I. GENERAL INFORMATION

A. File Number

NADA 141-008

B. Sponsor

Miles Inc.
Agriculture Division
Animal Health Products
Shawnee Mission, KS 66201

C. Proprietary Name

Drontal™ Tablets

D. Established Name

praziquantel + pyrantel pamoate

E. Dosage Form(s), Route of Administration, and Recommended Dosage

Drontal Tablets are to be administered as a single oral dosage (directly by mouth or offered in the food) as appropriate for the weight of the cat.

Scored tablets containing 18.2 mg praziquantel and 72.6 mg pyrantel base.

Body Weight* (Lb.)	Number of Tablets
1.5-1.9	¼
2-3	½
4-8	1
9-12	1½
13-16	2

* NOT FOR USE IN KITTENS LESS THAN ONE MONTH OF AGE OR WEIGHING LESS THAN 1.5 LBS.

The tablet formulation and dosage table were designed to provide the current approved dosage of praziquantel (Droncit®; Miles NADA No. 111-798) for 100% elimination of tapeworms and at least 20 mg/kg (9.09 mg/lb) pyrantel base for removal of hookworms and large roundworms.

F. Indication

Drontal Tablets will remove Tapeworms (Dipylidium caninum, Taenia taeniaeformis), Hookworms (Ancylostoma tubaeforme) and Large Roundworms (Toxocara cati) in kittens and cats.

II. EFFECTIVENESS

A. Reference to Droncit® (praziquantel) NADA

Praziquantel tablets are currently approved for use in cats for the removal of tapeworm infections (NADA No. 111-798). Data contained in the Droncit® NADA

are referenced to establish the efficacy of the praziquantel component in praziquantel/pyrantel tablets.

B. Pivotal Well-Controlled Laboratory Efficacy Studies.

Pyrantel pamoate administered at a dosage of at least 20 mg/kg (9.09 mg/lb) base was selected to provide efficacious removal of hookworms and large roundworms of cats. Two adequate and well-controlled laboratory studies were conducted to demonstrate that pyrantel does not interfere with the cestocidal activity of praziquantel for removal of tapeworms, to confirm that pyrantel is efficacious for the removal of hookworms and large roundworms of cats, and to demonstrate the combined formulation of praziquantel plus pyrantel provides efficacious removal of the parasites listed on the label.

A separate dose titration study to determine an optimal pyrantel pamoate dosage in cats was not necessary, as the sponsor documented efficacy of Drontal tablets of at least 90% for each parasite to be included in the labeling.

The following formulations were evaluated in the laboratory studies: Drontal Tablets was the formulation intended for the market.

Formulation and Dosage

Product	**Formulation**	**Dosage**
Pyrantel Tablets (Lab Study No. 1)	72.6 mg pyrantel base per tablet	20 mg/kg (9.09 mg/lb)
Drontal Tablets (Lab Study No. 1 and 2)	18.2 mg praziquantel + 72.6 mg pyrantel base per tablet (the formulation to be marketed)	5 mg/kg (2.27 mg/lb) praziquantel + 20mg/kg (9.09 mg/lb) pyrantel base
Placebo Tablets (Lab Study No. 1 and 2)	Blank (without active ingredient)	-

These studies were conducted in accordance with the FDA Canine/Feline Anthelmintic Guidelines. Parasite infections were diagnosed by fecal examinations prior to including the animals in each study. Each cat was then treated with the designated tablet formulation. Control cats in each study were treated with placebo (blank) tablets. The studies were blinded in that the investigators were not aware of the content of the tablet formulations until the studies were concluded. Seven days after treatment the cats were euthanized and the gastrointestinal tracts were removed and examined for all remaining parasites. Percent efficacy was calculated for each parasite species from the number of parasites recovered at necropsy using the following formula:

$$\frac{\text{Mean No.of Parasites in the Control Animals} - \text{Mean No.of Parasites in the Treated Animals}}{\text{Mean No.of Parasites in the Control Animals}} \times 100 = \text{Percent Efficacy}$$

Worm recovery data were analyzed statistically using nonparametric methodology.

