Date of Approval: September 20, 20000

FREEDOM OF INFORMATION SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION

ANADA 200-286

Phoenectin™ (ivermectin) Paste 1.87%

For the treatment of Large Strongyles, Small Strongyles, Pinworms, Roundworms, (Ascarids), Hairworms, Neck Threadworms, Largemouth Stomach Worms, and Bots (specific species listed within).

Sponsored by:

Phoenix Scientific, Inc.
3915 S. 48th Street Terrace
St. Joseph, MO 64503

1. GENERAL INFORMATION

ANADA : 200-286

Sponsor: Phoenix Scientific, Inc.
3915 South 48th Street Terrace
St. Joseph, MO 64503

Generic Name: Ivermectin Paste 1.87%

Trade Name: Phoenectin™ (ivermectin) Paste 1.87%

Dosage Form: Oral Paste

How Supplied: 6.08 g in 6 mL syringe

How Dispensed: OTC

Amount of Active Ingredients: 1.87%

Route of Administration: Oral

Species: Horses

Labeled Dosage: 200 mcg/kg of body weight (91 mcg/lb body weight)

Indications for Use: Ivermectin Paste 1.87% is indicated for the effective treatment and control of the following parasites or parasitic conditions in horses:

Large Strongyles:
Strongylus vulgaris (adults and arterial larval stages)
S.edentatus (adults and tissue stages)
S. equinus (adults)
Triodontophorus spp (adults)

Small Strongyles - including those resistant to some benzimidizole class compounds (adults and fourth-stage larvae):
Cyanthostomum spp
Cylicocyclus spp
Cylicostephanus spp
Cylicodontophorus spp

Pinworms
(adults and fourth-stage larvae)
Oxyuris equi

Ascarids (adults and third- and fourth-stage larvae)
Parascris equorum

Hairworms (adults):
Trichostrongylus axei

Large-mouth Stomach Worms (adults):
Habronema muscae

Bots (Oral and gastric stages):
Gastrophilus spp

Lungworms (adults and fourth-stages larvae):
Dictycaulus arnfieldi

Intestinal Threadworms (adults):
Strongyloides westeri

Summer Sores caused by *Habronema* and *Draschia* spp cutaneous third-stage larvae**.**

Dermatitis caused by neck threadworm microfilariae,
Ohchocerca spp.

Pioneer Product:	Eqvalan® Paste for Horses (ivermectin)
"Listed Product:	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 (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). New target animal safety data, drug effectiveness data, and human food safety data (other than tissue residue data) are required for approval of an ANADA. An ANADA approval is based on a demonstration that the generic product is bioequivalent to the pioneer product.

The following study was completed to provide evidence of blood-level bioequivalence of the generic and pioneer ivermectin pastes in horses.

Bioequivalence Study: PSI -0677-96E-003 (GLP)

SERUM BIOAVAILABILITY OF GENERIC AND PIONEER 1.87% IVERMECTIN PASTE (EQVALAN®) ADMINISTERED ORALLY IN THE HORSE

Study Location: Southwest Bio-Labs, Inc. (SBL)
401 N 17th Street
Las Cruces, NM 88005

Summary: Animals were observed and acclimated for 28 days prior to study start. After meeting entrance criteria, 12 adult horses (6 castrated males; 5 non-pregnant females and 1 pregnant female) were segregated by sex and ranked by ID number (lowest to highest) within each sex. Males and females within the block were randomly assigned to one of two treatment sequences, generic test article followed by pioneer control article or pioneer control article followed by generic test article, so that three males and three females were assigned to each sequence. Animals were given the first drug of the assigned sequence during the first treatment period and the second drug of the assigned sequence during the second treatment period. The treatment order (order in which the animals were dosed) was randomized for both treatment periods. Treatments consisted of a single oral administration of 22.75 mg of generic or pioneer ivermectin per 250 pounds of body weight, a washout period of 28 days between treatment periods, and a single oral administration of 22.75 mg of generic or pioneer ivermectin per 250 pounds of body weight during the second treatment period.

Blood (~10-12 mL) was collected for ivermectin serum analysis immediately pretreatment (0) and 1, 2, 3, 4, 6, 8, 10, 12, 24, and 36 hours and 2, 3, 4, 7, 10, 14, 17, and 21 days posttreatment (19 samples/animal/treatment period). Twenty-eight (28) days after the first treatment, animals were dosed with the alternate product and the blood collections repeated during the second treatment period. Serum samples were submitted to PPD Pharmaco, Inc., Middleton, WI for ivermectin analysis at the completion of the study.

The area under the curve (AUC) was computed using the trapezoidal rule. The natural logarithm of AUC was computed and used as the variable for analysis, denoted by LAUC. The maximum concentration measured for all time periods (C_{max}) was determined and the natural logarithm of C_{max}, denoted LC_{max}, was computed and used as the variable for analysis.

Results and Conclusions: The criteria for determining bioequivalence, as described in CVM's *Bioequivalence Guidance* (Final) Docket No. 94D-0401, 1996, is to construct a 90% confidence interval about the difference of the two means, generic minus pioneer, based on the log scale of AUC and C_{max} and then take the anti-log of

the confidence limits. The anti-log of the lower limit of LAUC was greater than or equal to 0.8 (0.81) and the anti-log of the upper limit was less than 1.25 (1.24). The anti-log of the lower limit of LC_{max} was greater than or equal to 0.8 (0.81) and the anti-log of the upper limit was less than or equal to 1.25 (1.25).

Both variables, LAUC and LC_{max}, satisfied the bioequivalence criteria. Therefore, the study objective to determine the bioequivalence of generic and pioneer ivermectin 1.87% paste by serum bioavailability was achieved.

Although the variable, T_{max} did not satisfy the criteria in the *Bioequivalence Guidance*, we are permitted to exercise clinical judgement when interpreting this variable as it relates to the efficacy of the proposed drug. In this case, there is no reason to expect the difference in T_{max} will affect the efficacy of the drug, since both AUC and C_{max} are bioequivalent and the product is administered as a single dose.

3. HUMAN SAFETY:

Human Safety Relative to Food Consumption:

None required as Ivermectin Paste 1.87% is intended for use only in horses. The labeling includes the statement:

"WARNING: Do not use in horses intended for food purposes."

Human Safety Relative to Possession, Handling, and Administration:

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, Ivermectin Paste1.87% were established by demonstration of bioequivalence to the pioneer product, Eqvalan® Paste for Horses (NADA 134-314, Merial Ltd).

This generic product and the pioneer product have identical labeling indications for the use in horses. The 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 ingredients.

This ANADA satisfies the requirements of section 512 of the Act and demonstrates that Ivermectin Paste 1.87 % , is safe and effective for its labeled indications when used under the proposed conditions of use.

Attachments:

1. **Generic labeling:**

   Package Insert

   Container Label

   Carton Label

2. **Pioneer Labeling**

   Package Insert

   Container Label

   Carton Label