

PRODUCT PERFORMANCE / EFFICACY REVIEW

Mark Suarez, Entomologist - IB



5 DECEMBER 2007

DATE: 5 December 2007

EPA REG. NUMBER: 2517-80
2517-85
2517-90

PRODUCT NAME(S): Sergeant's Cyphenothrin + IGR Squeeze-On for Dogs [2517-80]
Sergeant's Cyphenothrin Squeeze-On for Dogs [2517-85]
Sergeant's Cyphenothrin + Methoprene Squeeze-On for Dogs [2517-90]

REGISTRANT: Sergeant's Pet Care Products, Inc.

PM: George LaRocca, PM13
REVIEWER: Linda DeLuise

DECISION #s.: 381596 [2517-80]
381598 [2517-85]
381595 [2517-90]

DP BARCODE(S): 342540 [2517-80]
342541 [2517-85]
342544 [2517-90]

ACTION: R34

ACTIVE INGREDIENT(S): 129013, Cyphenothrin.....40.0% [2517-80]
129032, Pyriproxyfen.....2.0%
129013, Cyphenothrin.....40.0% [2517-85]
129013, Cyphenothrin.....40.0% [2517-90]
105402, s-Methoprene.....2.3%

TYPE: Wipe-On (Squeeze-On) for Dogs

OPPTS GUIDELINE(S): 810.3300

MRID: 47163701 Submitted GLP? No
47163702 Submitted GLP? No

SITES & PESTS Dogs, Puppies ≥12 weeks Fleas, Ticks, & Mosquitoes

PESTS: Fleas (adult); Fleas (eggs); Fleas (larvae); Ticks; Mosquitoes; Mosquitoes (vector of WNV); Mosquitoes (vector of Heartworm); Deer Ticks (vector of Lyme Disease)

STUDY APPLICATION RATE: Variable (see study summaries)

LABEL APPLICATION RATE: Cyphenothrin [All products]:
>66.14 mg Cyphenothrin per kg dog body mass for dogs <80 lbs

Pyriproxyfen [2517-80]:
>2.5 mg Cyphenothrin per kg dog body weight for dogs <80 lbs

s-Methoprene [2517-90]:
>2.875 mg Cyphenothrin per kg dog body weight for dogs <80 lbs

STUDY SUMMARIES:

MRID 47163701. Sharp, M.; Miller, T. (2007) Efficacy Evaluation of Sergeant's Cyphenothrin Squeeze-On for Dogs Against Fleas (*Ctenocephalides felis*), Ticks (*Rhipicenphalus sanguineus*) and Mosquitoes (*Aedes aegypti* and *Culex quinquefasciatus*) on Dogs. Project Number: MS/105/D. Unpublished study prepared by Sharp Veterinary Research. 39 p.

The data presented in MRID 47163701 were generated from tests of product performance against adult fleas, ticks, and mosquitoes using a 40% cyphenothrin formulation applied as a spot-on to dogs. The minimum application rate for which the product is labeled (0.075 mL cyphenothrin/lb or 66.14 mg Cyphenothrin/kg dog body mass) was exceeded in all cases (0.077 to 0.143 mL cyphenothrin/lb or 68.18 to 125.98 mg cyphenothrin/kg dog mass). In fact only two of 24 animals were treated at a dose rate approaching the minimum label rate. Therefore, the effectiveness of the product at the minimum label application rate can not be determined and the data do not support the desired registration.

Additionally, copies of all raw data sheets are to be included with any data submission. If these data are to be cited in the future, the MRID must be amended to include these data sheets.

MRID 47163702. Sharp, M.; Miller, T. (2007) Efficacy Evaluation of Sergeant's Cyphenothrin Squeeze-On Applied at Minimum Dose Rate Against Adult Cat Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicenphalus sanguineus*/*Dermacentor variabilis*) on Dogs. Project Number: MS/111D. Unpublished study prepared by Vetoquinol N.A. Inc. 34 p.