1. Laboratory Study No. 1: Dr. L. Cruthers, Corapeake, N.C.

   The purpose of this study was to evaluate the efficacy of pyrantel pamoate alone and in combination with praziquantel for the removal of hookworms and large roundworms of cats. A total of 65 mixed-breed cats (23 males and 42 females), ranging in age from young cats to adults, ranging in weight from 1.1-4.6 kg with naturally acquired infections of *Ancylostoma tubaeforme* and *Toxocara cati* were included in the study. The cats were randomized into 3 groups. The cats received treatment with either pyrantel tablets, Drontal Tablets or placebo tablets (control). The number of parasites recovered from each group at necropsy and efficacy data are given in Table 1.

   Table 1. Summary of Efficacy: Laboratory Study No. 1

Treatment	**Controlled Percent Efficacy (No. of Cats Infected) *Ancylostoma tubaeforme***	**Controlled Percent Efficacy (No. of Cats Infected) *Toxocara cati***
Pyrantel Tablets	75.92 (18)	95.37 (18)
Drontal Tablets (the formulation to be marketed)	99.53 (20	89.0 (17
Control: [mean worms/cat]	[11.37] (20)	[17.25] (19)

   Conclusions: There were no significant differences between pyrantel and Drontal Tablets for removal of *A. tubaeforme* (P= 0.0906) or *T. cati* (P= 0.6151). The results of the study demonstrated the efficacy of Drontal Tablets against hookworms *(Ancylostoma tubaeforme)* and roundworms (*Toxocara cati*). Praziquantel did not interfere with the activity of pyrantel for removal of either parasite, as the efficacies for both parasites were high, 99.53% for *Ancylostoma tubaeforme* and 89% for *Toxocara cati*). The 89% (slightly less than the acceptable standard of 90% for anthelmintics) can be explained by biological variation, as laboratory study #2 (see below) showed efficacy of Drontal tablets against *T. cati* of 99.28%.

2. Laboratory Study No. 2: Dr. D. Bowman, Stanwood, MI

   The purpose of this study was to confirm that pyrantel pamoate does not interfere with the activity of praziquantel for tapeworm removal and to demonstrate the efficacy of the combined formulation of praziquantel plus pyrantel for treatment of tapeworm, hookworm and large roundworm infections of cats. A total of 28 mixed-breed cats (13 males and 15 females) of various sizes and aged young to adults with naturally acquired infections of *Taenia taeniaeformis* , *Ancylostoma tubaeforme* and *Toxocara cati* were included in the study. The cats were randomized into 2 groups. One group was treated with Drontal Tablets and the other group received placebo tablets (control). The number of parasites recovered from the two groups at necropsy and efficacy data are given in Table 2.

Table 2. Summary of Efficacy: Laboratory Study No. 2

Treatment	**Controlled Percent Efficacy (No. of Cats Infected)** ***Taenia taeniaeformis***	**Controlled Percent Efficacy (No. of Cats Infected)** ***Ancylostoma tubaeforme***	**Controlled Percent Efficacy (No. of Cats Infected)** ***Toxocara cati***
Drontal Tablets (the formulation to be marketed)	100.0 (13)	98.10 (4)	99.28 (9)
Control: [mean worms/cat]	[7.0] (9)	[13.14] (7)	[17.8] (12)

Conclusions: Statistically significant differences in the worms remaining at necropsy were observed between the Drontal Tablet and the control group ($P < 0.0001$). The data demonstrated that when given as indicated, Drontal Tablets are efficacious for the removal of *Taenia taeniaeformis, Ancylostoma tubaeforme* and *Toxocara cati* in cats.

Summary of the Well Controlled Laboratory Studies

The laboratory efficacy studies provided the following:

1. A pyrantel dosage of 20 mg/kg provided efficacious removal of hookworms and large roundworms in cats.
2. Pyrantel did not interfere with the activity of praziquantel against tapeworms.
3. Praziquantel did not interfere with the activity of pyrantel against hookworms or large roundworms.
4. The combination of pyrantel with praziquantel provided effective removal of tapeworms, hookworms and large roundworms in cats.

