

# Efficacy of a topically applied formulation of metaflumizone on cats against the adult cat flea, flea egg production and hatch, and adult flea emergence

## Abstract

This study was undertaken to evaluate the efficacy of metaflumizone applied to cats in a spot-on formulation (ProMeris® for Cats, Fort Dodge Animal Health) against adult fleas, flea egg production and hatch, and the development of fleas from eggs to adults. 8 male and 8 female adult domestic shorthair cats were randomly assigned to either serve as non-treated controls or were treated topically with a minimum of 40 mg/kg metaflumizone in single spot on Day 0. On Days -2, 7, 14, 21, 28, 35, 42, 49 and 56, each cat was infested with approximately 100 unfed cat fleas, *Ctenocephalides felis felis*. On Days 1, 2, and 3, and at 48 and 72 hours after each post-treatment reinfestation, flea eggs were collected and counted. At approximately 72 hours after treatment or infestation, each cat was combed to remove and count live fleas. Egg viability was determined by examining hatched eggs after 5 days and adult emergence was determined 28 days after egg collection. Metaflumizone provided ≥99.6% efficacy against adult fleas from Day 3 to Day 45 following a single application. Following treatment, egg production fell by 51.6% within 24 hours and 99.2% within 48 hours. Following subsequent weekly infestations egg production from treated cats was negligible out to Day 38, with ≥99.5% reduction relative to nontreated cats. Where there were eggs to evaluate, metaflumizone treatment did not have any apparent effect on the hatching of eggs or on the development and emergence of adult fleas from the eggs produced by fleas from treated animals.

## 1. Materials and Methods

### 1.1. Animals

On Day -6, 19 purpose bred domestic shorthair cats were infested with approximately 100 *C. felis*. On Day -4, flea counts were conducted to assess the ability of cats to maintain infestations. After counting, fleas were removed by combing each cat thoroughly for 10-20 min. The 16 cats (>6 month old, 2.6 to 4.8 Kg.) used in the study were selected from these 19 cats based on highest pretreatment flea counts. These cats were ranked in descending order by flea count and gender and randomly allocated into two groups.



### 1.2. Experimental design

Cats (4M:4F) in Group A remained nontreated and served as controls. Cats (4M:4F) in Group B were treated with a metaflumizone formulation containing 200 mg active ingredient/ml. Animals were dosed with a minimum of 40 mg metaflumizone/kg according to pretreatment body weight. The dose was applied to the skin at a single spot on the dorsal neck at the base of the skull.

On Days -2, 7, 14, 21, 28, 35, 42, 49 and 56, each cat was infested with approximately 100 unfed cat fleas. On Days 1, 2, and 3, and at 2 and 3 days after each posttreatment reinfestation, flea eggs were collected from the pan under each cat cage. At approximately 72h after treatment or infestation, each cat was combed to remove and count live fleas. The fleas were not replaced on the animals following the 72 h count. Prior to the egg collections, cats were brushed vigorously by hand for ~20 seconds to dislodge any flea eggs from the cat's hair coat, allowing the eggs to fall into the drop pan below the cage. Eggs were collected and counted. Viability of eggs was determined by attaching up to 50 flea eggs from each collection to the lids of glass Petri dishes. The lid was inverted and placed over a corresponding lower dish containing growth media and held in a growth chamber at approximately 75-80% R.H. and 27-28 °C. Eggs were examined using a dissecting microscope 5 days after attachment to lids to determine hatch. Hatched larvae were allowed to continue development in the growth media. At 10 - 12 days after egg collection, pupae were sifted from the media and placed into plastic vials with lids. Adult emergence was determined by counting adult fleas at about 28 days after egg collection.