The data presented in MRID 47163702 were generated from tests of product performance against adult fleas, ticks, and mosquitoes using a 40% cyphenothrin formulation applied as a spot-on to dogs. The product was tested below (0.060 to 0.071 mL cyphenothrin/lb or 53.12 to 62.99 mg cyphenothrin/kg dog mass) the minimum application rate for which the product is

labeled (0.075 mL cyphenothrin/lb or 66.14 mg Cyphenothrin/kg dog body mass) in 5 out of 6 replicates. A sixth replicate were treated at a rate of 67.32 mg AI/kg – marginally higher than the minimum label rate.

The trial tested the performance of the subject formulation against fleas and ticks over the course of an 8 week trial. During the 8 weeks, the animals were infested with fleas and ticks, then treated with the product. The number of fleas and ticks present was recorded at 1, 4, 24, and 48 hours after treatment. Subsequently, the animals were challenged with fleas and ticks (either *D. variabilis* or *R. sanguineus*) weekly, with the number of pests present recorded at 1, 4, 24, and 48 post-infestation. The product provided a reduction in the number of both parasite populations of >90% for 56 days.

Copies of the raw data sheets were not provided in the MRIDs.

ENTOMOLOGIST'S COMMENTS AND RECOMMENDATIONS:

The data provided in MRID 47163701 do not support the desired registration due to an exceedance of the minimum label rate. The raw data sheets were not included with the original submission. The MRID must be amended to include said information within 6 months, if the data are to be used in the future.

The data provided in MRID 47163702 support the claims that the product is efficacious against adult fleas and ticks for up to 8 weeks. This was supported by weekly re-infestation of test animals with fleas and alternating species of ticks (i.e., *Dermacentor variabilis* and *Rhipicephalus sanguineus*) over the course of an 8 week study. Therefore, claims that the product is efficacious for up to 8 weeks against adult fleas and/or ticks are acceptable. The raw data sheets were not included with the original submission. The MRID must be amended to include said information within 6 months.

Outstanding data requirements remain for the efficacy of cypermethrin against mosquitoes, the efficacy and duration of effectiveness of s-Methoprene as a flea ovicidal, and the length of effectiveness of pyriproxyfen (Nylar®) against flea eggs and larvae. The data provided in the submission fail to satisfy these requirements. Therefore, the registrant must submit the requisite data or remove the unsupported claims. The registrant has committed to satisfy these data requirements and will work with the Agency to provide said data within the constraints imposed in the original notice of registrations.

1) General Labeling issues follow:

- a) All label claims regarding effectiveness up to 8 weeks/2 months (e.g., works, kills, repels, prevents, x week/y month dose) must be specific to adult fleas and ticks. Also,
 - i) EPA Reg. No. 2517-80 may bear claims that it Kills [flea eggs][flea larvae] for up to 63 day/9 weeks;
 - ii) EPA Reg. No. 2517-90 may bear claims Kills [flea eggs] for up to [24 days][4 weeks][1 month];
 - iii) EPA Reg. No. 2517-85 may bear no claims against flea eggs or larvae or references to “breaking the lifecycle”.
- b) Claims against mosquitoes must be explicitly stated as “for up to 28 days/4 weeks/1 month” for all labels.

2) Specific issues pertaining to the proposed labeling are presented below by product number:

a) EPA Reg. No. 2517-80

i) Remove the following marketing statements:

- (1) Kills [and Repels] 100% of [fleas] [and] [ticks] on Day 30
- (2) Long Lasting
- (3) Fast Acting
- (4) Kills [and Repels] 100% of [fleas] [and] [ticks] in as little as 1 hour
- (5) Kills[and repels] 93-100% of [fleas] [and] [ticks] for up to 8 weeks
- (6) Kills [and repels] 96.5%-100% of [fleas] [and] [ticks] for up to 7 weeks
- (7) Kills [and repels] 98-100% of [fleas] [and] [ticks] for [5] [6] weeks
- (8) Kills [and repels] up to 100% [fleas] [and ticks] for up to [30 days] [1 month]
[4weeks] [5 weeks] [6 weeks] [7 weeks] [8 weeks] [2 months]
- (9) [Kills [and Repels]
- (10) Fleas [in as little as 1 hour]
- (11) Ticks [in as little as [1] [3] hours]
- (12) [Mosquitoes]
- (13) [Kills for [9 weeks] [63 days]]
- (14) [flea eggs]
- (15) [flea larvae]
- (16) [(ICON Showing [4] [5] [6] [7] [8] Week Protection)]
- (17) [Nothing works faster, Nothing lasts longer]
- (18) [Outlasts, Outperforms, Outprotects]
- (19) [Speed-of-kill that lasts!]

