Efficacy Review

Date: April 23, 2010

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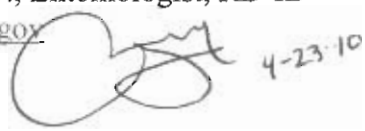

Risk Manager Rev.: Kevin Sweeney

Products: Etofenprox/Nylar Spot-On Flea and Tick for Dogs and Puppies

EPA Reg. #: 2517-RGG

A.I.'s: Etofenprox (55.0%), Pyriproxyfen (2.2%)

Decision #: 420097

DP #: 376747

Submission: Rebuttal, correspondence

MRIDs: None

GLP: No

Summary of Agency's previous product performance review(s):

1. Various studies were submitted in support of a pet product with a retreatment interval of 30 days, intended to protect small dogs from fleas and ticks. The data submitted did not support this claim, because at the appropriate dosages (which match the label dosages), efficacy was only demonstrated for 2-3 weeks for fleas and ticks, with some variability between studies.
2. Ultimately, the underlying conclusion of the data is that a 250 mg/kg dosage is required to provide adequate protection against fleas and ticks. For the most part, dosages under this threshold failed to offer adequate protection throughout the 30 day retreatment interval
3. Claims against black legged ticks (deer ticks), *Ixodes scapularis* were only supported by data going out to 3 days after treatment.
4. Claims against mosquitoes were not supported as the submitted study treated dogs at dosages exceeding those instructed on the product label.
5. Claims against flea eggs/larvae were not supported by any submitted data for pyriproxyfen.

Summary of Registrant submission/rebuttal:

1. For flea and tick data all data from dog studies was pooled and re-analyzed. When dogs that received treatments above the proposed label dose (i.e., >2.0 mL per animal) were eliminated from the analysis, flea efficacy was demonstrated from 9-29 days, with a mean protection time of 20 days. Out of 18 dogs, 11 were adequately protected for 16 days or less. For tick efficacy, the mean protection time was 26 days. Out of 18 dogs, 10 were protected for 23 days or less.
2. For mosquitoes, the registrant stated that only small dogs were used (hence, biasing the dosage toward dogs with a higher rate of ai/kg) because the available Gerberg type mosquito cages were not large enough to accommodate dogs of larger size. The registrant cites previous reviews where similar data was used to support a similar claim, including dogs over 60 lbs. Finally, while they concede that a controls or kills claim is not supported, they propose to retain a claim of repellency/prevention of blood feeding by female mosquitoes.
3. For black legged ticks, the registrant cites a previous protocol that was used to support a 30 day claim on another label, and proposes a retention of an open-ended controls claim for black legged ticks, since no explicit '30 day' claim is being proposed.
4. For the pyriproxyfen/IGR claims (i.e., kills flea larvae, eggs, breaks flea life cycle), the registrant cites previously submitted data that supported a similar claim on a product containing a smaller nominal concentration of pyriproxyfen a.i. than the submitted product.

Entomologist's Observations/Discussion:

1. The registrant's ultimate conclusions after re-anaylsis do not substantially differ from the conclusion reached in the previous review. At a 2.0 mL dose, efficacy against fleas is supported for 2 weeks and ticks for 3 weeks. Because this product's use directions indicate retreatment on a 30 day interval, the implied duration for all control claims should be 30 days. In order to support a 30 day claim, the registrant would have to increase the dosage applied, based on the data submitted previously, which indicate that a dose of approximately 250mg/kg is necessary to provide adequate 30 day control of both pests.
2. The availability of mosquito cages is a consideration that should be taken when designing efficacy studies. A number of much larger mosquito cages are available for conducting these types of mosquito exposure studies, as the Agency has reviewed data where significantly larger dogs were used for similar studies. Prior acceptance by the Agency of inadequate data to support such claims is not an adequate justification to repeat the same mistake again in this instance.
3. Open-ended controls claims are typically not allowed on any pesticide product with claims against pests of public health importance. Any claim of residual control must be qualified by an appropriate duration of control that is supported by the submitted/cited data. In the case of a pet spot on, the retreatment interval is considered an implicit duration of control claim. Consumers buying this product, and treating their pets on a 30 day retreatment interval will expect the product to adequately protect their pets for that interval of time. Therefore, data demonstrating control of black legged ticks for 30 days would be required to support a controls claim on this pet product. Since the submitted study was terminated at 3 days after treatment, it does not support such a claim.

Furthermore, as with point number 2, prior acceptance by the Agency of inadequate data to support such claims is not an adequate justification to repeat the same mistake again in this instance.

4. The dose-titration study cited (MRID 46346601) submitted in support of a similar IGR claims on another product and was found to be acceptable. This study supports IGR claims (i.e., kills/controls flea eggs and larvae, breaks the flea life cycle, etc.).

Entomologist's Label Recommendations:

1. Placement of 2 or 3 week claims on the label (for fleas and ticks) would be contradictory to the reapplication directions for 30 days. For such pet products, a 30 day retreatment interval implies a time duration for control of listed pets. In this case, efficacy considerations may be in conflict with animal safety. This labeling decision is deferred to the Risk Manager Reviewer and the Product Manager.
2. Claims against Mosquitoes are not supported for the application rate of 2.0 mL proposed on the current label. The dosage would have to be raised to support this claim, and the claim would only be for repellence/suppression of mosquito blood feeding. These claims must be removed from the product label.
3. Claims against black legged ticks, deer ticks, *Ixodes scapularis*, or ticks that may carry/transmit Lyme Disease are not supported and must be removed from the label.
4. While IGR claims are supported against flea eggs/larvae, the acceptance of this claim is contingent upon whether or not any general flea claims will be allowed at all, per point number 1. This labeling decision is deferred to the Risk Manager Reviewer and the Product Manager.