Date of Approval: April 18, 2005

FREEDOM OF INFORMATION SUMMARY

Supplemental NADA 200-342

Pyrantel Pamoate Paste

(Pyrantel Pamoate)

Pyrantel Pamoate Paste (pyrantel pamoate) is indicated for the removal and control of mature infections of large strongyles (*Strongylus vulgaris, S. edentatus, S. equinus*); small strongyles; pinworms (*Oxyuris equi*); large roundworms (*Parascaris equorum*) and tapeworms (*Anoplocephala perfoliata*) in horses and ponies.

Sponsored by:

Phoenix Scientific Inc.
3915 South 48th Street Ter.
St. Joseph, MO 64503

Table of Contents

1. GENERAL INFORMATION:

a.	File Number:	NADA 200-342
b.	Sponsor:	Phoenix Scientific, Inc. 3915 South 48th St. Ter. St. Joseph, MO 64503 Drug Labeler Code: 059130
c.	Established Name:	Pyrantel pamoate
d.	Proprietary Name:	Pyrantel Pamoate Paste
e.	Dosage Form:	Oral paste
f.	How Supplied:	Packaged in 37.6 gram (31.8 mL) syringes. Each syringe contains adequate Pyrantel Pamoate Paste to treat up to two 1200 lb. horses for large strongyles, small strongyles, pinworms and large roundworms or one 1200 lb. horse for tapeworms.
g.	How Dispensed:	OTC
h.	Amount of Active Ingredients:	Each syringe contains 7.20 grams pyrantel base in 37.6 grams of paste.
i.	Route of Administration:	Oral
j.	Species/Class:	Equine
k.	Recommended Dosage:	Strongyles, pinworms and roundworms - Administer as a single oral dose of 3 milligrams pyrantel base per pound of body weight for treatment of large strongyles, small strongyles, pinworms and large roundworms (ANADA 200-342) Tapeworms - Administer as a single oral dose of 6 milligrams pyrantel base per pound of body weight for treatment of tapeworms (*Anoplocephala perfoliata*) (NADA 200-342).
l.	Pharmacological Category:	Anthelmintic
m.	Indications:	For the removal and control of mature infections of large strongyles (*Strongylus vulgaris, S. edentatus,*

S. equinus); small strongyles; pinworms (*Oxyuris equi*); large roundworms (*Parascaris equorum*) and tapeworms (*Anoplocephala perfoliata*) in horses and ponies.

n. Effect of Supplement:

The supplement to NADA 200-342 provides revisions to 21 CFR 520.2044:

Addition of label claim for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata*) in horses and ponies, with a single oral dose of 6 milligrams pyrantel base per pound of body weight.

The sponsor conducted effectiveness and target animal safety studies in support of this label claim; thus, this supplemental application is a submission under section 512(b)(1) of the Federal Food, Drug, and Cosmetic Act. As a result, the application status of this supplemental approval for Pyrantel Pamoate Paste is designated NADA 200-342.

2. EFFECTIVENESS:

a. Dosage Characterization:

Dosage characterization of 6.0 mg pyrantel base/lb (13.2 mg/kg) body weight (b.w.) administered one time orally for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata*) in horses and ponies has been established by numerous reports in the published scientific literature. [1,2,3,4]

---

[1] Slocombe, J.O.D. 1979. Prevalence and treatment of tapeworms in horses. Canadian Veterinary Journal 20:136-140.

[2] Lyons, E.T., et al. 1986. Pyrantel pamoate: Evaluating its activity against equine tapeworms. Veterinary Medicine, 81:280-285.

[3] Slocombe, J.O.D. 1995. The critical test and efficacy of pyrantel pamoate for *Anoplocephala perfoliata* in equids. In Proceedings, Joint Meeting of the American Society of Parasitologists & the American Association of Veterinary Parasitologists, Pittsburgh, PA, p. 70.

[4] Höglund, J., et al. 1998. Epidemiology of *Anoplocephala perfoliata* infection in foals on a stud farm in south-western Sweden. Veterinary Parasitology 75:71-79.

b. Substantial Evidence:

A series of dose-confirmation and field studies were conducted to evaluate the effectiveness of Pyrantel Pamoate Paste for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata*) when administered to horses and ponies as a single oral dose at the recommended rate of 6.0 mg/lb (13.2 mg/kg) body weight. The final Pyrantel Pamoate Paste formulation was used in these studies.

i. Dose Confirmation Study No. PSI-0690-00E-19B

Title: Clinical Dose Confirmation Study of Tapeworm Removal in Horses Orally Administered PSI Pyrantel Pamoate Paste

Type of Study: Dose Confirmation Study

Investigator: Craig R. Reinemeyer, D.V.M., Ph.D.
East Tennessee Clinical Research
Knoxville, Tennessee

Purpose: The objective of this study was to provide confirmation of the effectiveness of the recommended dose level of Pyrantel Pamoate Paste for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata)*.

