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DATA ACCESSION NO(S). 456282-01,456127-01,456205-01,-04,-05 & -06; D282269;S613600;Case# 066320;AC:305

PRODUCT MGR. NO. 03-Layne/Sibold

PRODUCT NAME(S) FRONTLINE® Plus for Dogs

COMPANY NAME Merial Limited

SUBMISSION PURPOSE Provide performance data in support of claims for chewing lice and sarcoptic mange mites on dogs with standard label rate of subject product.

CHEMICAL & FORMULATION Fipronil 9.8%
(S)-Methoprene 8.8%
(1.02 gm/cc ready-to-use liquid concentrate)

CONCLUSIONS & RECOMMENDATIONS The data presented in EPA Accession (MRID) Number 456282-01, having been obtained from standard field testing conducted according to requirements of § 95-9(a)(1)-(3) on p. 263 and meeting the standard of § 95-9(b)(2)(ii) on p. 264 of the Product Performance Guidelines, are adequate to demonstrate the ability of a formulation nearly identical to the subject product to control biting dog louse, *Trichodectes canis*, when applied to naturally infested dogs at the appropriate rate for the weight of dogs involved in kilograms of body weight between June 27, 2000 and April 9, 2001. Observations were continued for 42 days after the single treatment and results were 98.3% reduction in total louse counts at day 2 and 100% reduction at days 28 and 42. The data presented in MRID No.456127-01, having been summarized from standard clinical studies conducted according to requirements of § 95-9(a)(1)-(3) on p. 263 and meeting the standards of § 95-9(b)(2)(ii) for lice and § 95-9 subpart (b)(2)(iii) for mites, both on p. 264 of the Guidelines, are adequate to demonstrate the ability of the subject product to control infestations of *T. canis* on dogs for 63 days following the application of (to be continued)

appropriate label rates on day 0 and day 28. Infestations were reduced by 100% at day 2 through day 63 by this treatment regime. This information is presented in Table 1 on p. 9. Also included in this volume are results of a standard clinical test of control of flea allergy dermatitis on dogs with the subject product as reported as summary of dermatological criteria and efficacy assessments in Table 1 on p. 16, geometric mean flea counts in Table 3 on p. 18, summary of pruritis scores in Table 6 on pp. 21-4, summary of data on investigator's assessment of improvement and overall assessment of efficacy for dogs treated with the subject product for dogs in Table 10 on p. 28. The results were as follows: % of pruritis positive improved from 100% on day 0 to 41.9% on day 90 and extent of lesions from 94.4% on day 0 to 51.6% on day 90 in Table 1; geometric mean flea counts improved from 7.37 on day 0 to 0.14 on day 90 in Table 3; % positive pruritis in Table 6 is same as in Table 1; % positive extent of lesions scores in Table 6 is same as in Table 1; summary of data on investigator's assessment of improvement and overall assessment of efficacy assessment from 86.1% at day 14 to 93.8% at day 60 in Table 10. Finally, included in this volume are results of standard clinical tests of control of infestation of dogs with sarcoptic mange mite, *Sarcoptes scabiei* var. *canis*, and of associated sarcoptic mange with the subject product. The results are as follows: 1st study from Centro Veterinario Oriolo in Italy: geometric mean counts of live *S. scabiei* var. *canis* 3.0 on day -1 to 0 on day 63 in Table 1 on p. 33; arithmetic mean *S. scabiei* var. *canis* lesions scores 2.7 on day -1 to 0 on day 63 in Table 2 on p. 34; 2nd study from Stillmeadow, Inc. in U.S.A.: geometric mean counts of live *S. scabiei* var. *canis* >14.7 on day -1 to >5.8 on day 63/70 in Table 3 on p. 35; arithmetic mean *S. scabiei* var. *canis* lesions scores 3.0 on day -1 to 2.2 on day 63/70 in Table 4 on p. 36; 3rd study from University of Sinaloa in Mexico: geometric mean counts of live *S. scabiei* var. *canis* 21.0 on day -1/0 to 0 on day 83/84 in Table 5 on p. 37; arithmetic mean *S. scabiei* var. *canis* lesions scores 3.3 on day -1/0 to 0.2 on day 83/84 in Table 6 on p. 38.

