FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

ANADA:	200-007
Sponsor:	Happy Jack® Inc. P.O. Box 475 Highway 258 South Snow Hill, NC 28580
Trade Name:	Liqui-Vict 2X™
Established Name:	pyrantel pamoate
Dosage Form:	Oral suspension
How Supplied:	2 oz. (60 mL) and 16 oz. (473 mL) bottles
How Dispensed:	OTC
Amount of Active Ingredients:	Each mL contains 4.54 mg of pyrantel base as pyrantel pamoate
Route of Administration:	Oral
Species:	Dogs
Labeled Dosage:	1 teaspoonful (5 mL) for each 10 pounds of body weight
Indications for Use:	To prevent reinfection of *Toxocara canis* in puppies and adult dogs and in lactating bitches after whelping. For removal of large roundworms (*Toxocara canis* and *Toxascaris leonina*) and hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*) in dogs and puppies.
Pioneer Product:	Nemex™-2, NADA 100-237, Pfizer Inc.

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). Under the Act, approval of a generic product requires a demonstration of bioequivalence to the pioneer product. Bioequivalence of the generic and pioneer products can be demonstrated by a clinical end-point study (61 FR 26182, May 24, 1996; Bioequivalence Guidance). The ANADA relies on the target animal safety and drug effectiveness data in the pioneer's New Animal Drug Application (NADA).

EFFECTIVENESS:

The effectiveness of pyrantel pamoate oral suspension has been established by data contained in approved NADA 100-237. The following clinical end-point studies establish the therapeutic bioequivalence of the generic Happy Jack product to the pioneer Pfizer product.

A. *Ancylostoma caninum* Controlled Anthelmintic Test

Study Title: Efficacy of Liqui-Vict 2X (liquid pyrantel pamoate, Happy Jack) for the removal of natural *Ancylostoma caninum* infections of dogs. A bioequivalency study.

Sponsor: Happy Jack, Inc.
P.O. Box 475
Snow Hill, NC 28580

Testing Facility: Professional Laboratory and Research Services, Inc.
Route 1, Box 3AA
Corapeake, NC 27926

Investigator: Dr. Larry R. Cruthers

Objective: The objective of this study was to compare the bioequivalent efficacy of Happy Jack's Liqui-Vict 2X (liquid pyrantel pamoate) to that of Pfizer's Nemex-2 Suspension (liquid pyrantel pamoate) against *A. caninum* infections of dogs.

Test Animals: 30 dogs of mixed breed, random size and ages, and both sexes were used in this study. The dogs were housed individually in stainless steel cages. Dogs were acclimated for at least 5 days prior to treatment.

Identification of parasite infection: Individual fecal samples were collected from each dog upon procurement for fecal egg counts to identify pre-existing natural

parasite infections. Mixed parasite infections were allowed; however, the study examined *A. caninum* infections only. With the exception of one dog where only one fecal sample was available, 3 pretreatment fecal egg counts were conducted during the pretreatment period.

Assignment of dogs to treatment groups: Each replicate of dogs was ranked by mean pretreatment fecal egg counts from highest to lowest. The counts were then blocked into groups of 3 dogs. Within each block, each dog was randomly assigned to a treatment group by drawing a numbered piece of paper from a container.

Treatment: Liqui-Vict 2X and Nemex-2 were administered in an identical manner. Both were administered according to individual body weights at a dose of 0.5 mL per pound. The body weights used for treatment were recorded on Study Day -1 for the animals in both replicates. Medication was administered by gently squirting the appropriate amount of the dewormer towards the back of the mouth. Each dog was held and the throat stroked until swallowing was completed. Dogs were observed once daily throughout the study for any adverse reactions to treatment.

Blinding: The technicians responsible for treatment, conduct of fecal egg counts, necropsy, and collection of worms were not aware of which treatment a dog received.

Parasite Enumeration: All dogs in each replicate were euthanized on the same day and at the same post-treatment interval (7 days post-treatment). Standard parasitological procedures were utilized to recover, count, and identify helminths remaining in the gastrointestinal tract at necropsy.

Efficacy was calculated by the following formula:

$$\frac{\text{Mean \# parasites in untreated controls} - \text{mean \# parasites in treated controls}}{\text{Mean \# parasites in untreated controls}} \times 100 = \% \text{ efficacy}$$

Results:

Replicate 1:

Treatment	Number of Dogs	Total (Mean) Parasites at Necropsy	Percent Efficacy
Liqui-Vict 2X	4	4 (1)	97%
Nemex-2	4	0 (0)	100%
Untreated Control	4	140 (35)	n/a

Replicate 2:

Treatment	Number of Dogs	Total (Mean) Parasites at Necropsy	Percent Efficacy
Liqui-Vict 2X	6	15 (2.5)	99%
Nemex-2	6	125 (20.8)	91.8%
Untreated Control	6	1522 (253.7)	n/a

Total:

Treatment	Number of Dogs	Total (Mean) Parasites at Necropsy	Percent Efficacy
Liqui-Vict 2X	10	19 (1.9)	98.8%
Nemex-2	10	125 (12.5)	92.5%
Untreated Control	10	1662 (166.2)	n/a

Conclusions:

Based on the results of this controlled anthelmintic study, Happy Jack's Liqui-Vict 2X is bioequivalent to Pfizer's Nemex-2 against *A. caninum*.

B. *Toxocara canis* Critical Anthelmintic Test

Title: Efficacy of Liqui-Vict 2X (liquid pyrantel pamoate, Happy Jack) for removal of natural *Toxocara canis* infections of dogs. A bioequivalency study.