Animals: A total of 22 horses weighing between 506-1126 lb diagnosed with naturally-acquired equine tapeworm infections within 45 days of study initiation.

Control: Placebo-treated with paste vehicle in oral syringe

Dosage Form: Final Pyrantel Pamoate Paste formulation in oral syringe

Route of Administration: Oral

Dose Groups: (11 horses per group)

Each test horse received one of the following treatments:

- Control group placebo-treated with paste vehicle formulation containing 0 mg pyrantel base/lb body weight in syringe
- Final Pyrantel Pamoate Paste formulation at 6.0 mg pyrantel base/lb (13.2 mg/kg) body weight

Test Duration: Animals were sacrificed ten, eleven or twelve days after the treatment day.

Pertinent Measurements/Observations: The presence of naturally-acquired equine tapeworm (*Anoplocephala* spp.) infection was demonstrated by fecal evaluation as a condition for inclusion in the study. Test animals were observed for general health at 8 hours post treatment and then daily for the duration of the study. On Days 10, 11

and 12 post treatment, the test horses were sacrificed, necropsied and cestodes present in the small and large intestines were counted and identified by genus and species.

Results:

Parasite recovery data and percent effectiveness calculated using geometric means for *Anoplocephala perfoliata* are provided in the table below.

Table 1. Summary of *A. perfoliata* data by treatment group

Treatment Group	Geometric Mean	Effectiveness (%)
Controls	26.2	n/a
Pyrantel Pamoate Paste	1.2	95.5

Ten out of eleven horses had positive worm counts in the control group at the end of the study, whereas five out of eleven had positive worm counts in the treated group. The log transformed worm counts (log(count+1)) were analyzed using a general linear model with treatment effect. There was a significant treatment difference between the control and the treated group ($p<0.05$).

There were no adverse reactions observed in any of the test horses.

Conclusion: The recommended dose level of the final Pyrantel Pamoate Paste formulation was effective against *Anoplocephala perfoliata*.

ii. Dose-Confirmation Study No. PSI-0690-00E-019C

Title: Clinical Dose Confirmation Study of Tapeworm Removal in Horses Orally Administered PSI Pyrantel Pamoate Paste

Type of Study: Dose Confirmation

Investigator: Douglas Hutchens, D.V.M., M.S.
University of Illinois Veterinary Medicine Research Farm
Urbana, Illinois

Purpose: The objective of this study was to provide confirmation of the effectiveness of the recommended dose level of Pyrantel Pamoate Paste for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata)*.

Animals: A total of 20 horses weighing between 473-1124 lb diagnosed with naturally-acquired equine tapeworm infections within 90 days of study initiation.

Control: Placebo-treated with paste vehicle in oral syringe

Dosage Form: Final Pyrantel Pamoate Paste formulation in oral syringe

Route of Administration: Oral

Dose Groups: (10 horses per group)

- Control group placebo-treated with paste vehicle formulation containing 0 mg pyrantel base/lb body weight in syringe
- Final Pyrantel Pamoate Paste formulation at 6.0 mg pyrantel base/lb (13.2 mg/kg) body weight

Test Duration: Animals were sacrificed ten or eleven days after the treatment day.

Pertinent Measurements/Observations: The presence of naturally-acquired equine tapeworm (*Anoplocephala* spp.) infection was demonstrated by fecal evaluation as a condition for inclusion in the study. Test animals were observed for general health at 8 hours post treatment and then daily for the duration of the study. On Days 10 and 11 post treatment, the test horses were sacrificed, necropsied and cestodes present in the small and large intestines were counted and identified by genus and species.

Results:

Parasite recovery data and percent effectiveness calculated using geometric means for *Anoplocephala perfoliata* are provided in the table below.

Table 2. Summary of *A. perfoliata* data by treatment group

Treatment Group	Geometric Mean	Effectiveness (%)
Controls	4.5	n/a
Pyrantel Pamoate Paste	0.1	98.4

Seven out of ten horses had positive worm counts in the control group at the end of the study whereas one out of ten had positive worm counts in the treated group. The log transformed worm counts (log(count+1)) were analyzed using a general linear model with treatment effect. There was a significant treatment difference between the control and the treated group ($p<0.05$).