3. Pivotal Clinical Trial

A clinical trial was conducted with a common protocol by investigators at 6 geographic locations in the United States to provide additional information regarding the performance of Drontal Tablets. The investigators are listed below:

Investigator	**Location**
Dr. S.F. Cheesman	Pine Bluff, AR
Dr. R. Clark	Benton, IL
Dr. J. Durling	Ft. Scott, KS
Dr. T. Lamp	Bellville, TX
Drs. R. Mauldin and C. Moe	Oklahoma City, OK
Dr. J. Strothers	Hartselle, AL

The purpose of this trial was to evaluate the efficacy and safety of Drontal Tablets for treatment of cats naturally infected with tapeworms plus

hookworms or large roundworms under practical conditions. Pretreatment fecal samples from each cat were examined microscopically for diagnosis of the parasite infections. Each animal served as its own control. The investigators were provided with Drontal Tablets containing 18.2 mg praziquantel and 72.6 pyrantel base as pyrantel pamoate per tablet (the formulation to be marketed).

Each cat was weighed prior to treatment and the following schedule was then utilized to determine the number of whole or one-half tablets for each cat based on body weight.

Body Weight (Lbs)	**Number of Tablets**
2-3	½
4-8	1
9-12	1½
13-16	2

This schedule provided a dosage range of 5-10 mg/kg (2.27 - 4.54mg/lb) praziquantel plus 20-40 mg/kg (9.09 - 18.18 mg/lb) pyrantel base. The tablets were given directly by mouth as a single treatment.

A post-treatment fecal sample was collected from each cat 7 - 10 days following treatment and examined for nematode eggs using the same flotation procedure used for pretreatment. Percent reduction of the fecal egg count was recorded.

In addition, feces from each cat were examined closely on Days 5, 6 and 7 after treatment for the presence of tapeworm proglottids. Any proglottids observed at this time were to be identified by the investigator.

A total of 85 cats (44 males and 41 females) were treated with Drontal Tablets. The cats ranged from the age of one month to 14 years with a weight range of one to sixteen pounds. The cases included a variety of breeds while domestic short hair, domestic, or mixed-breed were the most common, 94.4%. Efficacy evaluation was based upon 84 fully completed cases (post-treatment efficacy evaluation was not available for one of the cats). The number of parasite infections treated and the post-treatment reduction of the mean egg counts are given in Table 3.

Other animal health products were administered concurrently to 33 of the cats with no apparent incompatibility. These products were primarily antibiotics, insecticides, and immunizations.

Table 3. Drontal Tablet Clinical Trial Efficacy Results

Parasite	**Number of Infections Treated**	**Post-Treatment % Reduction of Mean Egg Counts or Presence of Proglottids**	**% of Cases Cleared to Zero (at 7 days post-Tx)**
Tapeworm - *Taenia taeniaeformis*	6	100	100
Tapeworm - *Dipylidium caninum*	78	100	100
Hookworm - *Ancylostoma tubaeforme*	61	98.5	98.4
Large Roundworm - *Toxocara cati*	51	98.3	94.1

Conclusion: Drontal Tablets were efficacious for the removal of tapeworms, hookworms and large roundworms of cats.

Summary of the Clinical Trial Results

The results of the pivotal clinical trial confirmed the data collected during the two pivotal laboratory efficacy studies. The recommended treatment dosage of Drontal Tablets was found to be safe and efficacious for the parasite species indicated on the label under conditions of practical use.

4. Corroborative Efficacy Studies

   a. Drs. C.R. Reinemeyer and R.C. DeNovo, Knoxville, TN

      Twenty-four cats were included in a controlled study to evaluate the efficacy of pyrantel pamoate for removal of naturally acquired *A. tubaeforme* and *T. cati* infections. Eight cats each received either pyrantel pamoate paste or granules at a dosage of 20 mg/kg. Eight cats did not receive medication and served as controls. The cats were euthanized 7 days after treatment and examined for all remaining gastrointestinal nematodes. The paste formulation was 100% efficacious for the removal of *A. tubaeforme* and 93.5% efficacious for the removal of *T. cati* . Pyrantel pamoate granules removed 100% of the *A. tubaeforme* and 88.9% of the *T. cati* . The control cats at necropsy harbored means of 29.5 and 19.1 *A. tubaeforme* and *T. cati* per cat, respectively.

