

Confirmation of the efficacy of a novel formulation of metaflumizone plus amitraz for the treatment and control of fleas and ticks on dogs

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Abstract

A novel spot-on formulation containing metaflumizone plus amitraz (ProMeris[®]/ProMeris Duo[®] for Dogs, Fort Dodge Animal Health, Overland Park, KS) was evaluated in four laboratory studies to confirm efficacy against fleas and ticks on dogs for 1 month. Three different strains of cat flea (*Ctenocephalides felis felis*) and four tick species were used. *Rhipicephalus sanguineus* and *Dermacentor variabilis* were evaluated concurrently in two studies and *Ixodes scapularis* and *Amblyomma americanum* in one study each. In all studies, dogs were randomly allocated to treatment groups and compared with nontreated dogs. One study also included a placebo treatment and a commercial product containing fipronil plus S-methoprene. All treatments were applied to the skin at a single spot between the scapulae on Day 0. Dogs were infested with fleas and/or ticks prior to treatment and then reinfested at weekly intervals for 6 weeks after treatment and evaluated for efficacy at 1 or 2 days after treatment and each reinfestation. These studies confirmed that treatment with ProMeris for Dogs at the proposed commercial dose rate rapidly controlled existing infestations of fleas and ticks on dogs. Treatment provided control of reinfesting fleas for up to 6 weeks and at least 4 weeks control of ticks. Efficacy was confirmed in a variety of dog breeds against three different flea strains and four common species of ticks found on dogs in the United States.

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Keywords: ProMeris[®]; ProMeris Duo[®]; *Ctenocephalides felis felis*; *Rhipicephalus sanguineus*; *Dermacentor variabilis*; *Ixodes scapularis*; *Amblyomma americanum*; Metaflumizone; Amitraz; Flea; Tick; Dog

1. Introduction

The cat flea *Ctenocephalides felis felis* is endemic worldwide and is considered the most important ectoparasite of dogs and cats (Rust and Dryden, 1997). Fleas are recognized as a major cause of allergic skin disease in dogs and are capable, when present in

sufficient numbers, of causing anemia (Krämer and Menke, 2001). They are intermediate hosts for the cestode *Dipylidium caninum*, and can transmit a number of pathogens including *Bartonella henselae*. Infestations of ticks can have widely varying effects on dogs; ticks may be an occasional nuisance or a continuous infestation, and they may cause virtually no adverse effects on health or cause life-threatening disease. The genera of ticks commonly infesting dogs in the US are *Amblyomma*, *Dermacentor*, *Ixodes* and *Rhipicephalus* (Dryden and Payne, 2004). Some tick species excrete

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toxic substances within their saliva and tick-borne diseases may be passed to their next host in saliva (Needham and Teel, 1991). A large infestation of ticks may cause anemia and ticks are responsible for the transmission of a number of diseases, some are dog-specific, some are zoonotic and some cause serious, even life-threatening, diseases (Dryden and Payne, 2004).

Control of fleas and ticks is primarily based on chemical means and recently, convenient on animal treatments have become the standard accepted method (Dryden and Payne, 2004; Rust, 2005). Despite the variety of available products and different application methods, both fleas and ticks remain an ongoing problem for many pet owners. In addition, the baseline susceptibility or tolerance of different flea and tick populations and the tick species to individual insecticides and acaricides can vary widely (Bossard et al., 1998; Ross et al., 1998; Rust, 2005). The US EPA recommends that new insecticides be evaluated against at least three geographically distinct cat flea populations (US EPA Guideline, OPPTS 810.3300).

Metaflumizone is a novel insecticide in the semicarbazone class of chemistry with potent activity against fleas *in vitro* and *in vivo* via topical application to dogs and cats (Takagi et al., 2007; Rugg and Hair, 2007) and no known cross-resistance to other chemistries (Salgado and Hayashi, 2007). This compound was combined with the formamidine acaricide amitraz in a novel spot-on formulation (ProMeris[®]/ProMeris Duo[®] for Dogs, Fort Dodge Animal Health, Overland Park, KS) to develop a product for flea and tick control on dogs (Sabnis and Zupan, 2007). The appropriate dose rate of a formulation of metaflumizone and amitraz applied as a single spot application to dogs to provide at least a month of control of fleas and ticks study was determined in a previous study (Rugg and Hair, 2007). Here we report studies conducted to confirm the efficacy of this formulation applied as unit doses to dogs to control different flea strains and the major tick species parasitizing dogs in the US.

2. Materials and methods

Four studies were conducted examining the efficacy of ProMeris for Dogs applied at the proposed commercial dose rates against a number of cat flea strains (three studies) and/or different species of ticks at three different sites in the US. Two studies (A and B) were conducted at Nu-Era Farms Inc. (NEF), OK, another (C) at AgResearch Consultants Inc. (ARC), AR,

and the fourth (D) at STILLMEADOW Inc. (STM), TX. All studies were conducted according to Good Laboratory Practices as outlined in US EPA 40CFR160, and followed the basic methodology of US EPA Guideline, OPPTS 810.3300.

2.1. Animals

2.1.1. Studies A and B

Eight male and eight female adult Beagle dogs from the NEF colony were used in each study. Each dog was individually identified by numbered or lettered ear tattoos. The dogs had not been treated with an ectoparasiticide for at least 30 days and were in good health when enrolled in the study and at treatment. The animals weighed from 7.3 to 16.1 kg on Day -2. These animals were selected from a group of nine male and nine female dogs (A) or 10 male and 10 female dogs (B) based on pretreatment flea and/or tick counts.

Dogs were housed individually in indoor runs that conformed to accepted animal welfare guidelines. Each run was approximately 3 m × 1 m with wire mesh walls on epoxy-coated concrete flooring and contained a raised mesh rest. Dog runs were grouped by treatment. Each individual run was labeled with the dog identification number only and was not identified by treatment. Dogs from different treatment groups were physically separated by space equivalent to at least one empty run.

Dogs were fed an appropriate maintenance ration of a commercial dry canine feed (27% Hi-Protein Complete Ration, A+M Feeds, Stillwater, OK 74074) for the duration of the study. Water was available *ad libitum*.

2.1.2. Study C

Sixteen male and 16 female adult mixed breed dogs from the ARC colony were used in the study. Each dog was individually identified by numbered tags attached to a neck chain. The dogs had not been treated with an ectoparasiticide for at least 14 days and were in good health when enrolled in the study. The animals weighed from 5.4 to 30.6 kg on Day -2. These animals were selected from a group of 19 male and 21 female dogs based on pretreatment flea and tick counts, skin condition and health. All dogs included in the study retained >30 fleas and >5 ticks at the pretreatment evaluation. Dogs were housed individually in indoor runs that conformed to accepted animal welfare guidelines. Each run was approximately 1.2 m × 1.2 m (small dogs) or 2.4 m × 1.2 m (large dogs) with wire mesh walls on concrete flooring. Dog runs were grouped by treatment. Each

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