Approval Date: November 14, 1978

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 101-331

B. Sponsor

Ralston Purina Co.
Checkerboard Square
St. Louis, MO 63188

C. Proprietary Name

Dog Wormer Tablets

D. Established Name

pyrantel pamoate

E. Dosage Form

Purina Dog Wormer Tablets are formulated in three sizes of oral tablets at concentrations of 22.7 mg., 45.4 mg. and 113.5 mg. pyrantel base as pyrantel pamoate per tablet.

F. Dosage Regimen

22.7 mg pyrantel base as pyrantel pamoate tablet 1 tablet per each 10 lbs of dog body weight.

45.4 mg pyrantel base as pyrantel pamoate tablet 1 tablet per 20 lbs of dog body weight. Tablet may be broken in half to provide 1/2 tablet for 10 lbs body weight.

113.5 mg pyrantel base as pyrantel pamoate tablet 1 tablet per 50 lbs of dog body weight. Tablet may be broken in half to provide 1/2 tablet for 25 lbs of body weight.

Label directions are designed to provide a minimum of 2.27 mg pyrantel base per pound body weight for dogs weighing more than 5 pounds body weight, and 4.54 mg pyrantel base per pound body weight for dogs weighing 5 lbs or less.

Tablets are scored to facilitate breaking of tablet for more accurate dosage.

G. Route of Administration

Pyrantel pamoate oral tablets are administered orally by placing the tablet in a small amount of meat to be hand fed to the dog or by placing the tablets directly into the back of the dog's mouth.

H. Indication

For the removal of large roundworms (ascarids), *Toxocara canis* and *Toxascaris leonina* and hookworms, *Anyclostoma caninum* and *Uncinaria stenocephala* in dogs.

The presence of these parasites should be confirmed by laboratory fecal examination. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

II. EFFECTIVENESS

A. Dosage Titration

It has been established in critical efficacy evaluations, control critical efficacy evaluations, and clinical nematode egg count studies that pyrantel pamoate at 2.27 mg pyrantel base/lb of body weight for dogs weighing more than 5 lbs body weight and 4.54 mg pyrantel base/ lb of body weight for dogs weighing less than 5 lbs body weight, administered orally to dogs, is safe and effective for the removal of large roundworms (ascarids) and hookworms as cited above.

The basic titration data supporting the dosage of 2.27 mg/lb (5 mg/kg) is contained by cross reference in Pfizer Inc's. approved NADA 100-237, Pyrantel Pamoate oral suspension. A letter of authorization dated May 20, 1975 from Pfizer is contained in NADA 101-331 for Ralston Purina to refer to NADA 100-237 for data supporting safety and efficacy of pyrantel pamoate.

Newer information gathered from specific studies with Pyrantel pamoate tablets indicated a somewhat higher dosage (4.54 mg/lb) is required in dogs weighing less than 5 pounds. Since no greater risk of toxicity would be present from this increased level, it was decided to provide in the labeling for the administration of one full 22.7 milligram tablet to dogs 10 pounds and under in order to insure satisfactory efficacy in the smaller animals.

B. Critical Laboratory Studies

In compliance with 21 CFR 514.111(a)(5)(vi) for controlled studies, the following adequate and well-controlled critical evaluations were conducted with the market product:

1. Trial

   R.P. Experiment #26 - University of Wisconsin

   a. Investigator:

      A.C. Todd, Ph.D.

   b. Institution

      Department of Veterinary Science
      University of Wisconsin
      Madison, Wisconsin

   c.Type of Investigation:

      Control Critical Efficacy Evaluation

d. Design of Investigation:

Ten dogs infected with *T. canis* were individually penned and treated with pyrantel pamoate oral tablets at the target dose level of 5 mg pyrantel base/kg of body weight.

Ten dogs were held as sham dosed controls.

All worms passed for 96 hours after treatment were recovered for identification and enumeration. The dogs were euthanized and the worms remaining in the intestinal tract recovered for identification and counted.

