added to the dish and the eggs/larvae were incubated for an additional 32 days. At that time adult emergence was determined.

All dogs were shampooed weekly with Bio-Groom So-Gentle Hypo-Allergenic Shampoo (non-insecticidal, non-acaricidal), which was supplied as a concentrate and diluted with two parts water prior to application. The dog's coat was wetted and the shampoo was applied and worked well through the coat. The dog was then rinsed with clean water for at least five minutes using a shower head with a flow rate of 2.8 gal/minute. The dogs were then dried with a towel and returned to the appropriate kennel.

List the treatments including untreated control:

TABLE 3. Treatments used in MRID 484058-09

Group	N	
1	7	Untreated control
2	7	TS# 13337, 0.065 mL/lb body weight
3	7	TS# 13338, 0.065 mL/lb body weight

Data from p. 7, MRID 484058-09

Number of replicates per treatment: 7

Number of individuals per replicate: 3

Length of exposure to treatment: Fleas, 2 days; ticks, 2 days.

Were tested specimens transferred to clean containers? Not applicable.

Experimental conditions: During the test, the temperature ranged from 16.8 to 30.8°C; relative humidity ranged from 23.7% to 88.1%. The photoperiod was 12 hrs light:12 hrs darkness.

Data or endpoints that were to be collected/recorded: Flea counts, tick counts, percent flea egg hatch, percent of flea eggs developing to adults.

MRID 484058-11:

Twelve adult, mixed-breed dogs of both sexes from the test facility colony were housed individually in 5 x 4 ft cages with chain-link walls and concrete floors. The dogs were acclimated to the test facility and were healthy at test start. The dogs were fed once daily with 2-3 cups of commercial dry ration (Loyall, Adult Maintenance Formula, Nutrena). Local municipal supply water was available *ad libitum*. Prior to assignment to treatment groups, the ability of each dog to maintain a flea infestation was determined. The dogs were blocked by the pre-test flea count. Six

replicate blocks of two dogs each were established, and within each replicate, dogs were randomly assigned to the treatment groups. Body weight of the dogs ranged from 26.1 to 46.7 lbs.

On day 0, the test material was applied to the test material group using a needleless syringe placed on the back between the shoulder blades. The tip of the syringe was used to part the hair so that the test material was applied at skin level. The test material was applied so as to form a stripe down the back to the base of the tail. Any fleas applied to the test animals after treatment were applied away from the treatment site.

On test day 2, each dog was infested with ~100 unfed cat fleas, and a flea count was made eight hours later by thoroughly combing the entire animal with a fine-tooth flea comb and removing all fleas. Each animal was then infested with ~100 fleas, and a flea count was made 15 minutes later. Each animal was then infested with ~100 fleas and a flea count was made 12 hours later on test day 3. Each animal was then infested with ~100 fleas and a flea count was made 30 minutes later.

List the treatments including untreated control:

TABLE 4. Treatments used in MRID 484058-11

Group	N	
1	6	TS# 13396, 0.065 mL/lb body weight
2	6	Untreated control

Data from p.8, MRID 484058-11

Number of replicates per treatment: 6

Number of individuals per replicate: 2

Length of exposure to treatment: 15 minutes, 30 minutes, 8 hours, 12 hours.

Were tested specimens transferred to clean containers? Not applicable.

Experimental conditions: Not provided.

Data or endpoints that were to be collected/recorded: Flea counts.

Statistical Analysis:

MRID 484058-06:

Flea and tick counts were transformed to the natural logarithm of (count + 1) to calculate geometric means. Percent efficacy for each treated group on each day was calculated as 100 * (GMC – GMT)/GMC, where GMC = geometric mean of the control group and GMT = geometric mean of the treated group. Treatments were compared using a t-test for means with poolable variances or for means with unequal variances, as appropriate. Variances were compared using an F-test, and Satterthwaite's Approximation was used to determine the degrees of freedom for the unequal variance tests. All three pairwise combinations of treatment groups were compared.

