Date of Approval: January 19, 2005

FREEDOM OF INFORMATION SUMMARY

Original Abbreviated New Animal Drug Application

ANADA 200-326

BIMECTIN Paste 1.87%
(ivermectin)

Oral Anthelmintic Paste for use in Horses

For the treatment and control of specific internal parasites in horses

Sponsor:

Cross Vetpharm Group Ltd.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-326
b. Sponsor:	Cross Vetpharm Group Ltd. Broomhill Road Tallaght, Dublin 24 Ireland Drug Labeler Code: 061623
c. Established Name:	Ivermectin
d. Proprietary Name:	BIMECTIN Paste 1.87%
e. Dosage Form:	Paste
f. How Supplied:	Individual syringe containing 6.08 g paste
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	1.87% ivermectin
i. Route of Administration:	Oral
j. Species/Class:	Horses, not intended for human consumption
k. Recommended Dosage:	This syringe contains sufficient paste to treat one 1250 lb horse at the recommended dose rate of 91 mcg ivermectin per lb (200 mcg/kg) body weight. Each weight marking on the syringe plunger delivers enough paste to treat 250 lb body weight. (1) While holding plunger, turn the knurled ring on the plunger ¼ turn to the left and slide it so the side nearest the barrel is at the prescribed weight marking. (2) Lock the ring in place by making a ¼ turn to the right. (3) Make sure the horse's mouth contains no feed. (4) Remove the cover from the tip of the syringe. (5) Insert the syringe tip into the horse's mouth at the space between the teeth. (6) Depress the plunger as far as it will go, depositing paste on the back of the tongue. (7) Immediately raise the horse's head for a few seconds after dosing.
l. Pharmacological Category:	Anthelmintic

m. Indications:	BIMECTIN Paste 1.87% provides effective treatment and control of the following parasites in horses: **Large Strongyles** (adults) – *Strongylus vulgaris* (also early forms in blood vessels), *S .edentatus* (also tissue stages), *S. equinus*; *Triodontophorus* spp. including *T. brevicauda* and *T. serratus*; **Small Strongyles** (adults, including those resistant to some benzimidizole class compounds) – *Cyathostomum* spp. including *C. catinatum* and *C. pateratum*; *Cylicocyclus* spp. including *C. insigne*, *C. leptostomum*, *C. nassatus*, and *C. brevicapsulatus*; *Cylicodontophorus* spp.; *Cylicostephanus* spp. including *C. calicatus*, *C. goldi*, *C. longibursatus*, and *C. minutus*; **Small Stronglyes** – Fourth-stage larvae; **Pinworms** (adults and fourth-stage larvae) – *Oxyuris equi*; **Ascarids** (adults, third-stage and fourth-stage larvae) *Parascaris equorum*; **Hairworms** (adults): *Trichostrongylus axei*; **Large-mouth Stomach Worms** (adults) – *Habronema muscae*; **Bots** (oral and gastric stages) – *Gasterophilus* spp. including *G. intestinalis* and *G. nasalis*; **Lungworms** (adults and fourth-stages larvae) – *Dictyocaulus arnfieldi*; **Intestinal Threadworms** (adults) – *Strongyloides westeri*; **Summer Sores** caused by *Habronema* and *Draschia* spp. cutaneous third-stage larvae; Dermatitis caused by **neck threadworm** microfilariae, *Onchocerca* sp.
n. Pioneer Product:	EQVALAN Paste 1.87%; ivermectin; NADA 134-314; Merial, Ltd.

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 (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Blood-level *in vivo* Bioequivalence Study:

Title: A Two-Way Single-Dose Bioequivalence Study with Ivermectin Oral Paste in Healthy Horses

Study Objective: To demonstrate that Cross Vetpharm Group Ltd's oral ivermectin paste is bioequivalent to Merial Ltd's EQVALAN Paste (NADA 134-314)

Principle Investigator: Dr. John Brennan

Study Location: Shur-Gain Agresearch, Inc.
Burford, Ontario
CANADA

This study was a randomized, single dose two-period crossover design. The pioneer product is Merial Ltd.'s EQVALAN (ivermectin) Paste approved under NADA 134-314 and the generic product is Cross Vetpharm Group Ltd's oral ivermectin paste. The study used 24 horses, 12 males and 12 females. The horses were randomly assigned to two groups containing 12 animals each. In Period 1, animals assigned to Group 1 received the reference product and animals assigned to Group 2 received the generic product. In Period 2, the animals in each Group received the opposite drug provided in Period 1. In each Period, blood samples were taken pre-dose and post-dose at 1, 3, 4, 5, 6, 7, 9, 12, 15, 18, 24, 36, 48, 72, 168, 336, and 504 hours. A washout time of 42 days was used.

Serum samples were submitted for ivermectin b1a analysis on an HPLC system at the completion of the study. The results were calculated using a linear regression analysis. Pen or gender or their interactions were not involved in the data analysis.

The table below summarizes the results of the *in vivo* bioequivalence study. Both pivotal parameters for determining bioequivalence, Area Under the Curve (AUC) and Maximum Concentration (C_{max}), are within the 80% to 125% bounds for logarithmically transformed data. Since the significance of Time to Maximum Concentration (T_{max}) is a veterinary medical decision, this parameter is represented in mean values only.

Variable	Bimeda Mean	Merial Mean	Lower	Upper
Time to Max. Concentration (hours)	4.39	4.70	NA	NA
Area under Curve $\log_e AUC_{0\text{-}log}$	8.2193	8.1273	100.0%	120.2%
Maximum Concentration $\log_e C_{MAX}$	4.2105	4.0948	101.1%	124.6%

Both variables, the logarithmic area under the curve and logarithmic maximum concentration, satisfied the bioequivalence criteria. These data confirm equivalent drug bioavailability between the generic and pioneer products.

3. 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 ANADA.

Human warnings are provided on the product label as follows: "Do not use in horses intended for human consumption. Not for use in humans. Keep this and all drugs out of reach of children. Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes."

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that BIMECTIN Paste 1.87% for use in horses, when used under the proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and current approved pioneer labeling are attached as indicated below:

Generic Labeling: BIMECTIN Paste, ANADA 200-326
Syringe label; carton label; package insert

Pioneer Labeling: EQVALAN Paste, NADA 134-314
Syringe label; carton label; package onsert