

29-Mar-00



Dr. Lonnie Luther
FDA, CVM HFC 102 Room 387
Generic Drug Branch
7500 Standish Place
Rockville, MD 20855

Dear Dr. Luther;

I have enclosed a Suitability Petition submission in reference to JINAD 10-664, ivermectin liquid for horses. The reference (pioneer) product is Eqvalan® Liquid for Horses; NADA 140-439 sponsored by Merial Ltd.

This submission is based on the Pre-ANADA Activities, ANADA Suitability Petition section in the second policy letter on the implementation of the Generic Animal Drug and Patent Term Restoration Act dated June 7, 1989.

Specifically the Pre-ANADA Activities, ANADA Suitability Petition section in the second policy letter states:

“The filing of a Suitability Petition provides a means by which a firm may request permission to file an ANADA for a product which differs from the approved pioneer product.

The specific variances under the Act for which a Suitability Petition may be submitted are as follows:

1. Change of one ingredient in a combination product or premix
2. Change of a dosage form
3. Change of a strength of an ingredient
4. Change in route of administration
5. Change in use with other animal drugs in animal feed.”

Equi Aid is requesting permission to file an ANADA that differs from the pioneer in that the pioneer is a liquid oral dosage form new animal drug containing 1% ivermectin for oral administration via stomach tube¹ or drench and the proposed product would be a liquid new animal drug for use in animal feeds (Type A medicated article) containing 5% ivermectin. Thus the proposed product would differ in dosage form, route of administration and strength.

Sincerely;



Peter R. Miller DVM MS

¹ Stomach tube is the term used in the CFR and on the reference product labeling. It is synonymous with nasogastric intubation.

00P-1225

CP1

**Equi Aid Suitability Petition
Ivermectin Liquid for Horses
JINAD 10-664
29-Mar-00**

Table of Contents

Suitability Petition	1
1. Identification of Petitioner and Statutory Citation.....	1
2. Action Requested.....	1
3. Statement of Grounds	1
(a) Identification of a single listed drug which is the basis of the petition	1
(b) Proposed Changes	3
(c) Justification for the proposed variances.....	4
4. Additional Essential Elements of a Petition	5
(a) Comparison of Pioneer and Proposed Product Labels.....	6
5. Environmental Impact.....	10
6. Economic Impact.	10
7. Certification.	10
<i>Supplemental information section</i>	
Pioneer Label	11
Proposed Product Label	14
<i>Other related product labels</i>	
Zimectrin®	16
Ivomec® Premix for Swine	17
Equi Aid CW® 48	19
MGA® 500	21
Bovatec® 20	23
Safe-Guard®	24
Environmental Impact (21 CFR 25.33)	25
AOAC Method for Assay of Ivermectin in feed	26
Green Book Chapter 7 (Suitability Petitions)	30
Transcript of Pre-ANADA activities 2nd GADPTRA Policy Letter	38

**Equi Aid Suitability Petition
Ivermectin Liquid for Horses
JINAD 10-664
29-Mar-00**

1. Identification of Petitioner and Statutory Citation

Petitioner

Equi Aid Products, Inc.
1517 W. Knudsen Drive
Phoenix AZ 85027

Statutory Citation

Section 512 (n) (3) of the Federal Food, Drug, and Cosmetic Act.

2. Action Requested

Equi Aid Products, Inc. is petitioning the Commissioner to permit filing of an ANADA which differs from the approved pioneer product in dosage form, strength of an ingredient and route of administration.

3. Statement of Grounds

(a) Identification of a single listed drug which is the basis of the petition

The reference (pioneer) product forming the basis for this petition is Eqvalan[®] Liquid for Horses; NADA 140-439 sponsored by Merial Ltd.

i) Description of the pioneer product Eqvalan[®] Liquid for Horses

140-439 Eqvalan Oral Liquid

Tradename: Eqvalan Oral Liquid

NADA Number: 140-439

Sponsor: Merck Research Laboratories

Ingredients: Ivermectin

Species: Equine, Horses not for meat production

Rx or OTC: Rx

Route of Administration: Per Os

Drug Forms: Liquid

- **21 CFR 520.1195**
- **CFR Information: 520.1195 Ivermectin liquid.**
- **Specifications.** Each milliliter contains 10 milligrams of ivermectin.
- **Conditions of use**

Amount.

200 micrograms per kilogram of body weight as a single dose.

Indications for use.

It is used in horses for the treatment and control of **large strongyles** (adult) (*Strongylus equinus*), (adult and arterial larval stages) (*Strongylus vulgaris*), (adult and migrating tissue stages) (*Strongylus endentatus*), (adult) (*Triodontophorus* spp.);

small strongyles, including those resistant to some benzimidazole class compounds (adult and fourth stage larvae) (*Cyathostomum* spp. *Cylicocyclus* spp., *Cylicodontophorus* spp. *Cylicostephanus* spp.);
pinworms (adult and fourth stage larvae) (*Oxyuris equi*);
ascarids (third- and fourth-stage larvae and adults) (*Parascaris equorum*);
hairworms (adult) (*Trichostongylus axei*);
large mouth stomach worms (adult) (*Habronema muscae*);
stomach bots (oral and gastric stages) (*Gastrophilus* spp.);
lungworms (adults and fourth stage larvae) (*Dictyocaulus arnfieldi*);
intestinal threadworms (adults) (*Strongyloides westeri*);
summer sores caused by *Habronema* and *Draschia* spp. cutaneous third stage larvae; and
dermatitis caused by neck threadworm microfilariae (*Onchocerca* spp.).