There were no adverse reactions observed in any of the test horses.

Conclusion: The recommended dose level of the final Pyrantel Pamoate Paste formulation was effective against *Anoplocephala perfoliata*.

iii. Field Studies

A series of five field studies were conducted in separate geographic locations in the U.S. These studies, which were performed in accordance with the same study design, furnished data pertaining to both the effectiveness and safety of Pyrantel Pamoate Paste under field use conditions. A combined summary of these five trials is presented below.

Type of Study: Clinical Field Study

Clinical Investigators & Locations:

Study No. PSI-0690-02E-008A

Dr. Gary W. White
GCT Consulting Services, Inc.
Sallisaw, Oklahoma

Study No. PSI-0690-02E-008B

Dr. Larry L. Smith
Larry Smith R&D, Inc.
Lodi, Wisconsin

Study No. PSI-0690-02E-008C

Dr. Craig R. Reinemeyer
East Tennessee Clinical Research
Knoxville, Tennessee

Study No. PSI-0690-02E-008D

Dr. John J. Dascanio
Virginia-Maryland Regional College
of Veterinary Medicine
Blacksburg, Virginia

Study No. PSI-0690-02E-008E

Dr. Edward G. Johnson
Johnson Research, L.L.C.
Parma, Idaho

Purpose: The purpose of these studies was to evaluate the safety and effectiveness of the recommended dose level of Pyrantel Pamoate Paste (6.0 mg pyrantel base/lb (13.2 mg/kg) body weight) when administered under field conditions.

Animals: A total of 241 client-owned horses or ponies ranging in age from 6 months to 30 years and ranging in weight from 330 to 1420 pounds completed the studies. The study population included various breeds of horses and ponies. Both infected (cestode positive) and non-infected (cestode negative) horses were evaluated. The cestode positive horses were infected naturally with *Anoplocephala* spp.

Dose Groups:

- Control group: 63 test animals administered vehicle formulation containing 0 mg pyrantel base/lb body weight in a syringe

- Treated group: 178 test animals given final Pyrantel Pamoate Paste formulation containing 6.0 mg pyrantel base/lb (13.2 mg/kg) body weight in a syringe

Route of Administration: Oral

Test Duration: Single administration with 16-day post treatment observation period.

Study Design: At each geographic location, client-owned animals over 6 months of age were enrolled in the study with no restrictions on sex or breed. For masking purposes, the test animals were randomly assigned to one of four treatment groups. Three of the treatment groups were given the recommended level of Pyrantel Pamoate Paste. The fourth group was treated with identically-appearing syringes containing blank vehicle. The owners and individuals treating and making health observations were not aware of the treatment being administered. The treated horses and ponies were observed for adverse reactions for a 16-day post treatment period.

Pertinent Measurements/Observations: Prior to treatment, all test animals were given a complete physical examination. Initial health observations were made approximately 4 and 8 hours post treatment, and then daily until day 16. Fecal samples were examined prior to treatment to determine the presence of cestode eggs. The 126 horses found to be cestode positive prior to treatment were re-sampled on test days 7, 8, 9, 14, 15 and 16 post treatment.

Results: The following table is a compilation of the cestode data:

Table 3. Cestode Data

Pre-Treatment Cestode Status	**Treatment**	**No. (n)**	**Post-Treatment Cestode Status**	
			Negative	Positive
Positive	Untreated Control	36	11 (31%)	25 (69%)
	Pyrantel Pamoate	90	69 (77%)	21 (23%)

The Fisher's Exact test was used to compare the two groups (control vs. treated). The (two-sided) p-value was $p<0.0001$.

There were no adverse reactions observed in any of the 178 treated and 63 control horses and ponies that participated in these five field studies.

Conclusion: Under field conditions, a single oral Pyrantel Pamoate Paste treatment at 13.2 mg pyrantel base/kg body weight was safe and effective against *Anoplocephala* spp. in a wide variety (in terms of age, sex and breed) of horses and ponies.

3. TARGET ANIMAL SAFETY:

The safety of Pyrantel Pamoate Paste in horses two to ten years of age was demonstrated in the study described below.

Title: Target Animal Safety and Tolerance Study of PSI Pyrantel Pamoate Paste Orally Administered to Horses. Study number PSI-0690-01E-008

Type of Study: Acute Toxicity and Tolerance

Investigator: HMS Veterinary Development, Inc.
Tulare, CA

Compliance: This study was conducted in accordance with Good Laboratory Practices For Nonclinical Laboratory Studies, U.S. Code of Federal Regulations, Title 21, Part 58.

