Date of Approval: March 25, 2003

FREEDOM OF INFORMATION SUMMARY

Abbreviated New Animal Drug Application

ANADA 200-350

Exodus™ (pyrantel pamoate) Paste

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

Sponsor:

Cross Vetpharm Group Limited
Tallaght, Dublin, Ireland

1. GENERAL INFORMATION:

a.	ANADA Number:	200-350
b.	Sponsor:	Cross Vetpharm Group Limited Tallaght, Dublin, Ireland
c.	Established Name:	Pyrantel Pamoate Oral Paste
d.	Proprietary Name:	Exodus™ (pyrantel pamoate) Paste
e.	Dosage Form:	Oral Paste
f.	How supplied:	23.6 gm syringes containing the equivalent of 3.6 gm of pyrantel base (171 mg pyrantel base as pyrantel pamoate per mL of paste)
g.	How Dispensed:	OTC
h.	Amount of Active Ingredients:	3.6 grams of pyrantel base in 23.6 g (171 mg pyrantel base as pyrantel pamoate per mL) of paste.
i.	Route of Administration:	Oral, via pre-filled syringe, adjustable to body weight by 300 pound increments.
j.	Species:	Equine
k.	Recommended Dosage:	The dose rate is 3 milligrams pyrantel base per pound of body weight.
l.	Pharmacological Category:	parasiticide/anthelmintic
m.	Indications for use:	Pyrantel pamoate paste is indicated for the removal and control of mature infections of large strongyles (*Strongylus vulgaris, S. edentatus, S. equinus*); small strongyles; pinworms (*Oxyuris equi*); and large roundworms (*Parascaris equorum*) in horses and ponies.

n. Pioneer Product: Strongid® (pyrantel pamoate) Paste, Pfizer Animal Health, NADA 129-831.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act, (53 FR 50460, December 15, 1988; First GADPTRA Policy Letter), an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). The sponsor has demonstrated *in vivo* bioequivalence, via clinical endpoint bioequivalence studies, of the generic product to the pioneer product to support safety and efficacy of the generic product.

Clinical endpoint bioequivalence studies were considered appropriate for pyrantel pamoate paste for horses because it is locally active in the intestinal tract, poorly absorbed into the circulatory system, and blood levels have not been shown to be reflective of clinical effectiveness. The parasite species selected for the studies below are among those labeled species more resistant to the effects of pyrantel. It is believed that bioequivalence demonstrated against these parasite species provides evidence to support the bioequivalence of the generic product for all claims found on the labeling.

Two clinical endpoint bioequivalence studies to assess the *in vivo* bioequivalence of Cross Vetpharm's formulation of pyrantel pamoate 43.9% paste, Exodus™ Paste (test product) in horses compared to Pfizer's Strongid® Paste (reference product) when administered at the recommended dosage were conducted. The studies are summarized below. The investigator for both studies was:

Craig R. Reinemeyer, D.V.M.
East Tennessee Clinical Research, Inc.
Knoxville, Tennessee 37921

a. Study One Summary and Results

Thirty adult male and female horses with natural infections of *Cylicocyclus nassatus*, *Strongylus edentatus* and other large strongyle species were randomly assigned to three groups containing 10 animals each for a total of thirty (30) test subjects. The study was conducted as a single period design in which one group received the test product, Exodus™ Paste and the second received the pioneer product, Strongid® Paste, and the third group received a placebo. All products were administered according to label directions.

Fourteen (14) days later, the horses were euthanized and measured samples of the gut contents were collected.

The study was completed May 1998 through August 1998. No adverse effects attributable to the medications given were seen.

The individual worm counts were made and "percent efficacy" was calculated for the groups administered the generic, pioneer, and control products. The only parasite for which efficacy calculations could be determined was *Cylicocyclus nassatus*, a small strongyle. Both the pioneer and the generic products demonstrated greater than 90 % efficacy and were considered bioequivalent. Another parasite (*Strongylus edentatus)* was found in numbers too small for a valid determination of efficacy to be established.