Criteria for pyrantel pamoate effectiveness was determined by comparing the number of worms eliminated in the feces versus the total number of worms eliminated in the feces plus those remaining in the gastrointestinal tract at necropsy.

e. Findings:

An average percent reduction of 81% was obtained in the ten treated dogs. Four-tenths percent reduction in the worm burden of the 10 control dogs occurred at the same time.

2. Trial

R.P. Experiment

a. Investigator:

C.W. Dickerson, M.S.

b. Institution

Ralston Purina Co. Research Farm

c.Type of Investigation:

Control Critical Efficacy Evaluation.

d. Design of Investigation:

Ten dogs infected with *Uncinaria Stenocephala* were individually penned and treated with pyrantel pamoate oral tablets at the target dose of 5 mg pyrantel base/kg of body weight (2.27 mg/lb).

Ten dogs were held as sham dosed controls.

All worms passed for 96 hours after treatment were recovered for identification and enumeration. The dogs were euthanized and the worms remaining in the intestinal tract recovered for identification and counted.

Criteria for pyrantel pamoate effectiveness was determined by comparing the number of worms eliminated in the feces versus the total number of worms eliminated in the feces plus those remaining in the gastrointestinal tract at necropsy.

e. Findings:

An average percent reduction of 88.6% was obtained in the ten treated dogs. 0.5% reduction in the worm burden of the 10 control dogs was observed concurrently. When worm burdens from treated dogs was compared to worm burdens of control dogs at necropsy an efficacy of greater than 95% was calculated for the drug.

The following partially-controlled critical laboratory studies were conducted in addition to the above two well-controlled evaluations:

1. Trial:

R.P. Experiments # 1 through # 11

a. Investigator:

C.W. Dickerson, M.S.

b. Institution:

Ralston Purina Co.
Research Farm
Gray Summit, MO

c.Type of Investigation:

Critical Efficacy Evaluations

d. Design of Investigation:

A total one-hundred and thirteen dogs infected with varying combinations of ascarids and hookworms were individually penned and treated with pyrantel pamoate oral tablets at the target dose level of 2.27 mg pyrantel base/lb of body weight. A total of sixteen dogs were retained as unmedicated controls.

All worms passed for 96 hours after treatment were recovered for identification and enumeration. The dogs were euthanized and the worms remaining in the intestinal tract recovered for identification and counted.

Criteria for pyrantel pamoate effectiveness was determined by comparing the number of worms eliminated in the feces versus the total number of worms eliminated in the feces plus those remaining in the gastrointestinal tract at necropsy.

e. Findings:

Pyrantel pamoate was highly efficacious at the target dose of 2.27 mg pyrantel base/lb against *T. canis* (95%), *T. leonina* (98%), *A. caninum* (96%), and *U. stenocephala* (92%7.

2. Trial

R.P. Experiment #12 - Kansas State

a. Investigator:

W.D. Lindquist, D.Sc.

b. Institution:

Department of Infectious Diseases
College of Veterinary Medicine
Kansas State University
Manhattan, Kansas

c.Type of Investigation:

Critical Efficacy Evaluation

d. Design of Investigation:

Eleven dogs infected with varying combinations of ascarids and hookworms were individually penned and treated with pyrantel pamoate oral tablets at the target dose level of 2.27 mg pyrantel base/lb or body weight.

All worms passed for 72 hours after treatment were recovered for identification and enumeration. The dogs were euthanized and the worms remaining in the intestinal tract recovered for identification and counted.

Criteria for pyrantel pamoate effectiveness was determined by comparing the number of worms eliminated in the feces versus the total number of worms eliminated in the feces plus those remaining in the gastrointestinal tract at necropsy.

e. Findings:

Pyrantel pamoate was highly efficacious at the target dose of 2.27 mg pyrantel base/lb against *T. canis* (90%), *T. leonina* (92%), and *A. caninure* (99%).

