

US EPA ARCHIVE DOCUMENT

**EFFICACY REVIEW
BY KEVIN J. SWEENEY, ENTOMOLOGIST**

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1/18/06

Date: Revised on January 18, 2006

Team Reviewer: Bonaventure Akinlosutu

EPA Reg. No. 2724-LNU

Registrant: Wellmark International

Product Manager: George LaRocca, PM13

Dec # 355865

DP#: 316838

Product Name: RF2004 (CCSO)

Active ingredient: 40% etofenprox and 3.6% s-methoprene

Formulation: RTU cat spot-on

Dose and application rate: 1.0 ml on cats under 5 lbs and 2.0 ml on cats 5 lbs or more.

Sites: cats

Pests: fleas, ticks and mosquitoes

OPPTS Guideline: 810.3300

GLP? Yes as indicated below.

Request: Evaluate efficacy data submitted in support of cat spot-on product performance claims. Efficacy data were not cited.

Study Submitted:

- MRID 46513410** Summary Report on RF2004 (CCSO) Development (non-GLP)
- MRID 46513411** GLP Efficacy Against Adult Cat Fleas of Formulation RF2004 (CCSO) (GLP)
- MRID 46513412** Efficacy Against cat Fleas of a RF2004(CCSO) Formulation.(non-GLP)
- MRID 46513413** Efficacy Comparison Against Adult Cat Fleas of Sergeant's Gold Squeeze-On and a Variation of RF2004 (CCSO). (Non-GLP)
- MRID 46513414** Efficacy Comparison Against Adult Cat Fleas of a Variation of RF2004 (CCSO) when Cats are Kept in Larger Enclosures. (non-GLP)
- MRID 46513415** GLP Repellency and Efficacy Against Adult Mosquitoes and Ticks on cats of

Formulation RF2-004 (CCSO) (GLP).

Summary of the Results from the Submitted Studies

The submitted data included non-GLP and GLP efficacy studies where in-vivo and in-vitro data were collected. The target dose of etofenprox was 231.1 mg/kg of cat. The effective product application rates were 1.0 to 3.0 ml per animal depending on the weight of the cat. The following table summarizes the submitted data:

Pest	Method	Days of 90% or greater control	Etofenprox dose delivered per cat	Product Application Volume per Cat
Mosquitoes (Aedes and Culex spp.)	Caged in-vivo	18	400mg etofenprox per cat weighing under 9 lbs. (100mg/kg or more) and 600 mg etofenprox per cat weighing 9 lbs or more (150 mg or less)	1.0 – 1.5 ml (0.9941 g and 1.49115 g)
Black-legged tick	in-vitro with treated hair	100% at day 7 89% at day 32	Same as for mosquitoes	Same as for mosquitoes
American dog tick	Caged in-vivo	11 days	Same as for mosquitoes	Same as for mosquitoes
Adult Flea	in-vivo	28 days --caged-- 21 days --caged-- 16 days --caged-- 16 days --caged-- 23 days penned -	205 mg/kg 108 - 129 mg/kg 110 mg/kg 266 mg/kg of etofenprox without product carrier 266 mg/kg of etofenprox without product carrier	1.5 – 3.0 ml 1.0 – 2.0 ml 1.0 – 1.5 ml

1. The dose for this study was expressed in terms of volume and the total number of grams applied per cat instead of being stated as mg of etofenprox per kg of cat. The values shown in the table are approximate calculations made by the EPA from the data.
2. Based on the density of the formulation and concentration of the active ingredient, 1 ml of the formulation delivers 397mg of etofenprox. 2.0 ml of formulation delivers 794 mg

of etofenprox. If the higher dose is reduced to 1.8 ml, the amount of etofenprox delivered would equal 714 mg.