Limitations.

Administer by stomach tube or as an oral drench.

Do not use in horses intended for food purposes. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

[52 FR 34637 Sept. 14, 1987, as amended at 53 FR 51273, Dec. 21, 1988]

- **Formulation of the pioneer product Eqvalan® Liquid for Horses**

The pioneer label lists each ml of Eqvalan Liquid for Horses as having:

10 mg ivermectin,
 0.2 ml propylene glycol
 80 mg polysorbate 80
 9 mg sodium phosphate monobasic monohydrate
 1.3 mg sodium phosphate dibasic anhydrous
 1 mg butylated hydroxytoluene
 0.1 mg disodium edetate
 3 % benzyl alcohol and
 purified water q.s. ad 100%

ii) **Description of the proposed product Equi Aid Ivermectin Liquid for Horses**

JINAD 10-664 Ivermectin Liquid for Horses

Tradename: Ivermectin Liquid for Horses

Ref Number: JINAD 10-664

Sponsor: Equi Aid Products, Inc.

Ingredients: Ivermectin

Species: Equine, Horses not for meat production

Rx or OTC: OTC

Route of Administration: Per Os (via feed)

Drug Forms: Liquid

- **21 CFR 558.300**
- **Proposed CFR Information: 558.300 Ivermectin.**
- **Specifications. Each milliliter contains 50 milligrams of ivermectin.**
- **Conditions of use**

It is used as follows:....

Horses**Amount.**

200 micrograms per kilogram of body weight as a single treatment.

Indications for use.

It is used in horses for the treatment and control of

large strongyles (adult) (*Strongylus equinus*), (adult and arterial larval stages) (*Strongylus vulgaris*), (adult and migrating tissue stages) (*Strongylus endentatus*), (adult);

small strongyles, including those resistant to some benzimidazole class compounds (adult and fourth stage larvae) (*Cyathostomum* spp. *Cylicocyclus* spp., *Cylicodontophorus* spp. *Cylicostephanus* spp.) (*Triodontophorus* spp.¹);

pinworms (adult and fourth stage larvae) (*Oxyuris equi*);

ascarids (third- and fourth-stage larvae and adults) (*Parascaris equorum*);

hairworms (adult) (*Trichostongylus axei*);

large mouth stomach worms (adult) (*Habronema muscae*);

stomach bots (oral and gastric stages) (*Gastrophilus* spp.);

lungworms (adults and fourth stage larvae) (*Dictyocaulus arnfieldi*);

intestinal threadworms (adults) (*Strongyloides westeri*);

summer sores caused by *Habronema* and

Draschia spp. cutaneous third stage larvae; and

dermatitis caused by neck threadworm microfilariae (*Onchocerca* spp.).

Limitations.

Administer either as a top-dress or mixed in the horse's grain ration for animals that have been at risk of exposure to parasites

Do not use in horses intended for food purposes.

Consult your veterinarian before using in severely debilitated animals and for assistance in the diagnosis, treatment, and control of parasitism.

- **Formulation of the proposed product Equi Aid Ivermectin Liquid for Horses**

Equi Aid proposes a formulation such that each ml of Equi Aid Ivermectin Liquid for Horses would contain:

50 mg ivermectin,

5 mg butylated hydroxytoluene

3 % benzyl alcohol and

propylene glycol q.s. ad 100%

(b) Proposed Changes**i) Dosage Form**

- **Pioneer**

The pioneer product is an oral dosage form New Animal Drug (CFR Reference: 21 CFR 520.1196).

- **Generic**

The proposed generic product would be a New Animal Drug for use in Animal Feeds (CFR Reference: 21 CFR 558.300).

ii) Active Ingredients

Equi Aid is not proposing changes in the active ingredient.

¹ *Triodontophorus* spp is not generally considered a large strongyle. Currently, it is typically classified as a small strongyle.

iii) **Strength**

- **Pioneer**
The pioneer product contains ivermectin at 1% (10 mg/ml).
- **Generic**
The proposed generic product would contain ivermectin at 5% (5 mg/ml).

iv) **Route of administration**

- **Pioneer**
The pioneer product is administered by stomach tube or as an oral drench.
- **Generic**
The proposed generic product is administered either as a top-dress or mixed in the horse's grain ration.

v) **Use with other animal drugs in animal feed**

Equi Aid is not proposing the use of ivermectin with other animal drugs in animal feed.

(c) **Justification for the proposed variances**

i) **Improvement in safety and efficacy because of change in dosage form.**

As stated on the pioneer label (See attached photocopy of pioneer label "Administration by stomach tube", "Administration by drench" and "Note to veterinarian" sections) there are risks to the horse when dosing the pioneer product via stomach tube or drench. In addition there is a need to alter the formulation by addition of water and a potential for rejection of the dose. The "Note to veterinarian" section of the pioneer label states that due to the consequences of improper administration the product is intended for use by a veterinarian only and is not recommended for dispensing.

Addition of the product to an animal feed (via top-dress or mixing on the horses grain ration) as proposed would be beneficial in regard to both safety and efficacy because feeding the product does not pose any "risks associated with tubing" and would help reduce difficulty of administration and rejection of the dose.

