EFFICACY REVIEW

DATE: IN 4-10-02 OUT 5- 8-02

FILE OR REG. NO. 65331-1

PETITION OR EXP. PERMIT NO.

DATE DIV. RECEIVED February 25, 2002

DATE OF SUBMISSION February 21, 2002

DATE SUBMISSION ACCEPTED

TYPE PRODUCT(S): (I,)D, H, F, N, R, S

DATA ACCESSION NO(S). 456282-01,456127-01,456205-01,-04,-05 & -06; D282304;S611827;Case# 014261;AC:305

PRODUCT MGR. NO. 03-Layne/Sibold

PRODUCT NAME(S) FRONTLINE® Spray Treatment

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 0.29% (0.859 Sp.Gr. ready-to-use liquid pump spray)

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 the subject product to kill and control the biting dog louse, *Trichodectes canis*, when applied to naturally infested dogs at the maximum label rate of 2 pumps per pound (4 pumps per kilo- gram) of body weight between June 27, 2000 and April 9, 2001. Ob- servations were continued for 42 days after the single treatment and results were 99.6% 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 the maximum label rate on day 0 and day 28. Infes- tations were reduced by 100% at day 2 through day 63 (to be cont'd) 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 cri- teria and efficacy assessments in Table 1 on p. 16, summary of flea count scores in Table 2 on p. 17, summary of flea dirt scores in Table 4 on p. 19, summary of pruritis scores in Table 5 on p. 20, summary of extent of lesions scores in Table 7 on p. 25, summary of lesion score index in Table 8 on p. 26, and summary of efficacy assessment in Table 9 on p. 27. The results were as follows: % of pruritis positive improved from 100% on day 0 to 26.6% on day 56/70 and extent of lesions from 100% on day 0 to 30.4% on day 56/70 in Table 1; % positive flea counts improved from 73.3% on day 0 to 0.0% on day 56/70 in Table 2; % positive flea dirt scores improved from 76.7% on day 0 to 6.3% on day 56/70 in Table 4; % of pruritis positive in Table 5 is same as in Table 1; % positive extent of lesions scores in Table 7 is same as in Table 1; summary of lesion score index improved from 4.7 on day 0 to 0.6 on day 56/70 in Table 8; % improved in efficacy assessment from 95.3% at day 14/21 to 96.2% at day 56/70 in Table 9. 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* 3.2 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 0.2 on day 63 in Table 2 on p. 34; 2nd study from Stillmeadow, Inc. in U.S.A.: geo- metric mean counts of live *S. scabiei* var. *canis* 6.2 on day -1 to 0.7 on day 63/70 in Table 3 on p. 35; arithmetic mean *S. scabiei* var. *canis* lesions scores 3.2 on day -1 to 1.4 on day 63/70 in Ta- ble 4 on p. 36; 3rd study from University of Sinaloa in Mexico: geo- metric mean counts of live *S. scabiei* var. *canis* 33.9 on day -1/0 to 0.1 on day 83/84 in Table 5 on p. 37; arithmetic mean *S. scabiei* var. *canis* lesions scores 2.7 on day -1/0 to 0.3 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 maximum label rate to dogs. No live lice were found on dogs treat- ed 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 oc- curred 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 demon- strate the ability of the subject product to control sarcoptic mange mite, *S. scabiei* var. *canis*, when applied at the maximum la- bel rate to dogs at Stillmeadow, Inc., in Sugarland, TX, U.S.A. Geometric mean live mite counts were reduced in scrapings from treated dogs after treatment. Counts from control (to be cont'd) 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 lowest 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 maximum label rate to dogs at the University of Sinaloa School of Veterinary Medicine in Culiacan, Sinaloa, Mexico. Dogs treated with the subject product had significantly ($p<0.05$) lower 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 the subject product group than in the control group on Days 7, 21, 35 and 42, and lesion scores were significantly ($p<0.05$) lower in an- other treated group than in the control group on Day 42. 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 the subject product to control sarcoptic mange mite, *S. scabiei* var. *canis*, when applied at the maximum label rate to dogs at Centro Veterinar- io 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 the subject product had signif- icantly ($p<0.05$) 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. Lesion scores were significantly ($p<0.05$) reduced in both treated groups at sev- eral 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 and control of mite (*S. scabiei* var. *canis*) infestations in dogs.

These data collectively are adequate to support the following label claims for the subject product: "Long Lasting Control of... Chewing Lice" on the front panel; "Kills fleas which may cause flea allergy dermatitis"; "Treats and controls flea allergy dermatitis"; "Rapidly eliminates infestations with chewing lice"; (continued)

and "Aids in control of sarcoptic mange infestations in dogs", all in bullets on the side panel; "...residual activity prevents rein- festation by...chewing lice for at least 30 days", also on the side panel.

RL Vern L. McFarland, IB