   b. Drs. P. Hedeman and T. Hopkins, Bahrs Hill, Australia

      Nine kittens 3-4 months of age were included in a critical anthelmintic study to evaluate efficacy of praziquantel + pyrantel tablets against

experimental *A. tubaeforme* infections. The kittens were each experimentally infected with 200 infective *A. tubaeforme* larvae. Twenty-four days after the experimental infections the kittens were given praziquantel + pyrantel tablets to provide 5 mg/kg praziquantel + 20 mg/kg pyrantel base. All feces were collected from each kitten and examined for eliminated worms for 4 days after treatment. The kittens were then euthanitized and examined for all worms remaining in the gastrointestinal tract. The praziquantel + pyrantel treatments were 94.4% efficacious for removal of *A. tubaeforme* .

c. Overall Efficacy Summary

A total of 93 cats with naturally acquired parasite infections were included in two well-controlled laboratory studies to establish the efficacy of Drontal Tablets. In addition, 85 cats and kittens of various sizes, ages and breeds were included in clinical field studies conducted at six veterinary clinics at different geographic locations throughout the United States. Data indicate most cats are cleared of their parasite infections within 7 days of treatment. These studies demonstrated Drontal Tablets are safe and efficacious for the removal of the parasite species indicated on the label when used as directed.

III. TARGET ANIMAL SAFETY

A. Pivotal Studies

Two preclinical safety studies were conducted in cats with the praziquantel/pyrantel pamoate tablet formulation in accordance with Good Laboratory Practice Regulations.

1. Drug Tolerance Test (Drug Tolerance Test for the use of Praziquantel/Pyrantel Tablets in Cats)

M. Kohlenberg of Shawnee Mission, Kansas conducted a drug tolerance evaluation in 3 adult cats (one male gray tabby and two females, a domestic longhair and a gray tabby) with the 18.2mg praziquantel/72.6mg pyrantel pamoate tablet. This evaluation determined the effects of administering 10 times the highest use rate of the tablet formulation in a single day. One male and one female cat received the treatment and the female control received an equivalent number of placebo tablets. The study was blinded because the individuals making clinical observations were not aware of the respective treatments. Further, the laboratories conducting the clinical chemistry/hematology evaluations and histological readings were not informed of the treatments. Parameters of the study included clinical signs, body weights, clinical chemistries, hematology, gross pathology and histopathology. The study concluded 7 days post-treatment. Vomition and salivation were the only clinical signs observed. Body weights remained stable. The post-treatment serum chemistry and hematology values were all within the normal ranges. The lesions (reddened or thickened urinary bladders, fallopian tube cyst, moderate redness of the lungs, hairballs, and kidneys firm to the cut) were observed at necropsy. None of these lesions were associated with

administration of Drontal tablets. All tissues were within normal limits histologically. Statistical analyses were unnecessary to the conclusions. It was concluded from this study that a single treatment of cats with this praziquantel/pyrantel pamoate formulation at 10 times the highest label use rate can induce vomition and salivation without other adverse effects. The results are summarized in Table 4.

Table 4. Drug Tolerance Test

Number of Animals	**Treatment Rate praziquantel/pyrantel mg/kg**	**Results**
1 female	Control (Placebo Tablets)	Normal
1 femals	100/400 mg/kg	Vomition at 1 hour post-treatment
1 male	100/400 mg/kg	Post-treatment; salivation at 1 and 2 hours