The change in strength and route of administration are necessitated by the change in dosage form.

The proposed formulation is similar to the pioneer with the water and related excipients removed.

ii) **Equi Aid Products, Inc. is skilled in production of medicated feeds for horses.**

Equi Aid currently holds an approval for a Type A medicated article (pyrantel tartrate for use as an anthelmintic in horses) and a medicated feed mill license. Equi Aid is the manufacturer of the Type A medicated article as well as medicated feeds for horses.

iii) **Medicated feeds are a common drug delivery system**

The use of medicated feed as a means of drug delivery, including anthelmintic drugs, is well established. Ivermectin is approved for use in swine feeds as an anthelmintic (21 CFR 558.3000). Pyrantel tartrate is approved for use in horse feed (21 CFR 558.485). Other anthelmintics currently approved for use in animal feeds include fenbendazole, levamisole, morantel tartrate, thiabendazole, etc.

iv) Liquid Type A Medicated Articles

The use of liquid Type A medicated articles for mixing with liquid or dry feeds is well established. One example MGA 500 Liquid Premix (Type A Medicated Article) (NADA 39-402, Pharmacia Upjohn Company) list propylene glycol as the only inactive ingredient and includes mixing directions for both liquid and dry feeds. Lasalocid (21 CFR 558.311) and Poloxalene (21 CFR 558.464) are other examples of approved Liquid Type A medicated articles.

v) Dosage form change (oral form to Type A medicated article) approval

The approval of suitability petitions requesting the change in dosage form is common and a suitability petition has been approved for the change from an oral dosage form to a Type A medicated article. (Pfizer petition 92P-0157/CP1 pioneer product NADA 011-315 approved 5/12/92). (See The Green Book Chapter 7 Suitability Petitions).

vi) Approved dosage forms

Various formulations of ivermectin products and other avermectin/milbemycin products are currently approved. Approved oral dosage form ivermectin formulations are listed in 21 CFR 520.1192, 520.1193, 520.1194, 520.1195, 520.1196 and 520.1197. Approved injectable dosage form ivermectin formulations are listed in 21 CFR 522.1192 and 522.1193. These drugs are approved for use in many species and formulations at 0.2 mg/kg including all oral and injectable forms for horses (paste, liquid and injectable). Approved topical (pour-on) formulations of avermectins are listed in 21 CFR 524 (Doramectin - 524.770, Eprinomectin - 524.814, Ivermectin - 524.1193, and Moxidectin - 524.1451).

The broad range of dosage forms with the same dosage regimen (0.2 mg/kg as a single treatment) indicate that ivermectin is not typically formulation sensitive. Ivermectin is currently approved and being used in feeds for another species (swine). These two facts render ivermectin a good candidate for use in medicated feeds for horses.

vii) Change in concentration

It is appropriate for a Type A medicated article to be more concentrated than a finished dosage form because the Type A article is intended for further mixing with feed. When the more concentrated Type A medicated article is diluted with feed it will contain an appropriate concentration of ivermectin in the Type C medicated feed.

viii) Change in route of administration

Even though both products would be per os (by mouth) the pioneer product is administered by stomach tube or drench. The proposed generic would be given via feed. The purpose of changing the dosage form and concentration is to allow for administration of the ivermectin via feed.

4. Additional Essential Elements of a Petition

The Pre-ANADA Activities, ANADA Suitability Petition section in the second policy letter on the implementation of the Generic Animal Drug and Patent Term Restoration Act dated June 7, 1989 under "Additional essential elements of a petition" lists two items:

- 1) identification of a single listed drug which is the basis of the petition (which is addressed above) and
- 2) pioneer and proposed product labeling with differences noted and explained.

(a) Comparison of Pioneer and Proposed Product Labels**i) Front of Pioneer Box Label**

- **FOR VETERINARY USE ONLY**

Appears first on the top of the pioneer label

Appears directly under the proposed product name and "Type A Medicated Article" statement.

- **Product Name**

The product name is prominently displayed on the front of both the pioneer product and the proposed product.

- **Liquid for Horses**

There is a "Liquid for Horses" statement on the pioneer product. The proposed product has "Liquid Premix for Horses" as part of the name. The word "premix" is added for clarification purposes.

- **Antiparasitic (Anthelmintic and Boticide)**

This verbiage was added to the proposed product label for clarification to non-veterinarians, similar to other ivermectin OTC products (see attached Zimectrin® paste label. It does not appear on the pioneer product.

- **Concentration of active ingredient**

Both the pioneer and proposed product display the ivermectin concentration on the front. The products differ in concentration (1% ivermectin in the pioneer and 5% ivermectin in the proposed product). The proposed product would list the ivermectin concentration in both percent and mg/ml and display it under the heading of Active Drug Ingredient which is typical of a Type A medicated article.

- **Prescription Statement**

The prescription statement "Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian." Only appears on the pioneer product because it would be inappropriate for the proposed Type A medicated article. The pioneer product requires a prescription because the route of administration (stomach tube or drench) requires special skills whereas dosing via feed does not require special skills.