Percent hatch and adult development of flea eggs were transformed to the arcsine (radians) of the square root of the proportion to calculate means; mean angle was back transformed. When no eggs were collected from a dog on a given day, the percent hatch and development were defined as zero,

and when none of the collected eggs hatched, the percent development was defined as zero. Percent efficacy was calculated as 100 * (RTMC – RTMT)/RTMC where RTMC = retransformed mean of the control group and RTMT = retransformed mean of the treated group. The data were analyzed as for the adult flea and tick counts above. Each treated group was compared with the control, the TS# 13321 group was compared with the TS# 13322 group, and the TS# 13323 group was compared with the TS# 13324 group.

All analyses were performed using SAS v. 8.2, with a significance level of 5%.

MRID 484058-08:

Tick counts were transformed to the natural logarithm of (count + 1) to calculate geometric means. Percent efficacy for the treated group on each day was calculated as 100 * (GMC – GMT)/GMC, where GMC = geometric mean of the control group and GMT = geometric mean of the treated group. Treatments were compared using a t-test for means with poolable variances or for means with unequal variances, as appropriate. Variances were compared using an F-test, and Satterthwaite's Approximation was used to determine the degrees of freedom for the unequal variance tests.

All analyses were performed using SAS v. 9.2, with a significance level of 5%.

MRID 484058-09:

Adulticidal efficacy was based on the geometric means of the tick or flea (count + 1) data. Percent efficacy for each treated group on each day was calculated as 100 * (GMC – GMT)/GMC, where GMC = geometric mean of the control group and GMT = geometric mean of the treated group.

Percent hatch and adult development of flea eggs were transformed to the arcsine of the square root and means of the transformed data were retransformed using the inverse function. When no eggs were collected from a dog on a given day, the percent hatch and development were defined as zero. Percent efficacy was calculated as 100 * (RTMC – RTMT)/RTMC where RTMC = retransformed mean of the control group and RTMT = retransformed mean of the treated group. Descriptive statistics (mean, minimum, maximum, standard deviation, CV%, geometric mean and medium) were calculated for the number of eggs incubated, number of larvae hatched, and number of emerged adults.

Between group comparisons were made using ANOVA with a treatment effect after logarithmic transformation of the tick or flea (count + 1) data. The significance level was 5%.

MRID 484058-11:

Flea counts were transformed to the natural logarithm of (count + 1) to calculate geometric means. Percent efficacy for each treated group on each day was calculated as 100 * (GMC – GMT)/GMC, where GMC = geometric mean of the control group and GMT = geometric mean of the treated group. The transformed data were analyzed using a t-test for means with poolable variances or for means with unequal variances, as appropriate. Variances were compared using the maximum F-test, and Satterthwaite's Approximation was used to determine the degrees of freedom for the unequal variance tests. The treated group was compared to the control group.

All analyses were performed using SAS v. 9.2, with a significance level of 5%.

RESULTS

MRID 484058-06:

Were the raw data included? Yes.

Protocol amendments and deviations: The protocol called for the test material to be applied from the base of the tail to the shoulder blades. In the study, the test material was applied from the shoulder blades to the base of the tail, to be consistent with the label directions.

All the test materials were well tolerated, with no adverse effects noted. Dogs in the TS# 13323 and TS# 13324 groups had significantly ($p<0.01$) lower flea counts at each examination day than dogs in the control group (Table 5). Efficacy for each of the test materials was ≥95% at each count. There was no significant difference ($p>0.05$) between the two test materials.