Nematode	**Quantitative Parameter**	**Exodus**	**Strongid**	**Controls**
Cylicocyclus nassatus	Geometric Mean Percent Efficacy	289.3 92.5%	342.6 91.1%	3847.2 (N/A)

The geometric mean numbers of adult *Cylicocyclus nassatus* for the generic and the pioneer products were each significantly less ($p<0.01$) than the placebo control group. The parasite burden was adequate. Percent efficacy against *C. nassatus* was greater than 90% and thus no further analysis was undertaken. The parasite burden for *Strongylus edentatus* was too low to establish significance in the study.

Conclusion

The test product, Exodus™ Paste was found to be bioequivalent to the Reference Product, Strongid® Paste with respect to claims for efficacy against *C. nassatus,* a small strongyle species.

b. Study Two Summary and Results

Thirty-six male and female horses, of mixed breeds, from 6 months to 20 years of age (34/36 horses were < 20 months of age), with natural infections of *Parascaris equorum* were randomly assigned to three groups containing 12 animals each for a total of thirty (36) test subjects. One group received the test product, Exodus™ Paste, another received the pioneer product, Strongid® Paste, and the third group received a placebo. All products were administered

according to label directions. Horses were observed once or twice daily to assess their health status. Ten to eleven (10 to 11) days later, the horses were euthanized and measured samples of the gut contents were collected for parasite counting and identification. Blinding during the study was accomplished through separation of function by the study employees. Those employees responsible for making observations and collecting data were unaware of the treatments given to the horses. The study was completed from March 2001 to May 2001. No adverse effects attributable to the medications given were noted.

The only parasite present in adequate numbers for evaluation was *Parascaris equorum*. The individual worm counts were made and "percent efficacy" was calculated for the groups administered the generic, pioneer, and control products. Both the pioneer and the generic product demonstrated greater than 90 % efficacy against *Parascaris equorum* and were considered bioequivalent.

Nematode	**Quantitative Parameter**	**Test**	**Reference**	**Controls**
Parascaris equorum	Geometric Mean Percent Efficacy	1.14 96.9%	0.95 97.4%	37.04 N/A

Adult *Parascaris equorum* geometric mean counts for the generic and pioneer groups were significantly less ($p<0.001$) than the placebo control group. The parasite burden was adequate. Percent efficacy against these nematodes was greater than 90% and no further analysis was undertaken.

Conclusion

The test product, Exodus™ Paste was found to be bioequivalent to the Reference Product, Strongid® Paste with respect to the claim for efficacy against *Parascaris equorum.*

3. HUMAN SAFETY:

Data on human safety, pertaining to consumption of drug residues in food, were not required for approval of this ANADA. The drug is approved for use only in horses that are not to be used for food and is labeled:

"**WARNING:** NOT FOR USE IN HORSES INTENDED FOR FOOD."

HUMAN SAFETY RELATIVE TO POSSESSION, HANDLING, AND ADMINISTRATION

The product labeling contains adequate caution/warning statements.

4. AGENCY CONCLUSIONS:

This is an Abbreviated New Animal Drug Application (ANADA) filed under section 512(b)(2) of the Federal, Food, Drug and Cosmetic (FFD&C) Act.

Safety and effectiveness for this generic animal drug, Exodus™ Paste, were established by the demonstration of clinical end-point bioequivalence to the pioneer product, Strongid Paste®, NADA 129-831.

This generic product and the pioneer product have identical labeling indications for use in horses. The marketing status, and, route and method of administration, of the two drugs are identical. Both drugs are administered orally. The generic and pioneer products contain the same active ingredient in the same concentration.

This ANADA satisfies the requirements of section 512(n) of the Act and demonstrates that Exodus™ Paste is safe and effective for its labeled indications, when used under the proposed conditions of use.

5. ATTACHMENTS:

a. Generic Labeling:

Syringe label
Carton label
Display carton label
Shipper carton label

b. Pioneer Labeling:

Package Insert
Syringe label
Carton label