Sponsor: Happy Jack, Inc.
P.O. Box 475
Snow Hill, NC 28580

Testing Facility: Professional Laboratory and Research Services, Inc.
Route 1, Box 3AA
Corapeake, NC 27926

Investigator: Dr. Larry R. Cruthers

Objective: The objective of this study was to compare the bioequivalent efficacy of Happy Jack's Liqui-Vict 2X (liquid pyrantel pamoate) to that of Pfizer's Nemex-2 suspension (liquid pyrantel pamoate) against *Toxocara canis* infections in dogs.

Study Design: Individual fecal samples were collected from each dog upon procurement for fecal egg counts to identify pre-existing natural parasite infections. Mixed parasite infections were allowed; however, the study examined *T. canis* infections only. Two to four pretreatment fecal egg counts were conducted during the pretreatment period. The mean roundworm egg count was based on the actual number of samples obtained and analyzed. The study was conducted in two replicates of 15 animals each, with five animals in each replicate assigned to each of the three treatment groups. Each replicate of dogs was ranked by mean pretreatment roundworm fecal egg count from highest to lowest. The counts were then blocked into groups of 3 dogs. Within each block, each dog was randomly assigned to a treatment group by drawing a numbered piece of paper from a container.

The dogs which received Liqui-Vict 2X and Nemex-2 were treated in an identical manner. Dewormer was administered according to individual body weight at a dose of 0.5 mL per pound of bodyweight. The body weights used for treatment were recorded on test day -1 for the animals in replicate 1 and on test day 0 for the animals in replicate 2.

Blinding: In order to maintain blinding, the two dewormers were placed in identical containers and were assigned a number code. The technicians responsible for treatment, conduct of fecal egg counts, necropsy, and collection of worms were not aware of which treatment a dog had received.

Treatment: Liqui-Vict 2X and Nemex-2 were administered in an identical manner. Both were administered according to individual body weights at a dose of 0.5 mL per pound. The body weights used for treatment were recorded on Study Day -1 for the animals in both replicates. Medication was administered by gently squirting the appropriate amount of the dewormer towards the back of the mouth. Each dog was held and the throat stroked until swallowing was completed. Dogs were observed once daily throughout the study for any adverse reactions to treatment

Parasite Enumeration: All dogs in each replicate were euthanized on the same day and at the same post-treatment interval (7 days post-treatment). Standard parasitological procedures were used to recover, count, and identify helminths remaining in the gastrointestinal tract at necropsy.

Only those dogs which were found to have total *T. canis* burdens of six or more worms (including worms expelled and present at necropsy) were included in the final analysis. If fewer parasites are present, it is difficult to differentiate between

treatment success and spontaneous expulsion of parasites, and results in less statistically signficant results.

Efficacy was determined using the critical test, where:

$$\frac{\text{Number of parasites expelled}}{\text{Number of parasites expelled + number of parasites remaining at necropsy}} \times 100 = \text{percent efficacy}$$

Treatment	Number of Dogs	Percent Efficacy (Critical Test)
Liqui-Vict 2X	8	83.75%
Nemex-2	7	78.25%
Untreated Control	6	11%

Because neither the test nor reference product achieved 90% or greater efficacy, the one-sided hypothesis test below was used to determine bioequivalence between Liqui-Vict 2X and Nemex-2. If H_{01} and H_{02} are rejected, then one concludes that the test and reference products are equivalent.

$H_{01} : 0.8R + 0.2P \geq T$
$H_{11} : 0.8R + 0.2P < T$

$H_{02} : T \geq 1.2R - 0.2P$
$H_{12} : T < 1.2R - 0.2P$

where T represents the test product, Liqui-Vict 2X, R represents the reference product, Nemex-2, and P represents the untreated control group.

Both H_{01} and H_{02} were rejected with $p = 0.04135$ and $p = 0.0166$, respectively.

This corresponds to a 90% confidence interval with bounds within $\pm$20% of the improvement over the untreated controls. The value chosen for η_o was 0.2. η_o was defined such that $| T - R | < \eta_o(R - P)$.

Conclusions:

Based on the results of this critical anthelmintic study as analyzed above, Happy Jack's Liqui-Vict 2X is bioequivalent to Pfizer's Nemex-2 against *T. canis*.

ANIMAL SAFETY

The animal safety of pyrantel pamoate oral suspension has been adequately demonstrated previously by Pfizer's approved NADA 100-237.

3. HUMAN SAFETY:

Human Safety Relative to Food Consumption:

Human safety data regarding consumption of drug residues in food were not required for approval of this ANADA. This drug is labeled for use in non-food animals (dogs).

Human Safety Relative to Possession, Handling and Administration:

Labeling contains adequate caution/warning statements.

4. AGENCY CONCLUSIONS:

This ANADA satisfies the requirements of section 512 of the Act and demonstrates that pyrantel pamoate oral suspension (Liqui-Vict 2X) is safe and effective for its labeled indications when used under its proposed conditions of use.

Attachments:

1. Generic labeling (FINAL):
   Liqui-Vict 2X: 2 oz. bottle and carton
   16 oz. bottle
   2 oz. bottle shipper carton
   16 oz. bottle shipper carton
   package insert

2. Pioneer Labeling (MOST CURRENT):
   Nemex: 2 oz. bottle and carton
   16 oz. bottle
   2 oz. bottle shipper carton
   16 oz. bottle shipper carton
   package insert