Data presented in MRID No. 456205-01, having been obtained from standard clinical testing meeting the same requirements and standard are adequate to demonstrate the ability of the subject product to control biting dog lice, *T. canis*, when applied at the appropriate label rates per kilogram of body weight for the dogs involved. No live lice were found on dogs treated from Day 2 to Day 63. Based on the whole body counts at Day 63, the efficacy was 100%. No health problems or adverse reactions occurred during this trial. The results of this study demonstrate that fipronil is highly effective for treatment and control of louse infestations (*T. canis*) in the dog.

Data presented in MRID No. 456205-04, having been obtained from standard clinical testing meeting the same requirements and the standard for § 95-9(b)(2)(iii) on p. 264 are adequate to demonstrate the ability of the subject product to control sarcoptic mange mite, *S. scabiei* var. *canis*, when applied at the appropriate label rates per kilogram of body weight for the dogs involved at Stillmeadow, Inc., in Sugarland, TX, U.S.A. Geometric mean live mite counts were reduced in scrapings from (to be continued)

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treated dogs after treatment. Counts from control animals also declined over the study period and mites were only present on 2 of 6 controls at the end of the study. Dogs treated with the subject product had the highest mean mite counts, but the number of mites were not significantly different ($p<0.05$) for any of the treatment groups relative to the controls. Mean lesion scores of treated animals were reduced, but due to improvement in lesion scores of controls over time, there were no significant ($p<0.05$) differences between scores for treated and control groups.

Data presented in MRID No. 456205-05, having been obtained from standard clinical testing meeting the same requirements and standard are adequate to demonstrate the ability of the subject product to control sarcoptic mange mite, *S. scabiei* var. *canis*, when applied at the appropriate label rates per kilogram of body weight for the dogs involved at the University of Sinaloa School of Veterinary Medicine in Culiacan, Sinaloa, Mexico. Dogs treated with the subject product had insignificantly ($p>0.10$) different mite counts than controls at the Day 35 count. This difference was significant ($p<0.05$) for all 3 treated groups at the Day 83/84 count. Lesion scores were significantly ($p<0.05$) reduced in all the treated groups starting with the Day 63 observation. In addition, lesion scores were significantly ($p<0.05$) lower in another treated group than in the control group on Days 7, 21, 35 and 42, and lesion scores were significantly ($p<0.05$) lower in the subject product group than in the control group on Day 77. All of the control dogs remaining at the end of the study had lower mite counts and improved lesion scores from baseline. The balanced diet and excellent living conditions provided during the study may have contributed to the decline in mite population in these dogs. Due to poor health, and for humane reasons, 1 dog from each of 2 groups were dropped from the study, and 1 dog from each of 2 groups died during the study. None of the health problems observed during the study were related to treatment.

Data presented in MRID No. 456205-06, having been obtained from standard clinical testing meeting the same requirements and standard are adequate to demonstrate the ability of a formulation similar to the subject product to control sarcoptic mange mite, *S. scabiei* var. *canis*, when applied at the appropriate label rates per kilogram of body weight for the dogs involved at Centro Veterinario Oriolo in Castelleone, Italy. One or more live mites were found on control animals throughout the trial, except for one animal on Days 49 and 63. Dogs treated with a similar product had significantly ($p<0.05$) fewer mites than did the controls at each post treatment counting time (Days 7 through 63). No live mites were found on these treated dogs on Days 7, 49 or 63. Dogs treated with the similar product had significantly ($p<0.05$) fewer mites than did the controls on Days 21 through 63. No live mites were found on these treated dogs on Days 35, 49 or 63. Lesion scores were significantly ($p<0.05$) reduced in both treated groups at several time points after the second treatment on Day 28. No health problems occurred during this trial. The results of this trial demonstrate that fipronil is effective for treatment (continued)

of mite (*S. scabiei* var. *canis*) infestations in dogs.

These data collectively are adequate to support the following label claims for the subject product: "Kills...chewing lice" on the front panel; "...provides fast, effective and convenient treatment and control of...chewing lice..."; "Rapidly eliminates infestations with chewing lice"; "Aids in control of sarcoptic mange infestations"; "Treats and controls flea allergy dermatitis"; "When used monthly,...completely breaks the flea life cycle and controls tick and chewing lice infestations"; and "Although...can control fleas for up to three months, if there is a high risk of reinfestation or if the pet has fleas which may cause flea allergy dermatitis, a once monthly application may be needed".

RL Vern L. McFarland, IB