TABLE 5. Summary of geometric mean flea counts and (percent efficacy)

Day	Control	TS# 13323	TS# 13324
2	77.8	3.0[b] (96.2%)	2.6[b] (96.7%)
9	85.8	0.0[b] (100.0%)	0.0[b] (100.0%)
16	93.1	0.2[b] (99.8%)	0.3[b] (99.7%)
23	90.2	0.2[b] (99.8%)	0.7[b] (99.2%)
30	81.4	0.9[b] (98.9%)	3.5[b] (95.7%)

[b]Significantly different from control ($p<0.01$)
Data from p. 21, MRID 484058-06

The TS# 13323 group had significantly lower tick counts than the control group only on days 9 and 23, with an efficacy ≥97% on those days (Table 6). The TS# 13324 group had significantly lower tick counts from day 9 until test end, with ≥93.8% efficacy on those days. The TS# 13324 group had significantly fewer ticks than the TS# 13323 group at day 30.

TABLE 6. Summary of geometric mean tick counts and (percent efficacy)

Day	Control	TS# 13323	TS# 13324
2	7.1	5.5 (21.7%)	2.7 (61.7%)
9	14.3	0.3[b] (97.6%)	0.0[b] (100.0%)
16	16.8	4.4 (74.0%)	0.4[b] (97.8%)
23	19.1	0.5[b] (97.3%)	0.8[b] (95.6%)
30	31.1	14.5[c] (98.9%)	1.9[b,c] (93.8%)

[b]Significantly different from control ($p<0.01$)
[c]Significant difference between TS#13323 and TS# 13324 ($p<0.05$)
Data from p. 21, MRID 484058-06

All the treated groups had significantly lower percent flea egg hatching than the control group throughout the test (Table 7). At all time points, efficacy was ≥97.8% for TS# 13321, ≥90.3% for TS# 13322, ≥96.4 for TS# 13323, and ≥97.6% for TS# 13324. There was no significance difference between the TS# 13321 and TS# 13322 groups, or between the TS# 13323 and TS# 13324 groups.

All the treated groups had significantly lower percent adult fleas developing from each of the weekly egg collections, compared to the control group. Efficacy was ≥98.9% for TS# 13321,

≥99.6% for TS# 13322, ≥97.3% for TS# 13323, and ≥98.6% for TS# 13324. There was no significance difference between the TS# 13321 and TS# 13322 groups, or between the TS# 13323 and TS# 13324 groups.

TABLE 7. Summary of retransformed[1] mean flea egg percent hatch and percent adult development (and percent efficacy)

Day	Control	TS# 13321	TS# 13322	TS# 13323	TS# 13324
Egg hatch (%)					
5	76.6	1.0[b] (98.8%)	7.4[a] (90.3%)	0.2[b] (99.8%)	0.0[b] (100%)
12	81.1	0.0[b] (100%)	0.0b (100%)	0.0[b] (100%)	0.0[b] (100%)
19	78.2	0.0[b] (100%)	0.0[b] (100%)	0.0[b] (100%)	0.0[b] (100%)
6	86.8	0.3[b] (99.7%)	0.3[b] (99.7%)	2.7[b] (96.9%)	0.0[b] (100%)
33	74.2	1.7[b] (97.8%)	1.5[b] (97.9%)	2.7b (96.4%)	1.8[b] (97.6%)
Adult emergence					
5	73.2	0.4[b] (99.4%)	0.1[b] (99.8%)	0.2[b] (99.8%)	0.0[b] (100%)
12	72.6	0.0[b] (100%)	0.0[b] (100%)	0.0[b] (100%)	0.0[b] (100%)
19	74.7	0.0[b] (100%)	0.0[b] (100%)	0.0b (100%)	0.0[b] (100%)
26	83.7	0.0[b] (100%)	0.0[b] (100%)	2.6[b] (96.9%)	0.0[b] (100%)
33	67.7	0.8[b] (98.9%)	0.3[b] (99.6%)	1.8[b] (97.3%)	0.0[b] (98.6%)

[1]Based on transformation to the arcsine of the square root of the proportion
[a]Signficantly different from control ($p<0.05$)
[b]Significantly different from control ($p<0.01$)
There were no significant differences ($p>0.05$) between groups treated with TS# 13321 and TS# 13322, or between groups treated with TS# 13323 or TS# 13324
Data from p. 22, MRID 484058-06

State if the data were corrected using Abbott's Formula or another applicable formula. Not applicable.