2. General Safety Evaluation (General Safety Evaluation for Use of Praziquantel/Pyrantel Tablets in Cats)

Group	**Animal #**	**Description**	**Sex**	**Initial Wt. (kg)**	**Tablet #**	**mg/kg**
I – nontreated controls	647	DSH	Female	2.86	-	-
I – nontreated controls	693	DSH	Female	3.01	-	-
I – nontreated controls	719	DSH	Neutered	4.91	-	-
I – nontreated controls	808	DSH	Male	3.63	-	-
II – 1X (use rate for 3 days)	686	DSH	Female	3.07	1	5.9/23.6
II – 1X (use rate for 3 days)	689	DSH	Male	3.68	1.5	7.4/29.6
II – 1X (use rate for 3 days)	725	DSH	Neutered	4.61	1.5	5.9/23.6
II – 1X (use rate for 3 days)	800	DSH	Female	2.70	1	6.7/26.9
III – 3X (use rate for 3 days)	690	DSH	Male	4.40	4.5	18.6/74.3
III – 3X (use rate for 3 days)	691	DLH	Female	2.55	3	21.4/85.4
III – 3X (use rate for 3 days)	692	DSH	Female	3.37	3	16.2/64.6
III – 3X (use rate for 3 days)	720	DSH	Neutered	3.73	4.5	22.0/87.6
IV – 5X (use rate for 3 days)	642	DSH	Female	2.20	5	41.4/165.0
IV – 5X (use rate for 3 days)	682	DSH	Female	3.54	5	25.7/102.5
IV – 5X (use rate for 3 days)	696	DSH	Male	3.93	7.5	34.7/138.5

M. Kohlenberg also conducted a general safety study in 16 adult cats of various breeds using the 18.2/72.6 mg tablet. Four of the cats, Group I, were nontreated controls. Groups II, III and IV (4 animals/group) received 1, 3 and 5 times the recommended use rate, respectively, for 3 consecutive days (3 times the labeled duration of treatment). Parameters evaluated were clinical signs, body weights, hematology, clinical chemistries, necropsy observations and histological readings. The study was completely blinded for the clinical sign observations, clinical laboratory procedures and histological readings.

Body weights were stable during the study. One incident of vomition and one of nonformed stool were obvserved in the nontreated control animals. No clinical signs were observed in the cats receiving use rate reeatments for the 3 days. Two of the 4 cats receiving 3X treatments had signs of vomition and an additional animal had diarrhea on one occasion. All 4 cats treated at the 5X rate showed vomition. Cat #720 from Group III had an elevated glucose value of 236 mg/dl (normal range of 60-125 mg/dl) 5 days post-treatment. Cat # 690 from Group III had an elevated CPK value of 1442 U/L (normal range of 45-890 U/L) 5 days post-treatment. These elevated values were not directly asociated with test aritcle administration, as other cats in this dosage group were not affected and the 5X group did not have elevated values (no post-treatment clinically significant trends). The group mean values for the hematology and clinical chemistry parameters when compared to the pretreatment values or to those of the nontreated controls were not elevated. None of the findings at necropsy (see below) or upon histological examination were judged to be directly related to administration of Drontal tablets. Statistical analyses, therefore, were unnecessary to the conclusions. It was concluded from this study that an adequate safety margin exists for the treatment of cats with a combination praziquantel/pyrantel tablet based upon these treatments of use rate, 3 times use and 5 times use rate for 3 times the labeled duration. The data are summarized in Table 5.

Gross Pathology Findings

Redness of the lungs and urinary bladder mucosa was noted in 14 of the 16 cats, including the control group.

Cat # 682 (5X) had a dark, firm area in the lung measuring 1/4 inches by 1/8 inches. The cat also showed slight mucosal redness to the urinary bladder and slight redness of the cortex of the kidney.

Cat # 690 (3X) showed a growth approximately 5 millimeters thick which covered the entire mucosal surface of the bladder. There was also mild to marked redness of the mucosal surface.

Cat # 691 (3X) showed a reddened cortex and medulla of the kidney.

Cat # 698 (5X) had a slightly reddened kidney cortex.

Cat # 720 (3X) had slightly bloody urine at necropsy. No lesions were seen in the bladder itself.

Histopathology

The consulting veterinary pathologist stated that there were no histopathologic changes found in any of the cats that would be interpreted to be treatment related.

