EFFICACY REVIEW
PROMERIS SPOT ON FOR CATS

DATE:	January 25, 2004
FILE SYMBOL:	80490-G
DP BARCODE:	D314412
CHEMICAL NUMBER:	CAS No. 35037-73-1
REGISTRANT:	Fort Dodge Animal Health
GLP:	No
CHEMICAL:	Metaflumizone (18.53%)
PURPOSE:	Provide efficacy data for product registration of a spot-on treatment for cats and kittens over eight weeks of age.
MRID:	46437609. M. Dryden and S. J. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-04-03; Performing Laboratory Kansas State Univerisyty, College of Veterinary Medicine, Manhatten, KS; Sponsor Fort Dodge Animal Health, Princeton, NJ. 46437610. L. Carter and S. Dunney 2004. Efficacy of Two Topically Applied Spot-On Formulations of R-28153 Against Fleas on Cats. Project Number 0817-F-US-08-04; Performing Laboratory STILLMEADOW, Inc., Sugar Land, TX; Sponsor Fort Dodge Animal Health, Princeton, NJ. 46437611. J. Hair and S. Dunney. 2004. Dose Determination of a Topically Applied Spot-On Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-02-03; Performing Laboratory Nu-Era Farms, Stillwater, OK; Sponsor Fort Dodge Animal Health, Princeton, NJ. 46437612. L. Carter and S. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-05-03; Performing Laboratory STILLMEADOWE, Inc., Princeton, NJ; Sponsor Fort Dodge Animal Health, Princeton, NJ. 46437613. D. Young and S. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-06-04; Performing Laboratory Young Veterinary Research Services, Turlock, CA; Sponsor Fort Dodge Animal Health, Princeton, NJ 46437614. J. Hair and S. Dunney. 2004. Dose Confirmation of a Topically Applied

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BACKGROUND:

Metaflumizone is a new active ingredient. The product "Promeris Spot on For Cats" is for the control and prevention of fleas on cats and kittens over eight weeks of age. The directions for use state that the material is to be applied as a single spot to the skin of the cat at the back of its head. For cats up to 9 pounds (4 kg) the rate is 0.027 fl oz (0.8 ml). For cats over 9 pounds the rate is 0.054 fl. oz (1.6 mL).

The directions for use state the product is effective for up to seven weeks.

Other label claims include:

"Effectiveness persists for up to seven weeks."
"Rapidly kills adult fleas which may cause dermatitis."
"Novel mode of action."
"It may also be used to prevent infestation in flea free animals being taken into a flea contaminated environment."

DATA REVIEW:

A summary of the results of the submitted data is provided below.

46437609. M. Dryden and S. J. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-04-03; Performing Laboratory Kansas State University, College of Veterinary Medicine, Manhatten, KS; Sponsor Fort Dodge Animal Health, Princeton, NJ.

An experiment was conducted to determine the efficacy of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats weighing from 2.5 to 4.7 kg. The product was compared to untreated controls (8 treated cats, 8 cats served as controls). After initially infestating cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult

fleas on days 4, 11, 18, 25, 32, 39, 46 and 55 with counts taken on days 6,13, 20, 27, 34, 41, 48, and 55. Cats were dosed according to label directions. Six cats were dosed at 0.8 ml and two cats were dosed at 1.6 ml.

Reported Results:

The percent mortality for adult fleas relative to the control was >98% after one day. Greater than 99% residual control was achieved through six weeks post-treatment (day 48). On day 55, it was below 90%. The authors reported no unexpected adverse effects that could be attributable to treatment.

46437610. L. Carter and S. Dunney 2004. Efficacy of Two Topically Applied Spot-On Formulations of R-28153 Against Fleas on Cats. Project Number 0817-F-US-08-04; Performing Laboratory STILLMEADOW, Inc., Sugar Land, TX; Sponsor Fort Dodge Animal Health, Princeton, NJ.

An experiment was conducted to determine the efficacy of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats weighing from 2.1 to 4.6 kg. The product was compared to untreated controls (16 cats treated with two different lots of R-28153, 8 cats served as controls). After initially infestating cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult fleas on days 5, 12, 19, 26, 33, 40, 47 and 54 with counts taken on days 7,14, 21, 28, 35, 42, 49, and 56. Eleven cats were dosed at 0.8 ml and five cats were dosed at 1.6 ml.

Reported Results:

The mean percent mortality for adult fleas relative to the control was 100% after two days. Greater than 90% residual control was achieved through seven weeks post-treatment (day 49 count). On day 56 it was below 90%. The authors reported no unexpected adverse effects that could be attributable to treatment.

46437611. J. Hair and S. Dunney. 2004. Dose Determination of a Topically Applied Spot-On Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-02-03; Performing Laboratory Nu-Era Farms, Stillwater, OK; Sponsor Fort Dodge Animal Health, Princeton, NJ.