MRID 484058-08:

Were the raw data included? Yes.

Protocol amendments and deviations: None reported.

The test material was well tolerated, with no adverse effects noted. The test material provided >90% control of brown dog ticks throughout the study (Table 8). Efficacy ranged from 92.1% to 97.8% for live ticks, and from 91.1% to 97.1% when moribund ticks were included in the live tick counts.

TABLE 8. Summary of geometric mean tick counts (and percent efficacy)		
Day	**Control**	**TS# 13377**
Live ticks		
9	29.6	0.7[a] (97.9%)
16	26.3	1.9[b] (92.8%)
23	19.5	0.4[b] (97.8%)
30	35.0	2.8[b] (92.1%)
Live + moribund ticks		
9	29.6	1.1[b] (96.2%)
16	26.3	2.2[b] (91.6%)
23	19.5	0.6[b] (97.1%)
30	35.0	3.1[b] (91.1%)

[a]Significantly different from control ($p<0.05$)
[b]Significantly different from control ($p<0.01$)
Data from p. 18, MRID 484058-08

State if the data were corrected using Abbott's Formula or another applicable formula: Not applicable.

MRID 484058-09:

Were the raw data included? Yes.

Protocol amendments and deviations: None reported.

The test materials were well tolerated, with no adverse effects noted. Results of the flea counts are summarized in Table 9, and efficacy of the test materials against adult fleas is summarized in Table 10. Both TS# 13337 and TS#13338 provided >90% efficacy up to day 16, with reduced efficacy afterwards. By day 30, efficacy of TS# 13337 was <19%, and efficacy of TS# 13338 was <42%.

TABLE 9. Arithmetic and geometric mean flea counts						
Day	**Negative control**		**TS# 13337**		**TS# 13338**	
	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean
2	69.3	67.2	3.0	1.4[a]	1.1	0.4[b]
9	75.7	74.6	0.4	0.2[a]	0.0	0.0[b]
16	80.0	78.2	4.0	2.3[a]	7.3	5.3[b]
23	75.0	71.7	23.0	19.9[a]	46.1	41.9[c]
30	76.6	76.0	64.4	61.7[a]	46.1	44.7[b,c]

[a]TS#13337 significantly different ($p<0.05$) from control
[b]TS# 13338 significantly different ($p<0.05$) from control
[c]TS# 13338 significantly different ($p<0.05$) from TS# 13337
Data from p. 9, MRID 484058-09

TABLE 10. Efficacy against fleas based on arithmetic and geometric mean flea counts				
Day	**TS# 13337**		**TS# 13338**	
	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean
2	95.7%	97.9%	98.4%	99.5%
9	99.4%	99.7%	100.0%	100.0%
16	95.0%	97.0%	90.9%	93.2%
23	69.3%	72.2%	38.5%	41.5%
30	15.9%	18.9%	39.7%	41.2%

Data from p. 9, MRID 484058-09

Neither test material was efficacious against the brown dog tick (Tables 11 and 12). The greatest efficacy (65.6%) was provided by TS# 13338 on day 9. By day 30, efficacy of TS# 13337 was <25%, and efficacy of TS# 1338 was <31%.

TABLE 11. Arithmetic and geometric mean tick counts

Day	Negative control		TS# 13337		TS# 13338	
	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean
2	22.6	21.7	13.4	12.6[a]	10.3	9.4[b]
9	27.6	27.2	5.4	4.1[a]	10.4	9.3[b,c]
16	27.6	27.4	15.9	15.8[a]	15.6	14.4[b]
23	29.4	28.6	24.0	23.7	24.4	23.9
30	28.6	28.2	22.0	21.2	20.9	19.5[b]

[a]TS13337 significantly different ($p<0.05$) from control
[b]TS# 13338 significantly different ($p<0.05$) from control
[c]TS# 13338 significantly different ($p<0.05$) from TS# 13337
Data from p. 8, MRID 484058-09