Table 5. General Safety Evaluation

Number of Animals	Treatment Rate	Results
4	Control	Once incident of vomition and one nonformed stool
4	Use Rate for 3 Days	Normal
4	3X Use Rate for 3 Days	Two of 4 had signs of vomition and one of diarrhea
4	5X Use Rate for 3 Days	Four of 4 had signs of vomition

3. Confirmation of Safety in Clinical Field Trials

   Confirmation of safety for the use of Drontal Tablets (praziquantel/pyrantel pamoate) for cats was achieved in clinical field trials. Six veterinary clinics in various geographical locations completed safety evaluations for 85 case reports. The cats were in an age range of one month to 14 years with a weight range of one to 16pounds. Both males (44) and females (41) were included and the cases included a variety of breeds while domestic short hair, domestic, or mixed-breed were the most common, 94.4%. Other animal health products were administered concurrently to 33 of the cats with no incompatibility. These products were primarily antibiotics, insecticides and immunizations. The clinical veterinarians rated overall safety as excellent for 83 of the cases (97.6%) with 2 of the cases (2.4%) rated good. No cases were rated as fair or poor. Of the 2 cases rated good, one owner observed loose stools from the cat 6 - 7 days following treatment and another owner indicated the cat had loss of appetite after treatment. In conclusion, the clinical field trial safety evaluations substantiated an adequate safety margin for the treatment of cats with Drontal Broad Spectrum Wormer Tablets.

B. Corroborative Safety Studies

Reference is made to an NADA containing one of the components. Additionally, clinical field trial safety studies were conducted at veterinary clinics in various geographical areas of the United States.

1. Reference to NADA 111-798

   Safety for the treatment of cats with a tablet formulation of praziquantel was evaluated and presented in NADA 111-798. This NADA concerned Droncit® Feline Cestocide Tablets and contained 5 preclinical safety studies conducted by GLP regulations. It further presented clinical field trial data for the treatment of 135 cats.

2. Drs. C.R. Reinemeyer and R.C. DeNovo, Knoxville, TN

   Thirty kittens between 4 and 6 weeks of age were included in a controlled study to evaluate the safety of pyrantel pamoate. Ten kittens received 100 mg/kg pyrantel pamoate paste for 3 consecutive days and 10 kittens received

the same dosage of pyrantel pamoate granules for 3 days. Ten kittens were untreated and served as controls. Kittens were weighed and complete physical examinations were performed 7 days before and 4 and 10 days after the initial treatment. No abnormal physical or clinical observations were noticed following 3 treatments with 5 times the recommended dose of pyrantel pamoate.

C. Overall Safety Summary

Cats treated with 10 times the highest recommended Drontal Tablet dosage during safety studies showed signs of vomition and salivation without other adverse effects. Eighty-three of 85 cats treated with the recommended dosages of Drontal Tablets in a clinical field study did not exhibit any drug related side effects. A temporary loss of appetite was reported for one cat and transient loose stools were observed in a second cat.

IV. HUMAN FOOD SAFETY

A. Human Food Safety

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this NADA. The formulation is labeled for use in cats only.

B. Safety Relative to Possession, Handling and Administration

The label contains an adequate warning statement: "WARNING: KEEP OUT OF REACH OF CHILDREN"

V. AGENCY CONCLUSIONS

GUIDELINE FOR DRUG COMBINATIONS FOR USE IN ANIMALS

Both of the drugs in this combination are approved individually, praziquantel for dogs and cats, and pyrantel pamoate for dogs. Safety and efficacy information is available on both components of this combination. There are no known safety or efficacy issues pending with regard to either pyrantel pamoate or praziquantel. Miles, Inc. owns the safety data for praziquantel and the combination praziquantel and pyrantel pamoate. It does not own the safety information for pyrantel alone. It does own efficacy data for both component drugs.

The Guideline for Drug Combinations is generally applied to new drug formulations. The Guideline states that a 2-way combination must be better than either drug used alone. In this application, the firm did not utilize a praziquantel alone treatment group, however 100% efficacy was achieved against tapeworms and reference was made to the firm's approved NADA 111-798 for this drug. Praziquantel is not effective alone against roundworms or hookworms [reference to NADA 133-953 (sponsored by Miles, Inc.) for dogs in which 2.4% efficacy was achieved against *Ancylostoma caninum* (hookworm) and 0% efficacy against *Toxocara canis* (roundworm)] . Pyrantel pamoate is not effective alone against cestodes as documented in the following references: 1) Howes, H.L. and Lynch, J.E. Anthelmintic Studies with Pyrantel. I. Therapeutic and Prophylactic Efficacy Against the Enteral Stages of