An experiment was conducted to determine an effective dose level of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats. Three dose rates (20, 30 and 40 mg ai/kg BW) were tested. Positive (imidacloprid 10%) and untreated controls were used. There were eight cats per treatment (total of 40 cats; 8 per group). After initially infesting cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult fleas on days 5, 12, 18, 25 and 32. Counts taken on days 6,13, 20, 27 and 34. Unfed fleas were replaced on each animal after combing and then counted on days 7, 14, 21, 28 and 35. Cat weights for the 40 mg

group ranged 1.7 to 5.6 kg.

Reported Results:

For the 20 mg treatment group, >90% control (based on geometric means) was not achieved at any time in the study. For the 30 mg treatment group, >90% control of fleas was only achieved on day 28. For the 40 mg treatment group, 92.6 % control occurred at the day two count. At only one other time period (day 7) was control >90%. The authors reported no unexpected adverse effects that could be attributable to treatment.

46437612. L. Carter and S. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-05-03; Performing Laboratory STILLMEADOWE, Inc., Princeton, NJ; Sponsor Fort Dodge Animal Health, Princeton, NJ.

An experiment was conducted to determine the efficacy of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats weighing from 2.2 to 4.6 kg. The product was compared to untreated controls. There were eight cats per treatment (untreated control, R-28153 spot-on and control substance/vehicle). After initially infesting cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult fleas on days 5, 12, 19, 26, 33, 40, 47 and 54 with counts taken on days 7,14, 21, 28, 35, 42, 49, and 56. Five cats were dosed at 0.8 ml and three cats were dosed at 1.6 ml.

Reported Results:

The mean percent mortality for adult fleas relative to the control was 100% after two days. Greater than 90% residual control was achieved through seven weeks post-treatment (day 49 count). Percent efficacy in the placebo relative to the untreated control was variable, ranging 5.4 to 32.1%. The authors reported no unexpected adverse effects that could be attributable to treatment.

46437613. D. Young and S. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-06-04; Performing Laboratory Young Veterinary Research Services, Turlock, CA; Sponsor Fort Dodge Animal Health, Princeton, NJ

An experiment was conducted to determine the efficacy of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats weighing from 2.7 to 5.2 kg. The product was compared to untreated controls. There were eight cats per treatment (untreated control and R-28153 spot-on). After initially infesting cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult fleas on days 5, 12, 19, 26, 33, 40, 47 and 54 with counts taken on days 7,14, 21, 28, 35, 42, 49, and 56. Five cats were dosed at 0.8 ml and three cats were dosed at 1.6 ml.

Reported Results:

The mean percent mortality for adult fleas relative to the control was 100% after two days. Greater than 90% residual control was achieved through seven weeks post-treatment (day 49 count). The authors reported no unexpected adverse effects that could be attributable to treatment.

46437614. J. Hair and S. Dunney 2004. Dose Confirmation of a Topically Applied Spot-on Formulation of R-28153 Against Fleas on Cats. Project Number 0817-F-US-04-03; Performing Laboratory Kansas State University, College of Veterinary Medicine, Manhatten, KS; Sponsor Fort Dodge Animal Health, Princeton, NJ

An experiment was conducted to determine the efficacy of R-28153 in a spot-on formulation against cat fleas (*Ctenocephalides felis*) infesting cats weighing from 2.4 to 5.9 kg. The product was compared to untreated controls. There were eight cats per treatment (untreated control and R-28153 spot-on). After initially infesting cats with adult unfed fleas (100 per cat), cats were reinfested with unfed adult fleas on days 5, 12, 19, 26, 33, 40, and 47 with counts taken on days 7,14, 21, 28, 35, 42, and 49. Two cats were dosed at 0.8 ml and six cats were dosed at 1.6 ml.

Reported Results:

The mean percent mortality for adult fleas relative to the control was 100% after two days. Greater than 90% residual control was achieved through six weeks post-treatment (day 42 count). The authors reported no unexpected adverse effects that could be attributable to treatment.

RECOMMENDATIONS:

The submitted data support the use of Promeris Spot On for control of fleas on cats and kittens over eight weeks of age.

The following label recommendations apply:

1. The label directions state the product is effective for up to seven weeks, but then also recommend monthly applications. Rephrase the statement "Monthly application is recommended to provide continuous effective control of fleas and prevent reinfestation" to read "Apply no more than once every seven weeks to provide continuous effective control of fleas and prevent reinfestation".

2. Delete the phrase "Novel mode of action." Alternatively, provide an explanation of what is meant by this.

3. Revise the statement "It may also be used to prevent infestation in flea free animals being taken into a flea contaminated environment." To read "It may also be used to prevent infestation in flea free cats and kittens over eight weeks of age being taken into a flea contaminated environment".