- **Size**

Both the pioneer and proposed products list the container size on the bottom of the front label. The pioneer product comes in 100 ml bottles. The proposed product lists both weight and volume in standard and metric measurements as is appropriate for liquid Type A medicated articles.

ii) Back Panel of Pioneer Box Label

- **Indications**

The indications are the same for the pioneer and proposed products. NOTE: Recently the Triodontophorus spp. have more commonly been included with the small strongyles as opposed to large strongyles as was done in the past.

- **Environmental Safety:**

Both the pioneer and proposed product have the same environmental safety information.

iii) **Left Side Panel of Pioneer Box Label**

- **Dosage and Administration**

Dosage: The dosage for both products (200 mcg of ivermectin per kilogram of body weight) is the same. The proposed product spell out micrograms while the pioneer abbreviates micrograms as "mcg" and indicates that "Each mL contains sufficient ivermectin to treat 110 lb (50 kg) of body weight; 10 mL. will treat an 1100 lb (500 kg) horse.

Administration: The pioneer product is labeled for administration via stomach tube or drench. Under the heading of "Mixing and Use Directions" the proposed product is labeled for administration either as a top-dress or mixed in the horse's ration. This difference in labeling is consistent with the proposed change in route of administration requested in this petition.

- **Reference to Package Insert:**

The side panel of the pioneer product box under the Dosage and Administration states "See Package insert for complete indications and use directions". The proposed product does not have a package insert. However, the front label does refer the reader to the back label for directions on mixing and use.

- **Storage**

Both products have the same storage instructions; "Store in a tightly closed container at room temperature. Protect Ivermectin Liquid (undiluted and diluted) from light.". The proposed product would have the storage instructions on the front label as opposed to the side of the box.

- **Lot number and Expiration Date**

Both the pioneer and proposed products would have a lot number and an expiration date. The proposed product would have the lot number and an expiration date on the back label as opposed to the side of the box.

- **Manufacturer/Distributor**

Both the pioneer and proposed product labels would have the manufacturers/distributors name and location. The proposed product would have the manufacturers/distributors name and location on the back label as opposed to the side of the box.

iv) **Right Side Panel of Pioneer Box Label**

- **Ingredients**

The pioneer product list the product ingredients and amounts as is typical for prescription animal drugs. The proposed product list the active and inactive ingredients on the front label in a manner consistent with Type A medicated feed labeling.

- **Warning Statements**
Both the pioneer and proposed product labels would have the warning statement "Warning : Not for use in horses intended for food". The proposed product label has the statement prominently displayed on the front label. In addition the warning "For the use in the manufacturing of equine feeds only" is also displayed on the front label of the proposed product. This additional warning is appropriate for and consistent with warnings on Type A medicated articles.
- **Caution Statements**
The caution statements:
"has been formulated specifically for use in horses only" and
"This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result"
are the same for both products.
A general caution on exposure to animal feeds and premixes is used in place of the "Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes." statements because the general caution statement is common and appropriate for a Type A medicated article.
- **Keep this and all drugs out of reach of children**
This statement appears on both labels. Following the "cautions".

v) **Package Insert**

The proposed product does not have a package insert.

- **Table of contents, Introduction and Product Description**
The information in these sections is not included in the proposed labeling, with the exception that ingredients are listed as addressed under the ingredients section above. The information included in these sections is typical of a finished dosage form product as opposed to a Type A medicated article.
- **Product Indications**
This section is essentially a duplicate of the indications found on the back panel of the box. See the section in this petition addressing the indications on the back panel of the box.
- **Dosage and Administration**
These sections cover the same information found on the left panel of the box. See the section in this petition addressing the dosage and administration on the left side panel of the box.
- **Suggested Parasite Control Program**
Similar parasite control programs are suggested on the pioneer package insert and the proposed product back label under "Mixing and Use Directions".
- **Mode of Action**
The information in this section is not included in the proposed labeling. The information included in this section is typical of a finished dosage form product as opposed to a Type A medicated article.

- **Safety, Precautions and Environmental Safety**
The proposed product has a safety statement on the back label under "Mixing and Use Directions" which is similar to the pioneer. The proposed product statement indicates that "Foals should be treated initially when consistent intake of grain mix is occurring (usually between two and three months of age)". This statement is appropriate when administration is via the feed. The other information has been covered previously in this petition. See the Caution, Warning, Storage and Environmental Safety sections above.
- **Note to Veterinarian**
The note to veterinarian section is similar to the note to user section in the proposed label which is the same as the note to user on other OTC ivermectin products for oral in horses.
- **Package Information**
The information in this section is not included in the proposed labeling. The information included in this section is typical of a finished dosage form product as opposed to a Type A medicated article.

vi) **Additional Information on the Proposed Product Label**

- **Antiparasitic (Anthelmintic and Boticide)**
This verbiage was added to the proposed product label for clarification to non-veterinarians, similar to other ivermectin OTC products (see attached Zimectrin® paste label. It does not appear on the pioneer product.
- **Follow Mixing Instructions and cGMP Statement**
The proposed product would have a statement in the "Mixing and Use Directions" stating "Follow mixing directions. Ivermectin Liquid Premix for Horses should be mixed in the feed in accordance with good manufacturing practices for medicated feeds". This section is appropriate for a Type A medicated article.
- **Mixing instructions for Dry and Liquid feeds**
The proposed product would have instructions and a table in the "Mixing and Use Directions" on mixing the proposed product with dry and liquid feeds. This section is appropriate for a Type A medicated article.