ii) Revise the following statements as indicated:

- (1) *Up to* [4] [5][6] [7] [8] Week [Flea & Tick Treatment]*
- (2) *Up to* [4] [5][6] [7] [8] Week [Flea and Tick Control]*
- (3) [Prevents ticks from attaching and feeding in as little as [+ 3 hours] after application]
- (4) [Kills for *up to* [9 weeks] [63 days]]
 - [flea eggs]
 - [flea larvae]
- (5) *Up to* [4 Week Dose!][5 week] [6week] [7 week] [8 week] Dose!
- (6) *Up to* [1 Month Dose!] [2 month dose]
- (7) *Up to* [4] [5] [6] [7] [8]Week flea and tick Protection!]
- (8) [• Kills Flea Eggs & Flea Larvae for ~~more than~~ *up to* [63 days], [9 weeks]!]*
- (9) *Up to* [• [4] [5] [6] [7] [8] week Flea and Tick Treatment!]
- (10) *Up to* [One] [2] Month Flea and Tick Treatment]
- (11) [Frequency of Application: When used monthly, product ~~completely~~ breaks the flea life cycle and controls flea, tick and mosquito infestations. Research demonstrates that [product brand name] kills adult fleas and ticks for up to 8 weeks, also prevents development of ~~all~~ *flea egg and larval* stages for up to nine weeks. A once monthly application is recommended where mosquito control is needed.]
- (12) [Sergeant's Squeeze-On Flea & Tick Control with Nylar® Insect Growth Regulator prevents eggs from fleas on treated dogs from developing into biting

adults for *up to* 63 days.] [7 weeks]

b) EPA Reg. No. 2517-85

i) Remove the following marketing statements:

- (1) [Kills [and Repels] 100% of [fleas] [and] [ticks] on Day 30]
- (2) [Long Lasting]
- (3) [Fast Acting]
- (4) [Kills [and Repels] 100% of [fleas [and] [ticks] in as little as 1 hour]
- (5) [Kills [and repels] 93-100% of [fleas] [and] [ticks] for up to 8 weeks]
- (6) [Kills [and repels] 96.5% - 100% of [fleas] [and] [ticks] for up to 7 weeks]
- (7) [Kills [and repels] 98%-100% of [fleas] [and] [ticks] for [5] [6] weeks]
- (8) [Kills [and repels] up to 100% of [fleas] [and ticks] for up to [30 days [1 month] [4 weeks] [5 weeks] [6 weeks] [7 weeks] [8 weeks] [2 months]]]
- (9) [Kills [& Repels] fleas and ticks for up to [4] [5] [6] [7] [8] weeks!]
- (10) [Reapply once every [4] [5] [6] [7] [8] weeks.] [Reapply monthly]
- (11) [Nothing works fast, Nothing lasts longer]
- (12) [Outlasts, Outperforms, Outprotects]
- (13) [Speed-of-kill that lasts]

ii) Revise the following marketing statements as indicated:

- (1) [Up to [4] [5] [6] [7] [8] week Flea and Tick Control] *up to* [4] [5] [6] [7] [8] week [monthly] protection]
- (2) *Up to* [[4] [5] [6] [7] [8] week dose]
- (3) *Up to* [[1] [2] Month Dose!]
- (4) *Up to* [[4] [5] [6] [7] [8] week flea and tick protection]
- (5) [Prevents ticks for attaching and feeding in as little as [~~1~~hour] [3 hours] after application]
- (6) [Kills [and Repels]
 - [Fleas [in as little as 1 hour]
 - [Ticks [in as little as [~~1~~] [3] hour[s]
 - Mosquitoes
- (7) [Prevents ticks from attaching and feeding in as little as [~~1~~][3] hour[s] after application]
- (8) [Up to [4] [5] [6] [7] [8] week Flea and Tick Control] *up to* [4] [5] [6] [7] [8] week [monthly] protection]
- (9) *Up to* [One] [1] [Two] [2] Month Flea and Tick Treatment
- (10) [Kills [and Repels] mosquitoes *for up to* [28 days][4 weeks][1 month]]
- (11) [Frequency of Application: When used monthly, the product [controls] [~~eliminates~~] [protects you pet from] flea, tick and mosquito infestations. Research demonstrates that {product brand name} kills adult fleas and ticks for up to 8 weeks. A once monthly application is recommended where mosquito control is needed.]

c) EPA Reg. No. 2517-90

i) Remove the following marketing statements:

- (1) [• [Five] [5] Way Protection [Kills fleas, ticks, mosquitoes, flea eggs & flea

- larvae]]*
- (2) [• Five Way Protection! Kills ticks, mosquitoes fleas, flea eggs & flea larvae]*
 - (3) [• 5 Way Protection! Kills ticks, mosquitoes, fleas, flea eggs & flea larvae]*
 - (4) [(ICON Showing [4] [5] [6] [7] [8] Week Protection)]
 - (5) [Long Lasting]
 - (6) [Fast Acting]
 - (7) [Kills [and Repels 100% of [fleas] [and] [ticks] in as little as 1 hour]
 - (8) [Kills [and repels] 93-100% of [fleas] [and] [ticks] for up to 8 weeks]
 - (9) [Kills [and repels] 96.5% - 100% of [fleas] [and] [ticks] for up to 7 weeks]
 - (10) [Kills [and repels] 98%-100% of [fleas] [and] [ticks] for [5] [6] weeks]
 - (11) [Kills [and repels] up to 100% of [fleas] [and ticks] for up to [30 days [1 month] [4 weeks] [5 weeks] [6 weeks] [7 weeks] [8 weeks] [2 months]
 - (12) [Nothing works faster, Nothing lasts longer]
 - (13) [100% Guaranteed!]
 - (14) [Outlasts, Outperforms, Outprotects]
 - (15) [Speed-of-kill that lasts]

ii) Revise the following statements as indicated:

- (1) [Sergeant's Squeeze-On Flea & Tick Control with methoprene is an effective and easy to use product.] [Sergeant's Squeeze-On Flea & Tick Control with methoprene prevents eggs from fleas on treated dogs from developing into biting adults for *up to* 30 days.] [As with all flea and tick control products, Sergeant's Squeeze-On Flea and Tick Control with methoprene should be used as part of a program aimed at reducing flea populations in the dog's environment (bedding, carpets, kennel, yard).] [Consult your retailer for program recommendations.]
- (2) *Up to* [• [Four [4] [5] [6] [7] [8] Week] [Flea and Tick Control]]*
- (3) *Up to* [•[4] [5] [6] [7] [8] Week Protection against fleas and ticks!]
- (4) [• [4] [5] [6] [7] [8] week][[1][2]month] Flea and Tick Treatment!]*
- (5) [• Kills [& Repels] [for [4] [5] [6] [7] [8] Weeks] Fleas [in as little as 1 hour], and ticks [in as little as [4][3] hour[s]] [for up to [4] [5] [6] [7] [8] weeks]]
- (6) *Up to* [[4] [5] [6] [7] [8] week dose]
- (7) [Frequency of Application: When used monthly, the product ~~completely~~ breaks the flea life cycle and controls flea, tick and mosquito infestations. Research demonstrates that [product brand name] kills adult fleas and ticks for up to 8 weeks, and also prevents development of ~~all~~ flea *egg and larval* stages for up to four weeks. A once monthly application is recommended where mosquito control is needed.]

Enclosure

002517-00080-00085-00090-4December2007revision-ER