### 1.3. Calculation of efficacy

Percent efficacies on adult and egg fleas, relative to the non-treated control group and based on geometric means, were calculated as follows:

$$\% \text{ Efficacy} = \frac{(\text{GMean Control} - \text{GMean Treated}) * 100}{\text{GMean Control}}$$

Percent egg hatch and percent adult emergence were calculated as follows:

$$\frac{\text{Number of Hatched Eggs or Number of Emerged Adults} * 100}{\text{Number of Eggs Incubated}}$$

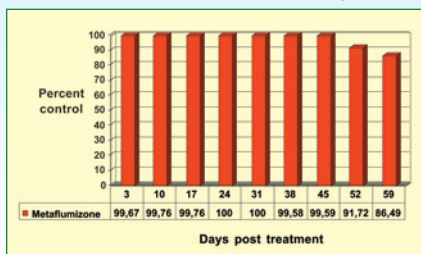
## 2. Results

All cats included in the study demonstrated adequate pretreatment flea retention with Day -4 flea counts ranging from 42 to 88. Untreated cats also maintained adequate flea infestations throughout the study with geometric mean flea counts ranging from 44.4 to 80.5.

Treated cats showed significantly lower geometric mean adult flea counts than counts on nontreated controls throughout the entire 8 weeks of the study (P < 0.05). Treatment with metaflumizone provided ≥99.6% efficacy for six weeks posttreatment and then 91.7 and 86.5% at 7 and 8 weeks post-treatment, respectively - Graphic 1.

Graphic 1

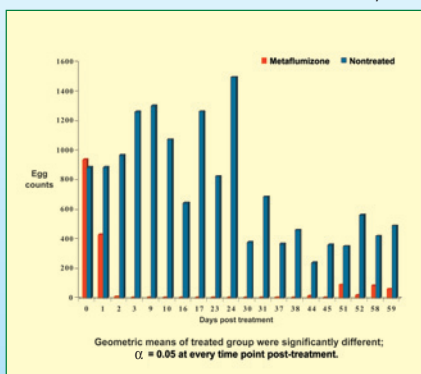
Percentage of efficacy relative to nontreated controls for cats treated with metaflumizone spot-on



Geometric mean flea egg counts for the metaflumizone-treated cats were also significantly lower than those for nontreated controls at all post-treatment evaluations (P < 0.05, Graphic 2). Egg production on metaflumizone treated cats was reduced by 55.3% within 24 hours after treatment and >99% over the next 24 hours. For subsequent infestations, egg production was negligible from treated cats out to at least 5 weeks after treatment (Day 38), with ≥99.5% reduction relative to nontreated cats at all evaluations. Egg production from treated cats increased slightly over the next three weeks, but was still reduced by 87.0% and 93.1% (based on geometric means) on Days 58 and 59 posttreatment.

Graphic 2

Geometric mean flea egg counts in nontreated controls and in cats treated with metaflumizone spot-on



Where there were eggs to evaluate, metaflumizone treatment did not have any effect on the hatching of eggs produced by fleas from treated animals. There were no significant differences between the percent hatch of flea eggs from treated or nontreated cats (P > 0.05, Table 1a). Similarly, the metaflumizone treatment did not have effects on the development and emergence of adult fleas from the eggs produced by fleas from treated animals. There were no significant differences between the percent hatch of flea eggs from treated or nontreated cats (P > 0.05, Table 1b) from Days 1 through 30, and from 52 on. While adult emergence was significantly lower for eggs from treated animals collected from Day 37 to 51,

this may not truly reflect a treatment effect as these comparisons were based on only a small number of eggs from treated animals.

Table 1a

Percent egg hatch and percent reductions relative to nontreated controls for cats treated with metaflumizone spot-on

Treatment	Count Day									
	0	1	2	3	9	10	16	17	23	24
Nontreated Control	92.65 <sup>a</sup>	94.93 <sup>a</sup>	91.79 <sup>a</sup>	93.03 <sup>a</sup>	96.17	71.73	82.71	89.54	91.56 <sup>a</sup>	94.79
Metaflumizone	93.58 <sup>a</sup>	96.78 <sup>a</sup>	95.8 <sup>a</sup>	100 <sup>a</sup>	--	--	--	--	85.36 <sup>b</sup>	--
% of reduction in egg hatching	0.0	0.0	0.0						6.8	

