Efficacy Review

Date: September 28, 2010

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Products: L899 INSECTICIDE

EPA Reg. #: 72642-O

A.I.'s: Spinetoram (39.6%)

Decision #s: 422561

DP #s: 371967

Submission: R270, New Use, Indoor, Includes RD Efficacy Review

MRIDs: Submitted: 47899914, 47899915, 47899916, 47920106

GLP: Yes, with some exceptions

MRID 47899914

Title: Efficacy Evaluation of Three Different Topical Dose Rates of L899 Insecticide Against Flea Infestations on Cats

Guideline: OPPTS 810.3300

Materials and Methods: A laboratory study was conducted to assess the efficacy of a new spinetoram spot-on product (39.6% w/w) at various application rates against fleas compared against a placebo spot-on treatment that was the identical formulation minus the active ingredient. 6 cats (3 male, 3 female each) were placed in one of 5 treatment groups (3 rates of spinetoram spot-on, placebo spot-on, untreated control). Cats were prequalified for flea retention by infestation of 100 fleas 14 days before treatment, from which 30 cats were selected. On treatment day, the first 4 groups received treatment according to proposed label directions, using a syringe to dispense the product in one spot on the back of each cat's neck. Hand counts for live fleas were conducted at 12 hours post-treatment and comb counts were conducted on day 2. Cats were reinfested with fleas (along each cat's back) on days 7, 14, 21, 28, 35, and 42, with comb counts for fleas conducted 48 hours after each reinfestation. Fleas were scored as live,

dead, or moribund and percent efficacy was calculated using Abbott's formula. Cat health was monitored.

Study Summary of the Results:

1. 97-100% flea efficacy was observed from 48 hours after treatment through 37 days after treatment for all rates of the spinetoram spot-on product (lowest was 0.3 mL)

Entomologist's Observations/Discussion:

This submitted data is adequate to support a controls claim for up to one month, four weeks, or 37 days for fleas on treated cats, and also supports a one month re-treatment interval for a dosage of 0.3 mL product or higher.

MRID 47899915 (non-GLP)

Title: Safety and Efficacy Evaluation of L8999 Insecticide Against Flea Infestations on Cats

Guideline: OPPTS 810.3300

Materials and Methods: A laboratory study was conducted to assess the efficacy of spinetoram spot-on products at various application rates against fleas compared against a placebo spot-on treatment that was the identical formulation minus the active ingredient. 4 cats were placed in one of treatment groups (control, positive control, 4 spinetoram groups, and one 6X group [for safety data only]). Some of the rates applied were above what is being proposed in the current product application submitted. Cats were prequalified for flea retention by infestation of fleas 7days before treatment, from which 28 cats were selected. On treatment day, treated cats received treatment using a syringe to dispense the product in one spot on the back of each cat's neck. A count for live fleas were conducted at 24 hours post-treatment and comb counts were conducted on day 2. Cats were reinfested with fleas (along each cat's back) on days 7, 14, 21, 28, 35, 42, 49, 56, and 63 with comb counts for fleas conducted 48 hours after each reinfestation. Percent efficacy was calculated using Abbott's formula. Cat health was monitored.

Study Summary of the Results:

2. 96-100% flea efficacy was observed for both the positive controls and the experimental spinetoram dosages, which equate to similar dosing as is proposed on the label (1.0 mL of 20% ai, 0.5 mL of 42% ai—label dosing is 0.55 mL of 39.6% ai).

Entomologist's Observations/Discussion:

This submitted data is adequate to support a controls claim for up to two months, eight weeks, or 65 days for fleas on treated cats, and also supports the proposed one month re-treatment interval for the proposed dosage of 0.55 mL of product.

MRID 47899916

Title: Speed of Kill Evaluation of L899 Insecticide Against Cat Fleas at Various Time Points During the Efficacy Period

Guideline: OPPTS 810.3300

Materials and Methods: A laboratory study was conducted to assess the efficacy and speed of kill of a new spinetoram spot-on product (39.6% w/w) against fleas compared against an untreated control group. 6 cats (3 male, 3 female each) were placed in one of 6 treatment groups (5 spinetoram treatments with evaluations at different times post-treatment, and an untreated control group). Cats were prequalified for flea retention by infestation of 100 fleas 8 days before treatment, from which 36 cats were selected. On treatment day, the treated groups received treatment according to proposed label directions, at the base of the skull. Infestation was made to all cats on day zero. Comb counts were conducted by treatment for live fleas at 1, 4, 8, 12, and 24 hours after treatment. Percent efficacy was calculated using Abbott's formula. Cat health was monitored.

Study Summary of the Results:

3. 94.3% efficacy was observed at 8 hours after treatment. Efficacy at 1 and 4 hours was 63% or below. Efficacy at 12-24 hours after treatment was 98-100%.

Entomologist's Observations/Discussion:

This submitted data is adequate to support claims that the product kills fleas within 8 hours of treatment, or "kills fleas within hours." Knockdown, fast kill, quick kill, or kills on contact claims are not supported.

MRID 47920106

Title: Knockdown and Speed of Kill Effectiveness of L899 Insecticide Administered to Cats for the Treatment of Adult Cat Fleas, and its Residual Efficacy.