Helminths in Mice and Dogs, **Journal of Parasitology** 53(5), 1967, pp. 1085-1091, 2) Lindquist, W.D. Drug Evaluation of Pyrantel Pamoate Against Ancylostoma, Toxocara, and Toxascaris in Eleven Dogs, **American Journal of Veterinary Research**, Vol. 36, No. 9, Sept. 1975, 3) Todd, A.C., Crowley, J. Jr., Scholl, P., Conway D.P. Critical Test with Pyrantel Pamoate Against Internal Parasites in Dogs from Wisconsin, **Veterinary Medicine/Small Animal Clinician**, 1975 (8), pp. 936-939, 4) Booth and McDonald, **Veterinary Pharmacology and Therapeutics**, Iowa State University Press, Ames Iowa, 1982, p. 828.

The dosage of pyrantel was determined from the approved products containing pyrantel pamoate and the sponsor confirmed this dosage against roundworms and hookworms at a minimum of 90% efficacy.

The sponsor provided evidence that each ingredient designated as active in the combination made a contribution to the effect in the manner claimed or suggested in the labeling. There is no evidence to suggest the possible interference of praziquantel with the effects of pyrantel pamoate, or the interference of pyrantel pamoate with the effects of praziquantel.

The benefits of this drug combination are that multiple parasite species are treated with an easily administered tablet, which is safe and effective enough to be marketed OTC.

In conclusion, the 2-way combination of praziquantel and pyrantel pamoate is better than either drug used alone for the parasites in which efficacy has been demonstrated. Therefore, the 2-way combination meets our requirements for approval.

FINAL CONCLUSIONS:

The data submitted in support of this NADA complies with the requirements of Section 512 of the Federal Food, Drug and Cosmetic Act and Section 514.111 of the implementing regulations. The data demonstrate that Drontal (praziquantel + pyrantel pamoate) Tablets are safe and efficacious when used as directed.

Under section 512(c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act, this approval for non-food producing animals qualifies for THREE years of marketing exclusivity beginning on the date of approval because the 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.

Parasitological surveys indicate cats and kittens are commonly infected with tapeworms plus intestinal nematodes. Tapeworms shed many proglottids in the feces which the general public can adequately diagnose. Praziquantel has been marketed for more than 10 years for the treatment of tapeworm infections in dogs and cats and currently has approval for marketing over-the-counter (OTC). There are no known contraindications to the use of praziquantel in cats. Pyrantel pamoate has been shown to be safe and efficacious for the removal of hookworm and large roundworm infections in cats at a dosage of 20 mg/kg. Drontal has an acceptable safety margin for cats since vomiting and salivation were the only significant side effects noted in animals treated with 10 times the labeled dosage rate.

The labeling contains adequate directions for use which were written for the layman. It is reasonably certain that the conditions of use prescribed, recommended, or suggested in the proposed labeling will be followed in practice. The effective use of Drontal tablets assumes that an accurate diagnosis can be made with a reasonable degree of certainty, including the diagnosis of tapeworm infections, how cats acquire hookworm and large roundworm infections, the proper administration of Drontal Tablets, and methods to prevent reinfection with parasites. The label contains directions for the lay person to consult their veterinarian before administration to a sick or pregnant animal and for assistance in the precise diagnosis, treatment, and control of parasites. The drug is therefore approved for OTC distribution.

VI. ATTACHMENTS

Drontal(TM) (praziquantel/pyrantel pamoate) Tablets 10 tablet bottle label
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets package insert
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets 10 tablet poly bag
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets inner shipper stencil
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets outer shipper stencil
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets 50 tablet bottle label
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets fix-a-form insert
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets 150 tablet bottle label
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets foil strip front and back
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets dispensing envelope
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets package insert
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets foil strip dispensing carton
Drontal(TM) (praziquantel/pyrantel pamoate) Tablets shipper stencil

Copies of these labels may be obtained by writing to the:

Freedom of Information Office
Center for Veterinary Medicine, FDA
7500 Standish Place
Rockville, MD 20855