Treatment	Count Day									
	30	31	37	38	44	45	51	52	58	59
Nontreated Control	93.17 <sup>a</sup>	89.32	97.93 <sup>a</sup>	96.63	91.85 <sup>a</sup>	94.82 <sup>a</sup>	94.42 <sup>a</sup>	96.34 <sup>a</sup>	90.09 <sup>a</sup>	93.72 <sup>a</sup>
Metaflumizone	75.36 <sup>b</sup>	--	97.56 <sup>a</sup>	--	78.64 <sup>b</sup>	95.85 <sup>a</sup>	90.71 <sup>a</sup>	95.53 <sup>a</sup>	88.54 <sup>a</sup>	88.30 <sup>a</sup>
% of reduction in egg hatching	19.1		0.4		14.38	0.0	3.9	0.9	1.7	5.8

Geometric means for each parameter in each column with the same superscript letter are not significantly different; -- indicates that there were no eggs/adults to evaluate α = 0.05.

Table 1b

Percent adult emergence and percent reductions relative to nontreated controls for cats treated with metaflumizone spot-on

Treatment	Count Day									
	0	1	2	3	9	10	16	17	23	24
Nontreated Control	71.98 <sup>a</sup>	44.30 <sup>a</sup>	32.04 <sup>a</sup>	56.56 <sup>a</sup>	68.68	35.68	63.42	80.72	80.98 <sup>a</sup>	84.76
Metaflumizone	57.98 <sup>a</sup>	45.01 <sup>a</sup>	35.70 <sup>a</sup>	50.38 <sup>a</sup>	--	--	--	50.00 <sup>a</sup>	--	--
% of reduction in emergence	0.0	0.0	10.9					38.3		

Treatment	Count Day									
	30	31	37	38	44	45	51	52	58	59
Nontreated Control	84.66 <sup>a</sup>	79.77 <sup>a</sup>	89.14 <sup>a</sup>	93.29	71.55 <sup>a</sup>	91.31 <sup>a</sup>	90.61 <sup>a</sup>	90.42 <sup>a</sup>	79.77 <sup>a</sup>	87.85 <sup>a</sup>
Metaflumizone	76.50 <sup>a</sup>	--	53.21 <sup>b</sup>	--	35.00 <sup>b</sup>	53.06 <sup>b</sup>	69.34 <sup>b</sup>	81.73 <sup>a</sup>	67.87 <sup>a</sup>	83.54 <sup>a</sup>
% of reduction in emergence	9.6		40.3		51.1	41.9	23.5	9.6	14.9	4.9

Geometric means for each parameter in each column with the same superscript letter are not significantly different; -- indicates that there were no eggs/adults to evaluate α = 0.05.



## 4. Discussion and Conclusions

Treatment of cats with a metaflumizone spot on almost completely halted egg production (99.2% reduction) within 48 h of application and provided 99.7% control of the existing flea burden within 72 h. Therefore, within 2 days of treatment, no egg dissemination should occur from treated cats. Currently available topical spot-on insecticide formulations such as fipronil-(S) methoprene, imidacloprid and selamectin are marketed to provide at least 30 days of effective flea control. A single application of metaflumizone provided greater than 99% control of adult cat fleas for at least 42 days after treatment and should provide highly effective flea control when used as a monthly treatment. Following treatment, egg production was reduced by over 99% for at least 5 weeks. At 6 weeks posttreatment, the control of egg production at 48 hours after reinfestation was 96.5%, and 99.7% between 48 and 72 hours after reinfestation. In this study it was demonstrated that metaflumizone had a profound effect upon egg production. This indirectly indicates that metaflumizone is producing rapid toxicity and thus markedly reducing blood feeding by fleas.

Where there were eggs to assess metaflumizone treatment appeared to have little effect on the hatchability of eggs or the survival and development of fleas from eggs recovered.

Dryden, M.\*\*; Payne, P.ª; Lowe, A.ª; Mailen, S.ª; Smith, V.ª; Rugg, D.ª  
ªDepartment of Diagnostic Medicine /Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS. 66503.

\*Fort Dodge Animal Health, PO Box 5366, Princeton, NJ 08543-5366.

\*\*Corresponding author.