3. In the study, half of the cats weighed 5-9 lbs (2.27 kg – 4.09 kg) and the other half weighed 9 to 17 lbs (4.09 kg – 7.73 kg). This should have resulted in an etofenprox dose range in the lower weight group of 176.6 mg/kg – 97.7 mg/kg and in the higher weight group of 146.6 mg/kg – 77.61 mg/kg. Note that no cats below 5 lbs were evaluated.
4. The average dose rate in the study groups was not stated. In the study tables summarizing the data for mosquito and tick testing there were 5 cats in each group. In the lower weight group the average weight was 7.8 lbs. or 3.54 kg yielding an average dose of etofenprox of $400\text{mg}/3.54\text{ kg} = 112.99\text{ mg/kg}$ of cat. In the higher weight group the average weight was 9.98 lbs. or 4.53 kg yielding an average dose of $600\text{mg}/4.53\text{kg} = 132.54\text{ mg/kg}$ of cat. Note that both these values are well below the target dose of 231 mg etofenprox /kg of cat. The 17 lbs cat was not listed in the results.
5. These data show that when cats are dosed at up to 132.54 mg of etofenprox/kg of cat the product provides:
 - a. only 18 days of repellency protection against mosquitoes based on blood-feeding success of questing female mosquitoes exposed to cats;
 - b. 11 days of control against the American dog tick exposed to cats; and
 - c. in the in-vitro testing with Ixodes sp. (black-legged ticks) exposed to treated cat hair (fur) 100% control at 24 hours post-exposure on day 7, 50% control at 24 hours post-exposure on day 32 and 89% at 48 hours post-exposure on day 32. To achieve a higher degree of efficacy more product is required per animal.
6. The registrant claims that the carrier in the formulation is tied to the residual efficacy of the product. Tests were conducted with and without the carrier and the carrier effect appears significant. Comparative testing also was done with the registered Sergeant's product formulation containing 55% etofenprox. The subject product performed better than the registered product in these studies. Registrant claims it is due to the carrier but these results are not meaningful to the subject label claims.
7. For control of flea larva and eggs, at least 1.0 ml of product is required per animal as this is the lowest dose rate stated on 2724-488, a product with the same % of pyriproxifen.

Entomologist's Recommendations

1. At 1.0 ml per cat, the subject product will deliver 397 mg of etofenprox equivalent to a dose of $(397\text{ mg}/0.45\text{kg} = 882\text{ mg/kg})$ 882mg/kg when applied to a 1 lb cat and $(397\text{ mg}/2.23\text{ kg} = 178\text{mg/kg})$ 178 mg/kg when applied to a 4.9 lbs. cat.
2. At 2.0 ml/cat, the subject product will deliver $(714\text{mg}/2.27\text{ kg} = 314\text{ mg/kg})$ 314mg/kg to a 5 lbs cat and 157 mg/kg to a 10 lbs cat. For a 15 lbs cat, the dose would equal 104 mg/kg. NOTE: as a result flea control for cats over 10 lbs is likely to only be 3 weeks

based on the data showing that 205 mg/kg was necessary to achieve 28 day flea control.

3. The submitted efficacy testing for the subject product when applied according to draft label directions supports the following claims for mosquitoes: Repels mosquitoes for up to 18 days. From the draft label the following mosquito claims are acceptable: "Direct on-animal protection for mosquitoes." Remove West Nile virus claims.
4. The submitted efficacy testing for the subject product when applied according to draft label directions supports label claims for **black-legged ticks/deer ticks only** of up to one-month. The label should be revised and refer to these ticks only. Lyme disease claims are acceptable. Rocky Mountain Spotted fever claims should be removed.
5. The submitted efficacy testing for the subject product when applied according to draft label directions supports the label claims for flea control up to one-month.
6. The reapplication interval of once per month supports the flea and black-legged tick claims only. Mosquito claims must be reduced to 18 days.
7. The acceptance of the above claims is based on the dose rates used in these studies and on the revised labeling. The 1.8 ml/animal dose is supported as discussed above.