

Efficacy of a novel formulation of metaflumizone for the control of fleas (*Ctenocephalides felis*) on cats

S. Holzmer^{a,*}, J.A. Hair^b, M.W. Dryden^c, D.R. Young^d, L. Carter^e

^a Fort Dodge Animal Health, P.O. Box 5366, Princeton, NJ 08543, USA

^b Nu-Era Farms, 320 N. Range Road, Stillwater, OK 74075, USA

^c Kansas State University, 1800 Denison Avenue, Manhattan, KS 66506, USA

^d Young Veterinary Research Services, Inc., 7243 East Avenue, Turlock, CA 95380, USA

^e Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX, USA

Abstract

A novel spot-on formulation containing metaflumizone (ProMeris[®] for Cats, Fort Dodge Animal Health, Overland Park, KS) was evaluated in five laboratory studies to determine the duration of residual efficacy in cats against fleas after a single spot treatment. In each study, eight domestic shorthair cats were randomly allocated to each treatment group and individually housed. One group in each study remained non-treated. In one study, an additional group of eight cats was treated with a placebo formulation. Cats were treated topically with metaflumizone formulation to provide a dose of at least 40 mg metaflumizone/kg. Cats were infested with 100 cat fleas (*Ctenocephalides felis felis*) once per week for approximately 8 weeks. Cats were comb counted 48 h after treatment and each infestation to determine the number of viable fleas present. There were no significant differences in flea counts between the non-treated control and the placebo-treated control ($P > 0.05$) other than a 26% reduction at week 1, demonstrating that the formulation excipients had no activity. Metaflumizone treatment resulted in significantly lower flea numbers relative to non-treated controls on all post-treatment count days ($P < 0.05$). Metaflumizone provided >90% control of flea infestations up to 7 weeks following a single treatment. © 2007 Elsevier B.V. All rights reserved.

Keywords: ProMeris[®]; *Ctenocephalides felis felis*; Metaflumizone; Flea; Cat

1. Introduction

The cat flea, *Ctenocephalides felis felis*, is endemic worldwide and considered to be the most important ectoparasite of companion animals (Rust and Dryden, 1997). Adult fleas are blood feeders, penetrating the skin with their sucking mouthparts and injecting salivary antigens as they feed (Dryden, 1989; Dryden and Rust, 1993). They are recognized as a major cause of allergic skin disease in companion animals and are capable, when

present in sufficient numbers, of causing anemia. They are intermediate hosts for the dog tapeworm, *Dipylidium caninum*, and can transmit a number of pathogens including *Bartonella henselae* (Kwochka, 1987; Foil et al., 1998; Krämer and Menke, 2001).

Control of fleas is primarily based on chemical means and recently, convenient on-animal treatments have become the standard accepted method (Dryden and Payne, 2004; Rust, 2005). The most widely used products are generally applied as spot-on applications on a monthly schedule. The spot-on treatments include active ingredients from a number of chemical classes, including phenyl pyrazoles, fipronil; neonicotinoids, imidacloprid; the pyrethroids, permethrin and phenothrin; and selamectin, an avermectin (Rust, 2005).

* Corresponding author. Tel.: +1 732 631 5858; fax: +1 732 631 5864.

E-mail address: holzmes@pt.fdah.com (S. Holzmer).

These chemistries have direct insecticidal activity and control fleas on the animal. In addition, there are products such as the insect growth regulators, lufenuron and methoprene, that may be applied or ingested and control fleas by disrupting the development of eggs and larvae. Despite the variety of available products and different application methods, fleas remain an ongoing problem for many pet owners. Fleas have developed resistance to a number of insecticides and pest management strategies to reduce the development of resistance are needed (Bossard et al., 1998; Ross et al., 1998; Rust, 2005), especially if we want to conserve these new active ingredients.

Metaflumizone is a novel insecticide belonging to the semicarbazones with no known cross-resistance to other chemistries (Salgado and Hayashi, 2007). Metaflumizone has been found to have potent activity against fleas *in vivo* by a single topical application to cats (Takagi et al., 2007). The following studies were designed to evaluate the residual efficacy of a single spot-on dose of metaflumizone (ProMeris[®] for Cats, Fort Dodge Animal Health, Overland Park, KS) for the control of fleas on cats.

2. Materials and methods

Five studies were conducted at four laboratories in different geographical regions of the US (Table 1). All studies were conducted according to good laboratory practices as outlined in US EPA 40CFR160 (http://www.access.gpo.gov/nara/cfr/waisidx_00/40cfr160_00.html), and followed the basic methodology of US EPA Guideline, OPPTS 810.3300

Table 1

Design and locations of five studies conducted to evaluate the efficacy of a single topical dose of ≥ 40 mg metaflumizone/kg against *Ctenocephalides felis felis* in cats

| Study | Treatment | No. of cats | Study location |
|-------|----------------------|-------------|----------------|
| A | Metaflumizone | 8 | Kansas |
| | Non-treated | 8 | |
| B | Metaflumizone | 8 | Texas |
| | Non-treated | 8 | |
| | Placebo ^a | 8 | |
| C | Metaflumizone | 8 | California |
| | Non-treated | 8 | |
| D | Metaflumizone | 8 | Oklahoma |
| | Non-treated | 8 | |
| E | Metaflumizone | 16 | Texas |
| | Non-treated | 8 | |

^a Placebo consisted of inert ingredients from the commercial formulation of metaflumizone.

(http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/810_Product_Performance_Test_Guidelines/Series/index.html).

2.1. Animals

Domestic shorthair cats obtained from commercial sources were used in these studies. Ninety-six cats (46 males and 50 females) were selected to enter the treatment phase of these studies. The cats ranged from 6 months to 9 years of age and weighed between 2.1 and 6.2 kg at the time of treatment. These animals were selected from larger groups of cats based on pretreatment flea counts.

Cats were housed individually in indoor cages that conformed to accepted guidelines for floor area and type, lighting, temperature and welfare (including environmental enrichment) as required by local and national animal welfare legislation. They were housed in such a manner as to avoid contamination with fleas or transfer of test materials between animals. Water was available *ad libitum* and an appropriate quantity of commercial dry feline ration was provided daily throughout the study. Animals had not been treated with any ectoparasiticide for at least 60 days and were in good health when enrolled in the study and at treatment. Cats were grouped by treatment and were individually identified by numbered or lettered ear tattoos and/or cage identification cards. Each individual cage was labeled with the cat identification number only and was not identified by treatment. Cats from different treatment groups were physically separated by space equivalent to at least one empty cage.

2.2. Experimental design and methods

Efficacy of metaflumizone against adult fleas on cats following administration of a single topical dose unit was evaluated in five controlled studies (Table 1).

Cats were acclimated to the study conditions for 14 days prior to treatment. The cats were observed for general health once daily during the preconditioning period. Prior to treatment, a physical exam was performed on each cat by a veterinarian to determine health and suitability for inclusion in the trial. Cats were infested prior to treatment to determine if they were good flea hosts. Approximately 7 days prior to treatment, each cat was infested with approximately 100 unfed cat fleas. Twenty-four hours following infestation, each cat was thoroughly examined and combed to remove and count fleas. Using the pretreatment flea counts, cats with the highest flea

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