TABLE 12. Efficacy against ticks based on arithmetic and geometric mean tick counts

Day	TS# 13337		TS# 13338	
	Arithmetic mean	Geometric mean	Arithmetic mean	Geometric mean
2	40.5%	42.1%	54.4%	56.6%
9	80.3%	85.0%	62.2%	65.6%
16	42.5%	42.5%	43.5%	47.5%
23	18.4%	17.2%	17.0%	16.3%
30	23.0%	24.8%	27.0%	30.7%

Data from p. 8, MRID 484058-09

Both test materials were effective at preventing flea egg hatch and adult flea emergence (Table 13). TS# 13337 was 100% effective through day 28, and 99.9% effective at day 35. TS# 13338 was 100% effective throughout the test.

TABLE 13. Efficacy against further development of flea eggs

Egg collection day	TS# 13337		TS# 13338	
	Egg hatch	Adult emergence	Egg hatch	Adult emergence
7	100%	100%	100%	100%
14	100%	100%	100%	100%
21	100%	100%	100%	100%
28	100%	100%	100%	100%
35	97.9%	99.9%	100%	100%

Data from p. 8, MRID 484058-09

State if the data were corrected using Abbott's Formula or another applicable formula: Not applicable.

MRID 484058-11:

Were the raw data included? Yes.

Protocol amendments and deviations: Two of the dogs exceeded the protocol upper weight limit of 40 lbs. One dog weighed 46.7 lb and one dog weight 43.0 lb. The protocol specified flea count times of 15 minutes, 30 minutes, 8 hours, and 12 hours after the respective infestations.

There were minor variations in the times the flea counts were conducted. Neither of these deviations would be expected to affect the outcome of the study.

TS# 13396 was effective for short-time kill of adult cat fleas at all time points. Efficacy was 90.0%, 98.9%, 95.3%, and 99.1% at 15 minutes, 30 minutes, 8 hours, and 12 hours, respectively, after infestation (Table 14).

TABLE 14. Summary of geometric mean flea counts and percent efficacy

Time after infestation	Control	TS# 13396	Efficacy	p-value
15 minutes	97.1	9.7[a]	90.0%	0.0070
30 minutes	99.5	1.1[a]	98.9%	0.0005
8 hours	96.1	4.5[a]	95.3%	0.0014
12 hours	95.3	0.9[a]	99.1%	0.0001

[a]Signficantly different from control ($p<0.01$)
Data from p. 18, MRID 484058-11

Study Author's Conclusions

MRID 484058-06:

The study author concluded that TS# 13323 and TS# 13324 were highly effective against fleas, with both initial activity and residual activity above 95% at all time points. Initial control (day 2) of ticks was 21.7% for TS# 13323 and 61.7% for TS# 13324. Residual control of ticks ranged from 53.4% to 97.6% for TS# 13323 and from 93.8% to 100% for TS# 13324 during the study. Efficacy of both test substances for inhibition of egg hatch and adult emergence was excellent (>90%) at all time points.

MRID 484058-08:

The study author concluded that application of TS# 13377 resulted in excellent control (>90%) of ticks for at least 30 days.

MRID 484058-09:

The study author concluded that TS# 13337 and TS# 13338 were <90% effective against ticks. Also, TS# 13337 and TS# 13338 were >90%effective against adult fleas for two weeks, and >97% effective against further development of flea eggs for five weeks.

MRID 484058-11:

The study author concluded that, at two and three days post-treatment, TS# 13396 showed speed of kill efficacy against adult fleas of 90.0%, 98.9%, 95.3%, and 99.1% at 15 minutes, 30 minutes, 8 hours, and 12 hours after infestation, respectively.

Reviewer's Conclusions

MRID 484058-06:

The test results support the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 label claims for control of adult fleas for up to four weeks. The TS# 13323 and TS# 13324 test materials provided >90% control of adult fleas at all time points in the study.