The Pre-ANADA Activities, ANADA Suitability Petition section in the second policy letter on the implementation of the Generic Animal Drug and Patent Term Restoration Act dated June 7, 1989 states that the Suitability Petition will be approved unless the Secretary finds that:

- 1) "investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which differ from the approved new animal drug, or
- 2) investigations must be conducted to show the safety for human consumption of any residues in food resulting from proposed active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which is different from the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug."

Equi Aid has addressed route of administration, dosage form, and strength in the sections above. Equi Aid proposes no changes in active ingredient or use with other animal drugs in animal feeds. Neither the pioneer nor the proposed generic product are intended for use in food producing animals nor is it likely that the product will be diverted into food producing animals. 1) the pioneer and proposed product labels clearly state not to use the product in other animals, 2) veterinarians and producers of food animals are well aware of the laws governing extra-label use of drugs in food animals because of recent new legislation and educational programs related to extra-label use of drugs, and 3) it is unlikely that the product would be more cost effective or significantly easier to use than currently approved ivermectin products for use in food animals.. Therefore safety for human consumption should not be impacted because of the proposed changes.

5. Environmental Impact

Equi Aid Products, Inc. requests, under 21 CFR 25.33 (a) categorical exclusion from the requirement for an environmental assessment.

6. Economic Impact

An "Economic Impact" section has not been requested. Equi Aid Products, Inc. will provide an "Economic Impact" statement upon the Commissioner's request.

7. Certification

I, Peter R. Miller DVM, MS, acting as Equi Aid's representative, have included all information known to me which is unfavorable to this petition.

Peter R. Miller DVM, MS
Equi Aid Products, Inc.
1517 W. Knudsen Dr.
Phoenix, AZ 85027
(623) 587 6082.



Peter R. Miller DVM MS

29-Mar-00

Photocopy of Eqvalan® Liquid for Horses container (bottle) label and carton (box). Enlarged to 110%

Indications: For the treatment and control of large strongyles, small strongyles, hairworms, pinworms, roundworms (ascarids), intestinal threadworms, large-mouth stomach worms, bots, lungworms, summer sores and cutaneous onchocerciasis.

Recommended Dose: 200 mcg of ivermectin per kilogram (91 mcg/lb) of body weight. Each mL contains sufficient ivermectin to treat 110 lb (50 kg) of body weight; 10 mL will treat an 1100 lb (500 kg) horse.

See package insert for complete indications and use directions.

U.S. Pat. 4,199,569 Made in U.S.A.
EQVALAN REG TM MERCK & CO., Inc.
8688303 Lot No & Exp Date ▼

FOR VETERINARY USE ONLY

Eqvalan®
(ivermectin)

Liquid for Horses
10 mg per mL

Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

Precautions:

WARNING: Do not use in horses intended for food purposes

CAUTION: EQVALAN® (ivermectin) Liquid has been formulated specifically for use in horses only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result. Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes.

Keep this and all drugs out of the reach of children. Store in a tightly closed container at room temperature. Protect EQVALAN Liquid (undiluted or diluted) from light.



Merck & Co., Inc.
Rahway, New Jersey 07065-0912, U.S.A.

EBY033 07-2001

100 mL

Product 25877

Top Panel of Box



10 mg per mL
Liquid for Horses
(ivermectin)

Eqvalan®

Product 25877

100 mL

Container Label

FOR VETERINARY USE ONLY

Eqvalan®
(ivermectin)

Liquid for Horses
10 mg per mL

Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

100 mL

Product 25877

Each mL contains 10 mg ivermectin, 0.2 mL propylene glycol, 80 mg poly-sorbate 80, 9 mg sodium phosphate monobasic monohydrate, 1.3 mg sodium phosphate dibasic anhydrous, 1 mg butylated hydroxytoluene, 0.1 mg disodium edetate, 3% benzyl alcohol and purified water q.s. ad 100%.

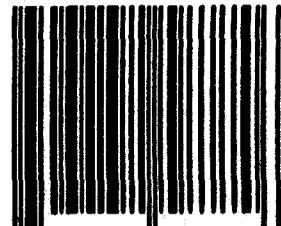
Precautions:

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

CAUTION: EQVALAN® (ivermectin) Liquid has been formulated specifically for use in horses only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes.

Keep this and all drugs out of the reach of children.



3 0373-258770 3

INDICATIONS:

EQVALAN® (ivermectin) Liquid provides effective control of the following parasites or parasitic conditions in horses: Large Strongyles — adults and arterial larval stages of *Strongylus vulgaris*, adults and tissue stages of *S. edentatus*, adults of *S. equinus* and *Triodontophorus* spp; Small Strongyles — including those resistant to some benzimidazole class compounds (adults and fourth-stage larvae) — *Cyathostomum* spp, *Cylicocycilus* spp, *Cylicostephanus* spp, *Cylicodontophorus* spp; Pinworms (adults and fourth-stage larvae) — *Oxyuris equi*; Ascarids (adults and third- and fourth-stage larvae) — *Parascaris equorum*; Hairworms (adults) — *Trichostrongylus axei*; Large-mouth Stomach Worms (adults) — *Habronema muscae*; Bots (oral and gastric stages) — *Gastrophilus* spp; Lungworms (adults and fourth-stage larvae) — *Dictyocaulus arnfieldi*; Intestinal Threadworms (adults) — *Strongyloides westeri*; Summer Sores caused by *Habronema* and *Dracchia* spp cutaneous third-stage larvae; Dermatitis caused by neck threadworm microfilariae, *Onchocerca* sp.