C. Clinical (Field) Studies

1. Trial

R.P. Experiment #18

a. Investigator:

William M. Stone, M.S.

b. Institution:

Veterinary Diagnostic and Investigational Laboratory
School of Veterinary Medicine
University of Georgia
Tifton, Georgia

c. Type of Investigation:

Clinical nematode egg count

d. Design of Study:

Thirteen racing Greyhounds were medicated with pyrantel pamoate oral tablets at the target dose level of 2.27 mg pyrantel base/lb or body weight. Fecal samples were obtained for nematode egg counts on day 4.

e. Findings:

Pyrantel pamoate was highly efficacious (97%) against hookworm infections.

2. Three (3) clinical trials were conducted with Purina Dog Wormer Tablets which included 33 treated dogs. No signs of toxicity or other related side effects were noted.

a. First trial

William A. Krumrey, D.V.M.
Yorkshire Animal Hospital
8088 Watson Road
St. Louis, Missouri 63119

Treated twelve (12) dogs between August 21, 1974, to October 1, 1974. All were totally cleared of Ascarids and/or hookworm eggs following treatment.

b. Second trial

John C. Eckert, D.V.M.
Concord Animal Hospital
11705 Concord Village Avenue
St. Louis, Missouri 63128

Treated twelve (12) dogs between August 29, 1974, to October 28, 1974. Five (5) of seven (7) dogs treated were totally cleared of Ascarids and for hookworms eggs following treatment. Five (5) dogs were either not infected or no post treatment fecal sample was obtained.

c. Third trial

Suzanne Saueressig, D.V.M.
Humane Society of Missouri
1210 Macklind Avenue
St. Louis, Missouri 63110

Treated nine (9) dogs between August 26, 1974 and November 16, 1974 Of the two (2) dogs trested in which post-treatment examinations were made, one roundworm and two hookworm infections were controlled.

The field studies described above were open evaluations and not in direct compliance with 21 CFR 514.111(a)(5)(vi) for controlled comparisons. Accordingly, the requirement for controlled field evaluations was waived by the agency. The basis for waiver is that the results of the critical laboratory trials are considered to be adequate to establish the effectiveness of the product.

At the time of conduct of these trials, several years ago, controlled field studies were not a recommended or required procedure.

As a result, in addition to the limited trials outlined above, several hundred other animals were dosed with either pyrantel pamoate tablets or suspension in individual field evaluations. These studies were primarily designed to assess the clinical safety of the formulations and not so much the actual efficacy of the drug. As stated previously, critical anthelmintic measurements provide more substantial and objective evidence on the effectiveness of a compound, than do non-critical observations.

D. Supportive Data:

In addition to the above studies, critical efficacy evaluations were conducted with a susupension formulation of pyrantel pamoate, covered by NADA 100-237. A total of 5 additional studies involving 90 critical efficacy observations with the suspension were submitted to support the effectivemess of the tablet formulation of pyrantel pamoate for dogs. The results of these related efficacy studies with the suspension formulation are summarized in Table 1 and compared to the efficacy results obtained for the tablets which were reported induvidually above. Foreign critical and clinical trials are contained in the cross-referenced NADA 100-237 as supportive information.

The names and addresses of investigators conducting the related safety and efficacy studies are presented Table 2.

III. TARGET ANIMAL SAFETY

Animal safety of pyrantel pamoate oral dosage forms has been adequately demonstrated per Pfizer, Inc. approved NADA 100-237. Pfizer, Inc. provided authorization to Ralston Purina Company on May 20, 1975 to refer to safety data contained in Pfizer, Inc. NADA's 091-739, 100-237 and 016-883 in support of NADA 101-331 on page 00035.

IV. HUMAN FOOD SAFETY

Pyrantel pamoate oral tablets are indicated for use only in non-food producing animals. The risk of toxicity from accidental human exposure is considered low since it is intended for limited dosing. The drug is approved for use in humans and is considered to have a wide margin of safety.

V. AGENCY CONCLUSIONS

The data submitted in support of this NADA complies with the requirements of 512 of the Act and demonstrate that Purina Dog Wormer Tablets when used under its proposed conditions of use is safe and effective for the treatment of roundworm and hookworm infection in dogs.