Guideline: OPPTS 810.3300

Materials and Methods: A laboratory study was conducted to assess the speed of kill and residual efficacy of 2 rates of a spinetoram spot-on product (39.6% w/w) against fleas compared against an untreated control group. 21 groups (3 cats per group) were placed in one of 3 treatment groups (2 spinetoram treatments with evaluations at different rates, and an untreated control group). Cats were prequalified for flea retention by infestation of 100 fleas 14 days before treatment, from which 63 cats were selected. On treatment day, the treated groups received treatment according to proposed label directions, at the base of the skull. Infestation

was made to all cats on day zero. Speed of kill was assessed by comb counts for live fleas at 0.5, 1, 4, 8, 12, and 24 hours after treatment. Residual flea control was determined approximately 48 hours after infestations on test days 8, 15, 22, 29, 36, 43, and 50. Percent efficacy was calculated using Abbott's formula. Cat health was monitored.

Study Summary of the Results:

4. Adequate efficacy was not observed within 24 hours for the 0.5 mL product application rate. Efficacy was 100% at 24 hours for the 0.7 mL rate, but this rate is above the proposed label application rate, so it is not valid to support any claims.
5. Residual efficacy exceeded 99% for both rates through 50 days after treatment.

Entomologist's Observations/Discussion:

This submitted data is adequate to support controls claims for up to 50 days for applications of the product at 0.5 mL or greater to cats. No speed of kill claims are supported by this data.

Overall Review of Label Claims and Directions:

Based upon submitted efficacy data, control claims are supported for fleas for up to 2 months (or 8 weeks) and support a 30 day re-treatment interval, using a rate of 0.5 mL product per cat or greater. The data is also adequate to support claims that the product kills fleas within 8 hours of treatment, or "kills fleas within hours." However, because rapid short term knockdown was not demonstrated, claims such as knockdown, fast kill, quick kill, or kills on contact are not supported. Claims that the product "starts working" quickly, on contact, etc. are acceptable, because they do not imply immediate efficacy, only that the product is starting to work.

Line by Line Review of Label Claims:

(0.55 mL dispenser)

A once a month topical solution for the prevention and treatment of flea infestations for cats and kittens eight weeks of age (and older): Acceptable.

L899 INSECTICIDE kills adult fleas before they lay eggs and breaks the flea life cycle: The claim of breaking the flea life cycle is typically associated with products that kill flea eggs and larvae, such as IGR products. Because there is no data for efficacy against eggs and larvae the 'breaks the flea life cycle claim' must be deleted. However, the claim "kills adult fleas before they lay eggs" is acceptable.

L899 INSECTICIDE starts working in 30 minutes (on contact) and research has shown it can remain effective for up to 10 (7, 8, 9) weeks: 9 and 10 must be deleted. The control claim is valid for up to 8 weeks.

Optional Marketing Claims Related to Efficacy:

Fast-Acting: Unacceptable, as "fast" is too subjective and there is no data to demonstrate quick knockdown, such as would be seen with a pyrethroid—a claim of 'kills within hours' would be acceptable

Long-Lasting: Unacceptable, as this is also subjective. The controls claim associated with the approved duration up to 8 weeks is acceptable.

For the prevention and treatment of flea infestations [*Ctenocephalides felis*] on cats (and kittens 8 weeks of age or older): Acceptable

Kills fleas, Kills fleas on cats within 8 hours: Acceptable

Starts killing fleas in 30 minutes, Starts killing fleas quickly, Starts working in 30 minutes: Acceptable

Starts killing fleas on contact: Acceptable

Kills fleas which may cause flea allergy dermatitis (FAD): Acceptable

Kills fleas and may reduce the incidence of FAD: Unacceptable—the product claim may only address the insect efficacy itself, as listed above—no direct claims against FAD are permitted, as this is an implied medicinal claim.

Kills fleas before they lay eggs: Acceptable

One treatment prevents further flea infestations through 9 (6, 7, 8) weeks, "remains effective", "kills fleas and prevents reinfestation for up to 10 (7, 8, 9) weeks": delete 10 and 9. Claims are acceptable for up to 8 weeks.

Provides complete flea control for a full month (30 days, 4 weeks, through 4 weeks, over 4 weeks): Acceptable

One application provides 100% flea control from 24 hours through 50 (37) days: Acceptable

Waterproof: Unacceptable, as no data was submitted to demonstrate the product remains effective after animal bathing, immersion in water, or exposure to rain.

Remains effective after exposure to sunlight: Unacceptable, as no data was submitted to demonstrate photostability, and this is an implied enhanced efficacy claim.

Spinetoram, the active ingredient in L899 Insecticide, is photostable (stable after UV exposure, stable after exposure to sunlight): Unacceptable, as no data was submitted to demonstrate photostability, and this is an implied enhanced efficacy claim.

(Regular use) Breaks the flea life-cycle, Breaks the flea life-cycle by killing the adult flea (before they lay eggs: Again, the claim of breaking the flea life cycle is typically associated with products that kill flea eggs and larvae, such as IGR products. Because there is no data for efficacy against eggs and larvae, the 'breaks the flea life cycle claim' must be deleted. However, the claim "kills adult fleas before they lay eggs" is acceptable.

Protects cats and kittens from fleas that may carry and transmit *Rikettsia felis* and *Rikettsia typhi*, *Francisella tularensis*: Acceptable

Kills (protects cats and kittens from) fleas that may carry and transmit diseases such as bartonellosis, tapeworm, and tularemia: "diseases such as" is unacceptable, because it implies an open-ended list of diseases.