ENVIRONMENTAL SAFETY:

Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not contaminate lakes, streams, or ground water by direct application or by improper disposal of drug containers. Dispose of drug container in an approved landfill or by incineration.

U.S. Pat 4,199,569
EQVALAN REG TM MERCK & CO., INC.

Made in U.S.A.
83939

Left Panel of Box

Front Panel of Box

Right Panel of Box

Back Panel of Box



Merck & Co., Inc.
Rahway, New Jersey 07065-0912, U.S.A.

EQVALAN (ivermectin)**EQVALAN** (ivermectin)**EQVALAN** (ivermectin)**EQVALAN** (ivermectin)**EQVALAN** (ivermectin)

	Page
Introduction	3
Description	4
Indications	5, 6
Dosage	7
Administration	7, 8
Suggested Parasite Control Program	9
Mode of Action	10, 11
Safety	12
Precautions	13
Environmental Safety	14
Notes to Veterinarian	15, 16
Package Information	17

Introduction

EQVALAN® (ivermectin) Liquid for Horses has been formulated for professional administration by stomach tube or oral drench. One low-volume dose is effective against important internal parasites, including the arterial stages of *Strongylus vulgaris*, and bots.

Discovered and developed by scientists from Merck Research Laboratories, ivermectin is a potent antiparasitic agent whose chemical structure is different from those of other antiparasitic agents. Its convenience, broad-spectrum efficacy and safety margin make EQVALAN Liquid an ideal parasite control product for horses.

EQVALAN is a registered trademark of Merck & Co., Inc., Whitehouse Station, N.J., U.S.A.

2

3

Product Description

Ivermectin is derived from the avermectins, a family of potent, broad-spectrum antiparasitic agents, which are isolated from fermentation of *Streptomyces avermitilis*.

EQVALAN Liquid is a clear, ready-to-use solution with each mL containing 1% ivermectin (10 mg), 0.2 mL propylene glycol, 80 mg polysorbate 80, 9 mg sodium phosphate monobasic monohydrate, 1.3 mg sodium phosphate dibasic anhydrous, 1 mg butylated hydroxytoluene, 0.1 mg disodium edelate, 3% benzyl alcohol and purified water q.s. ad 100%.

4

Product Indications

EQVALAN Liquid 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 benzimidazole class compounds (adults and fourth-stage larvae):

Cyathostomum spp
Cylicocyclus spp
Cylicostephanus spp
Cylicodontophorus spp

Pinworms

(adults and fourth-stage larvae):
Oxyuris equi

5

Ascarids (adults and third- and fourth-stage larvae):

Parascaris equorum

Hairworms (adults):

Trichostrongylus axei

Large-mouth Stomach Worms

(adults):

Habronema muscae

Bots (oral and gastric stages):

Gastrophilus spp

Lungworms

(adults and fourth-stage 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.

6

EQVALAN (ivermectin)**EQVALAN** (ivermectin)**EQVALAN** (ivermectin)**EQVALAN** (ivermectin)**Dosage**

EQVALAN Liquid for Horses is formulated for administration by stomach tube (nasogastric intubation) or as an oral drench. The recommended dose is 200 mcg of ivermectin per kilogram (91 mcg/lb) of body weight. Each mL contains sufficient ivermectin to treat 110 lb (50 kg) of body weight; 10 mL will treat an 1100 lb (500 kg) horse.

Administration

Use a calibrated dosing syringe inserted into the bottle to measure the appropriate dose, or pour the EQVALAN Liquid into a graduated cylinder for dose measurement. Use a clean syringe if accessing the bottle to avoid contaminating the remaining product.

Administration by stomach tube (gravity or positive flow): The recom-

7

mended dose can be used undiluted or diluted up to 40 times with clean tepid water (see Notes to Veterinarian). Use tepid water to flush any drug remaining in the tube into the horse's stomach.

Administration by drench: For administration by this method, an undiluted dose is usually preferred. Clear the horse's mouth of any food material, elevate the horse's head, and using a syringe, deposit the appropriate dose in the back of the mouth. In order to avoid unnecessary coughing or the potential for material to enter the trachea and lungs, do not use excessive pressure (squirting), do not use a large (diluted) dose volume, and do not deposit the dose in the laryngeal area. Increased dose rejection may occur if the dose is deposited in the buccal space. Keep the horse's head elevated and observe the horse to insure the dose is retained.

8

Suggested Parasite Control Program

All horses should be included in a regular parasite control program with particular attention being paid to mares, foals and yearlings. Foals should be treated initially at 6 to 8 weeks of age, and routine treatment repeated as appropriate. EQVALAN effectively controls gastrointestinal nematodes and bots in horses. Regular treatment will reduce the chances of verminous arteritis and colic caused by *S. vulgaris*. With its broad spectrum, EQVALAN is well suited to be the major product in a parasite control program.

9

Mode of Action

Ivermectin, one of the avermectins, kills certain parasitic roundworms and ectoparasites such as mites and lice. The avermectins are different in their action from other antiparasitic agents. This action involves a chemical that serves as a signal from one nerve cell to another, or from a nerve cell to a muscle cell. This chemical, a neurotransmitter, is called gamma-aminobutyric acid or GABA.

