Approval Date: September 9, 1996

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 140-915

B. Sponsor

Ciba-Geigy Corporation
Animal Health Division
Post Office Box 18300
Greensboro, NC 27419-8300

C. Proprietary Name

Interceptor®

D. Established Name

Milbemycin Oxime Tablets

E. Dosage Form, Route of Administration and Recommended Dosage

The ingredients of INTERCEPTOR FLAVOR TABS are formulated into various sized tablets to be administered orally (swallow or chew), as appropriate for the weight of the dog (see below), at monthly dosing intervals. The tablets supply the recommended minimum dose level of 0.5 mg milbemycin oxime per kilogram (0.23 mg/lb.) of body weight.

Tablet Milbemycin Oxime

Dog Weight	Per Month	Per Tablet
Up to 10 lbs.	1	2.3 mg
11 to 25 lbs.	1	5.75 mg
26 to 50 lbs.	1	11.5 mg
51 to 100 lbs.	1	23.0 mg

Dogs over 100 lbs. are provided the appropriate combination of these tablets.

F. Indication

INTERCEPTOR FLAVOR TABS are indicated for use in the prevention of heartworm disease caused by *Dirofilaria immitis*, the control of adult *Ancylostoma caninum* (hookworm), and the removal and control of adult *Toxocara canis* and *Toxascaris leonina* (roundworms), and *Trichuris vulpis* (whipworm) infections in dogs and in puppies four weeks of age or greater and two pounds of body weight or greater.

G. Effect of Supplement

This supplement expands the indications to include the removal and control of adult roundworms *Toxascaris leonina*. Laboratory data support the efficacy of the drug against this species.

II. EFFECTIVENESS

A. Dose Establishment

No additional dose establishment work was required. The minimum target dose of milbemycin oxime 0.5 mg/kg body weight was established in the original NADA 140-915 for the currently approved label indications.

B. Dose Confirmation

One dose confirmation study (Trial AH-93-0045) was conducted to evaluate the effectiveness of milbemycin oxime in the removal and control of the adult roundworm, *Toxascaris leonina*. Twenty-four dogs were infected with eggs of *Toxascaris leonina* by oral inoculation 75-77 days pre-treatment. Twelve dogs were given a treatment of 0.5 mg/kg minimum dose of milbemycin oxime one time and 12 were untreated. All dogs were necropsied 7 days post-treatment, and all intestinal parasites were recovered, identified and counted.

Study Site:

CHK-R&D
17190 Polk Road
Stanwood, MI 49346

Study Director:

Dwight D. Bowman, Ph.D.

Animals:
21.5 to 27 week old Beagle dogs
13 males and 11 females
5.3 to 10.6 kg

Results:

One adult worm was recovered from the 12 treated dogs compared to 159 worms from the 12 untreated control dogs. The milbemycin oxime treatment was calculated to be 99.4% efficacious.

Conclusion:

This study demonstrated the efficacy of Interceptor Flavor Tabs against *T. leonina*.

C. 1989 Clinical Field Trial

A clinical field trial (MT-147-00-89) was conducted during 1989-90 to evaluate the safety and efficacy of monthly administration of milbemycin oxime for the additional indications of removal and control of roundworms and whipworms when used under typical veterinary conditions. Safety and efficacy data from animals infected with

roundworms was extracted to support the label change for this supplement to the NADA. In this study, 100% (62 of 62) of the roundworm cases were successfully treated by study completion (See Table 1).

TABLE 1 : Effects of Milbemycin Oxime on Removal and Control of Adult Roundworm Infections in Dogs During Clinical Field Trials.

Investigator/Location	Treatment	No. of Dogs Completing Study	Roundworm Infections
Legg/Texas	Milbemycin	15	5/5
	Filaribits Plus	14	3/3
Stocks/California	Milbemycin	9	9/9
	Filaribits Plus	8	8/8
Utgard/Florida	Milbemycin	62	48/48
	Filaribits Plus	63	56/55
Totals	Milbemycin	86	62/62=100%
	Filaribits Plus	85	67/66=98%

2 - "Cured" means no eggs found at final fecal examination.

D. Prevalence Study

National Prevalence of Canine Parasites based on Centrifugal Sucrose Flotation Examinations of Fecal Specimens, B. L. Blagburn, D. S. Lindsay, J. L. Vaughan, R. C. Lynn, W. J. Kelch, G. C. Ritchie, D. I. Hepler, July 6-10, 1995, Joint Meeting of the American Association of Veterinary Parasitologists/American Society of Parasitologists, Pittsburg, PA.

Fecal specimens (6,458 in total) were collected from dogs housed in animal shelters and analyzed by Dr. Byron L. Blagburn, Auburn University. The animal shelters were selected from the largest cities in each state. Fresh fecal specimens, collected individually into 120 ml plastic specimen cups were examined using the centrifugal sucrose flotation procedure. Specimen cups were placed in styrofoam shipping boxes containing "cold pack" inserts, and shipped to Dr. Blagburn's laboratory at Auburn University via overnight courier. Specimens could contain more than one type of parasite. Thus, the percentages presented below indicate the percent of specimens that contained the particular parasite and do not add to 100 percent.

Parasite	% of Total
Toxocara canis	14.5M
Toxascaris leonine	0.74
Ancylostoma caninum	19.20
Uncinaria stenocephala	1.00
Trichuris vulpis	14.30
Capillaria spp	0.40
Giardia spp.	0.60
Isospora spp.	4.80
Sarcocystis spp.	0.80
Hammondia spp.	0.06
Physaloptera spp.	0.05
Diplydium caninum	0.09
Taeniidae	0.60

Conclusion: Based upon the 99.4% efficacy demonstrated in the dose confirmation study, the 100% efficacy in the MT-147-00-89 Clinical Field Trial (including the probability albeit low that some of the roundworms may have been *Toxascaris leonina* cases), this data is adequate to support the expansion of the roundworm claim.

III. ANIMAL SAFETY

This supplemental NADA does not require re-evaluation of target animal safety data submitted in support of the initial NADA No. 140-915. Please refer to the original Freedom of Information Summary (NADA 140-915) for additional information on target animal safety studies.

IV. HUMAN SAFETY

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this supplemental NADA. The drug is to be labeled for use in dogs, which are non-food animals.

V. AGENCY CONCLUSIONS

The data in support of this supplemental NADA application complies with the requirements of Section 512 of the Act and Section 514.111 of the implementing regulations. It demonstrates that Interceptor® Flavor Tabs, when used under the labeled conditions of use, are safe and effective.

According to the Center's supplemental approval policy (21 CFR 514.106), this is a category II change. This supplement provides for an additional claim for the removal and control of the adult roundworm, *Toxascaris leonina*. This approval relied upon the safety and effectiveness data in the parent application and evaluation of new efficacy data submitted in the supplemental application.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act (FFDCA), this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval because the supplemental application contains reports of new clinical or field investigations (other than bioequivalence studies) essential to the approval of the application and conducted or sponsored by the applicant. The three years of marketing exclusivity applies only to the additional roundworm claim (*Toxascaris leonina*) for which the supplemental application was approved. This exclusivity period will expire three years from the date of the approval letter.

The drug is restricted to use by or on the order of a licensed veterinarian because professional expertise is required to determine the existence of hookworm roundworm and/or whipworm infection. In addition, professional expertise is required to determine the existence of heartworm infection, and then properly treat existing heartworm infection prior to starting treatment with Interceptor® (milbemycin oxime) Flavor Tabs in a prevention program.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.