TABLE 1 Worm Count Summary

COMPARATIVE EFFICACY OF PYRANTEL PAMOATE ORAL DOSAGE FORMULATIONS*

PARASITE	FORMULATION	NO. DOGS	TOTAL NO. WORMS.** -PASSED	TOTAL NO. WORMS.** - RECOVERED	PERCENT EFFICACY
T. canis	Tablet	99	1,506	309	83
	Suspension	28	178	27	85
	Sum	127	1,684	336	83
T. leonina	Tablet	37	1,670	31	98
	Suspension	10	216	1	99
	Sum	47	1,886	32	98
A. caninum	Tablet	115	6,022	265	96
	Suspension	50	1,574	40	99
	Sum	165	7,596	305	96
U. stenocephala	Tablet	29	5,789	680	89
	Suspension	20	379	26	94
	Sum	49	6,168	706	90

*Dosage rate of 2.27 mg. base/lb. of body weight.

**Worms passed after treatment (96 hr.) and recovered in the intestinal tract at necropsy.

TABLE 2

Names and Locations of Investigators Who Participated in Related Efficacy (Suspension Formulation) and Safety Evaluation Programs

Name and Address	**# of Studies**	**Type of Studies**
C.W. Dickerson. M.S.	7	Clinical Safety Evaluation
Ralston Purina Research Farm Gray Summit. Missouri	1	Clinical Reproductive Safety Evaluation
D.P. Conway, Ph.D. Pfizer, Inc. Terre Haute, Ind.	1	Clinical Safety Evaluation
R.R. Rainier. D.V.M. 2821 Bee Ridge Road Sarasota, Fl.	1	Clinical Safety Evaluation
E. Schobert. D.V.M. 14212 Florida Avenue Tampa, FL	1	Clinical Safety Evaluation
N.L. Williams. D.V.M. East Side Animal Hospital 357 Edgewood S. E. Atlanta, GA.	1	Clinical Safety Evaluation
Pat Riggins. D.V.M. 2907 Buick-Cadillac Blvd. Bloomington. In.	1	Clinical Safety Evaluation
M.G. Shew, D.V.M. Shew Veterinary Clinic Seelyville. In.	1	Clinical Safety Evaluation
F.M. Lee, D.V.M. Archer Memorial Hospital 3122 Wallace Avenue Terre Haute, In.	1	Clinical Safety Evaluation
L. Dorner, D.V.M. Laboratory Research Enterprises, Inc. Kalamazoo, MI	2	Clinical Reproductive Safety Evaluation
W. Stone. M.S. Vet. Diag. & Invest. Lab. Tifton, GA. 31794	2	Clinical Safety Evaluation
J. Flipo, D.V.M. U. Montreal School of Vet. Med. St. Hyacinthe P.Q.	1	Clinical Safety Evaluation
J.F. Lautenslager, D.V.M. Vet. Ser. Branch Ontario Dept. Agric. & Food, Guelph, Ont.	1	Clinical Safety Evaluation

Name and Address	**# of Studies**	**Type of Studies**
G A. McGowan. D.V.M. 431 Pitt Street Cornwall, Ont.	1	Clinical Safety Evaluation
J.B. Millington, D.V.M. 45 Woodlawn Road Guelph, Ont.	1	Clinical Safety Evaluation
GA.. Call, D.V.M. A.T. O'Connor, D.V.M Stouffville Vet. Clinic Stouffville. Ont.	1	Clinical Safety Evaluation
Drug Safety Evaluation	1	Acute Toxicity
Medical Research Laboratories Groton, Connecticut 06340	1	Safety Evaluation with Organophosphates
Drug Safety Evaluation Pfizer Ltd. Sandwich, Kent England	3	Subacute and Chronic Toxicity
Dr. Kenneth A. Larsen Bioresearch Laboratories P.O. Box 2211 Fort Collins, CO	1	Safety Evaluation with Chlorinated Hydrocarbons

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