In roundworms, ivermectin stimulates the release of GABA from nerve endings and enhances binding of GABA to special receptors at nerve junctions, thus interrupting nerve impulses — thereby paralyzing and killing the parasite.

The enhancement of the GABA effect in arthropods such as mites and lice resembles that in round-

10

Eqvalan (ivermectin)

worms except that nerve impulses are interrupted between the nerve ending and the muscle cell. Again, this leads to paralysis and death.

The principal peripheral neurotransmitter in mammals, acetylcholine, is unaffected by ivermectin. Ivermectin does not readily penetrate the central nervous system of mammals where GABA functions as a neurotransmitter.

11

Eqvalan (ivermectin)**Safety**

EQVALAN® (ivermectin) Liquid may be used in horses of all ages including mares at any stage of pregnancy. Stallions may be treated without adversely affecting their fertility. These horses have been treated with no adverse effects other than those noted under **Notes to Veterinarian**.

Warning: Do not use in horses intended for food purposes.

12

Eqvalan (ivermectin)**Precautions**

- **Caution:** EQVALAN Liquid has been formulated specifically for use in horses only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
- Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes. **Keep this and all drugs out of the reach of children.**
- Store in a tightly closed container at room temperature.
- Protect EQVALAN Liquid (undiluted or diluted) from light.

13

Eqvalan (ivermectin)

For customer service, contact Technical Services Department, U.S. Operations, Merck AgVet Division of Merck & Co., Inc. Box 2000, Rahway, New Jersey 07065-0915.

Environmental Safety

Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not contaminate lakes, streams, or ground water by direct application or by improper disposal of drug containers. Dispose of drug container in an approved landfill or by incineration.

14

Eqvalan (ivermectin)**Notes to Veterinarian**

Swelling and itching reactions after treatment with EQVALAN have occurred in horses carrying heavy infections of neck threadworm microfilariae, *Onchocerca* sp. These reactions were most likely the result of microfilariae dying in large numbers. Symptomatic treatment may be advisable.

Healing of summer sores involving extensive tissue changes may require other therapy in conjunction with EQVALAN. Reinfection, and measures for its prevention, should also be considered.

Special consideration should be given to the effects or potential for injury from handling, restraint, and placement of the tube during administration by stomach tube. EQVALAN Liquid should be administered by drench if the risks asso-

15

Eqvalan (ivermectin)

ciated with tubing are of concern. Due to the consequences of improper administration (also see **Dosage and Administration**), EQVALAN Liquid is intended for use by a veterinarian only and is not recommended for dispensing.

EQVALAN Liquid in 1 to 20 and 1 to 40 dilutions with tap water has been shown to be stable for 72 hours under the conditions recommended for the product (i.e., at room temperature, in a tightly closed container, protected from light). The diluted product does not promote the growth of common organisms. However, prolonged storage of the diluted product cannot be recommended, as the effects of possible contaminants and interactions with untested materials are unknown.

16

Eqvalan (ivermectin)**Package Information**

EQVALAN Liquid for Horses (Product 25877) is available in a 100 mL plastic bottle. Each bottle contains sufficient ivermectin to treat 10–500 kg (1100 lb) horses. Contents may be poured into a graduated cylinder for dose measurement. Alternatively, a clean syringe may be inserted directly into the bottle to draw off the appropriate dose.

17

FOR VETERINARY USE ONLY

Eqvalan
(ivermectin)
Liquid for Horses
10 mg per mL



MERCK
AgVet Division

Merck & Co., Inc.
Rahway, New Jersey 07065-0912 U.S.A.

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8888408 March 1994

Caution: Federal (U.S.) law restricts this drug to use by or on the order of a licensed veterinarian.

EQUI AID PRODUCTS, INC.

IVERMECTIN



LIQUID PREMIX FOR HORSES Type A Medicated Article

FOR VETERINARY USE ONLY

Antiparasitic (Anthelmintic and Boticide)

ACTIVE DRUG INGREDIENT:

Ivermectin 5% (50 mg/ml)

INACTIVE INGREDIENTS:

Propylene Glycol, Butylated Hydroxytoluene (BHT) and Benzyl Alcohol

INDICATIONS FOR USE.

For the treatment and control of the following parasites or parasitic conditions in horses

Large Strongyles (adult) (*Strongylus equinus*), (adult and arterial larval stages) (*Strongylus vulgaris*), (adult and migrating tissue stages) (*Strongylus edentatus*),

Small Strongyles, including those resistant to some benzimidazole class compounds (adult and fourth stage larvae) (*Cyathostomum* spp. *Cylicocyclus* spp., *Cylicodontophorus* spp. *Cylicostephanus* spp.), (adult) (*Triodontophorus* spp.);

Pinworms (adult and fourth stage larvae) (*Oxyuris equi*);

Ascarids (third- and fourth-stage larvae and adults) (*Parascaris equorum*);

Hairworms (adult) (*Trichostongylus axei*);

Large Mouth Stomach Worms (adult) (*Habronema muscae*);

Stomach Bots (oral and gastric stages) (*Gastrophilus* spp.);

Lungworms (adults and fourth stage larvae) (*Dictyocaulus arnfieldi*);

Intestinal Threadworms (adults) (*Strongyloides westeri*);

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

Dermatitis caused by neck threadworm microfilariae (*Onchocerca* spp.)

when administered either as a top-dress or mixed in the horses grain ration.