The test results support the Hartz Reference # 134 and Hartz Reference #135 label claims for killing all stages of the flea life cycle. Both TS# 13323 and TS# 13324 were >90% effective against flea egg hatch and adult emergence for up to 33 days. The reviewer notes that TS# 13324 contains a concentration of 0.9% Nylar, compared to 0.5% Nylar in Hartz Reference # 134 and Hartz Reference #135.

The test results do not support the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 label claims for control of brown dog ticks for up to four weeks. Both test materials were <90% effective on test day 2, and the TS# 13323 test material was <90% effective on test day 16, although it was >90% effective for the remainder of the 30-day test.

MRID 484058-08:

This study was conducted to confirm the results reported in MRID 484058-06. The test results support the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 label claims for control of brown dog ticks for up to four weeks. The TS# 13377 test material produced >90% control at all time points up to 30 days. No other organisms were included in the test. The reviewer finds the study to be acceptable.

MRID 484058-09:

The test results do not support the four week claim of control for brown dog ticks on the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 labels. Neither test material TS# 13337 nor TS# 13338 provided the required >90% efficacy at any time point during the study.

The test results also do not support the four week claim on the product labels for control of adult fleas; however, both test materials were >90% effective against adult fleas for the first two weeks of the test.

The reviewer notes that this was the only test in which the dogs were shampooed and rinsed weekly, which probably reduced the effectiveness of the single application of one or more of the active ingredients against adult cat fleas and brown dog ticks over time. The product labels for Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 state that dogs may be bathed 48 hours after product application. The reviewer suggests that a statement that bathing the dog may reduce product effectiveness against ticks and adult fleas be added to the product labels. The reviewer finds this study to be unacceptable for the claimed four-week control of adult cat fleas and brown dog ticks.

The test results support the Hartz Reference #134 and Hartz Reference #135 label claims for killing all stages of the flea life cycle. Both TS# 13337 and TS# 13338 were >97% effective

against flea egg hatch and adult emergence for up to five weeks. The results also support the Hartz Reference #134 and Hartz Reference #135 label claim of waterproof control of flea eggs and larvae. Evidently, shampooing did not reduce effectiveness of the Nylar IGR. The reviewer finds this study to be acceptable for the claim of killing all stages of the flea life cycle and the claim of waterproof control of flea eggs and larvae.

MRID 484058-11:

The test results support the short-term flea control claims on the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 labels. The product was >90.0% effective against fleas at 15 minutes, 98.9% effective at 30 minutes, 95.3% at 8 hours, and 99.1% effective at 12 hours post-treatment. These results meet the label claims of kill within 15 minutes, 95% kill at 8 hours, and 99% kill at 12 hours post-treatment. No other organisms were included in the test. The reviewer finds this study to be acceptable.

Reviewer Recommendations

The reviewer recommends that the Hartz Reference #132, Hartz Reference #134, and Hartz Reference # 135 label claims for four-week control of adult cat fleas and brown dog ticks be accepted. Although the test results reported in MRID 484058-06 did not support the claim for brown dog ticks, the follow-up study (MRID 484058-08) found the test material did meet the required >90% control of ticks for four weeks.

The test results in MRID 484058-09 did not support the label claims for four week control of ticks and adult fleas, but the dogs in that study were bathed weekly, which likely reduced the effectiveness of the test material against adult fleas and ticks. The reviewer recommends that a statement be added to the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 labels indicating that bathing the dog after treatment may reduce the efficacy of the product against ticks and adult fleas. The test results in MRID 484058-09 did support the Hartz Reference #134 and Hartz Reference #135 label claims for waterproof control of flea eggs and larvae, and the reviewer recommends that these claims be accepted.

The reviewer recommends that the Hartz Reference #134 and Hartz Reference #135 label claims for control of flea life cycle be accepted. The test results in MRIDs 484058-06 and 484058-09 confirm these claims.

The reviewer recommends that the Hartz Reference #132, Hartz Reference #134, and Hartz Reference #135 label claims for speed of kill on fleas be accepted. The test results in MRID 484058-11 confirm these claims.