Purpose of Study: To determine the safety of Pyrantel Pamoate Paste in the horse. Toxicity was assessed under a six-day treatment regimen of one, three, or five times the recommended dose. Tolerance was determined with a six day treatment regimen of ten times the recommended dose.

Test Animal Allocation and Drug Administration: For the toxicity and tolerance study, horses were assigned to one of five groups as follows:

Table 4. Test Animal Allocation and Drug Administration

Group	No. Animals[a]	Type	Route	Dose	Frequency	Regimen
1	8	Control	Oral	5x[b]	Single dose	Six days
2	8	Test	Oral	1x	Single dose	Six days
3	8	Test	Oral	3x	Single dose	Six days
4	8	Test	Oral	5x	Single dose	Six days
5	8	Test	Oral	10x	Single dose	Six days

[a] Four males and four females per group
[b] Control article: 5x = an amount corresponding to the volume of test article given at five times the recommended dose of each active ingredient.
Test article: 1x, 3x, 5x, 10x = one, three, five, and ten times the recommended dose of each active ingredient, respectively.

Test Duration: April 17, 2002 to May 17, 2002

Pertinent Variables Measured: Physical examinations were conducted on study Days -14, -1, and 24 hours after every dose. Body weights were taken on the same dates as physical examinations and two additional pre-study measurements were taken on Days -21 and -7. Clinical observations were conducted to assess survival, general condition, body temperature, and any abnormal clinical signs once daily during the pre-treatment period and then both immediately following treatment and at 1, 2, 4, 8, 12, and 24 hours post-treatment. Clinical pathology testing (hematology, serum biochemistry, urinalysis) was conducted on baseline samples on Day -14, Day -1, and 24 hours following each dose. Gross postmortem examination was performed on all treatment groups in the toxicity study. Additionally, histopathology was conducted on the placebo and 10X animals. The continuous outcomes were analyzed by a repeated measures analysis of variance and dichotomous outcomes were analyzed by the Fisher's exact test.

Results:

No horses became clinically ill during the conduct of this study.

Two horses in the 1X dose group and two horses in the 5X dose group experienced transient elevations in body temperature during the dosing period. One horse in the 3X dose group had prolonged clotting times (PT and PTT) on day 3 of the study, with a normal platelet count. One horse in the 5X dose group exhibited neutropenia with a normal overall leukocyte count. The clinical significance of these findings is unknown. There were no clinically significant serum chemistry abnormalities in the treated horses that were not present prior to the start of dosing. There were no clinically significant abnormalities on urinalysis, fecal examination, body weights, or for feed and water consumption.

No post-mortem gross pathologic findings were observed that were associated with the administration of the test or control articles. There were no lesions seen in the 10X treatment group at gross necropsy or on histopathology.

Conclusions: This study demonstrated that Pyrantel Pamoate Paste is safe for use in horses two to ten years of age. No signs of toxicity were observed when this oral paste was administered for six consecutive days at 1, 3, 5, and 10 times the recommended dose.

4. HUMAN SAFETY:

This drug is intended for use in horses, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this supplemental NADA.

Human Warnings are provided on the product label as follows: “Do not use in horses intended for human consumption. Keep out of reach of children.”

5. AGENCY CONCLUSIONS:

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that Pyrantel Pamoate Paste when used under the labeled conditions of use is safe and effective for the removal and control of mature infections of tapeworms (*Anoplocephala perfoliata*) in horses and ponies.

The drug is available over-the-counter for lay use. Routine deworming of horses is a widely accepted and recommended practice performed by the lay person. It is recommended that a veterinarian be consulted for assistance in the diagnosis, treatment and control of parasitism.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval. The three years of marketing exclusivity applies only to the new indication for which the supplemental application was approved. Studies conducted in support of substantial evidence of effectiveness for the new indication, as well as new target animal safety data, are the basis for this marketing exclusivity.

According to the Center's supplemental approval policy (21 CFR 514.106), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

Package Insert
Syringe Label-37.6g (31.8mL)
Carton Label-37.6g (31.8mL)
Carton Display Label-6 x 37.6g (31.8mL)
Shipper Label-6 x 37.6g (31.8mL)
Carton Display Label-12 x 37.6g (31.8mL)
Shipper Label-6 x 37.6g (31.8mL)