**WARNING : NOT FOR USE IN HORSES INTENDED FOR FOOD
FOR THE USE IN THE MANUFACTURING OF EQUINE FEEDS ONLY**

**STORE IN A TIGHTLY CLOSED CONTAINER AT ROOM TEMPERATURE
PROTECT IVERMECTIN LIQUID (UNDILUTED AND DILUTED) FROM LIGHT**

**SEE MIXING AND USE DIRECTIONS ON BACK PANEL
TO BE USED ONLY IN THE MANUFACTURE OF HORSE FEEDS
IMPORTANT: Must be diluted in feed before use.**

NET WT. 2.2 lb (1 kg)

(0.26 gal [1L])

IVM40-FL-0C1

IVERMECTIN LIQUID PREMIX FOR HORSES**TYPE A MEDICATED ARTICLE****ANTIPARASITIC (Anthelmintic and Boticide)**

CAUTION: IVERMECTIN LIQUID PREMIX FOR HORSES has been formulated specifically for use in horses only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result. Certain components of animal feeds, including medicated premixes, possess properties that may be a potential health hazard or a source of personal discomfort to certain individuals who are exposed to them. Human exposure should, therefore, be minimized by observing the general industry standards for occupational health and safety. Precautions such as the following should be considered: dust mask or respirators and protective clothing should be worn; dust-arresting equipment and adequate ventilation should be utilized; personal hygiene should be observed; wash before eating or leaving a work site; be alert for signs of allergic reactions—seek prompt medical treatment if such reactions are suspected.

KEEP THIS AND ALL DRUGS OUT OF REACH OF CHILDREN.**Mixing and Use Directions.**

IVERMECTIN LIQUID PREMIX FOR HORSES is to be administered either as a top-dress or mixed in the horse's ration at a rate of 200 micrograms ivermectin per kilogram body weight (0.2 mg/kg or .091 mg/lb).

All horses should be included in a regular parasite control program with particular attention being paid to mares, foals and yearlings. Routine treatment should be repeated as appropriate. Consult your veterinarian for a control program to meet your specific needs. Ivermectin effectively controls gastrointestinal nematodes and bots in horses. Regular treatment will reduce the chances of verminous arteritis and colic caused by *S. vulgaris*. With its broad spectrum, ivermectin, is well suited to be the major product in a parasite control program.

IVERMECTIN LIQUID PREMIX FOR HORSES may be used in horses at any stage of pregnancy or lactation. Stallions may be treated without adversely affecting their fertility. Foals should be treated initially when consistent intake of grain mix is occurring (usually between two and three months of age).

Follow mixing directions. Ivermectin Liquid Premix for Horses should be mixed in the feed in accordance with good manufacturing practices for medicated feeds.

Typical Dry Feed Mixing Directions to Deliver 200 Micrograms Ivermectin per Kilogram Body Weight

LB MEDICATED GRAIN MIX PER 100 LB BODY WEIGHT	ML OF IVERMECTIN LIQUID PREMIX	LB NON-MEDICATED DRY FEED	(g/ton) RESULTING CONCENTRATION
2.00	181	1,999.6	9
1.5	242	1,999.5	12
1.0	363	1,999.2	18
0.5	726	1,998.4	36
0.2	1,814	1,996.0	91
LB MEDICATED TOP-DRESS PER 100 LB OF BODY WEIGHT			
0.04	9,076	1,980.0	454
0.025	14,529	1,968.0	726
0.025	18,171	1,960.0	907
0.0125	29,088	1,936.1	1,451

Liquid Medicated Feeds

Type B and C medicated feeds containing 0.1% to 1% ivermectin may be manufactured by thoroughly mixing 2 to 20 gallons of IVERMECTIN LIQUID PREMIX FOR HORSES TYPE A MEDICATED ARTICLE to 100 gallons of non-medicated liquid.

ENVIRONMENTAL SAFETY: Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not contaminate lakes, streams, or ground water by direct application or by improper disposal of drug containers. Dispose of drug container in an approved landfill or by incineration.

Note to User: Swelling and itching reactions after treatment with ivermectin have occurred in horses carrying heavy infestations of neck threadworm (*Onchocera* sp.) microfilariae. These reactions were most likely the result of microfilariae dying in large numbers. Symptomatic treatment may be advisable. Consult your veterinarian should any such reactions occur. Healing of summer sores involving extensive tissue changes may require appropriate therapy in conjunction with treatment with ivermectin. Reinfestation, and measures for its prevention, should be considered. Consult your veterinarian if the condition does not improve.

ANADA # Approved by FDA

Distributed by

Lot No.

Expiration Date

BAR CODE



IVM40-BL-0C1

ZIMECTERIN® (Ivermectin) Paste 1.87% ANTHELMINTIC AND BOTICIDE

Lot No & Exp Date
HBK018 05-2001

For treatment of Large Strongyles, Small Strongyles, Pinworms, Roundworms (Ascarids), Hairworms, Neck Threadworms, Large-mouth Stomach Worms, Bots. See carton for complete indications and use directions. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

CAUTION: Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes. Keep this and all drugs out of the reach of children. 8615303 Made in U.S.A.

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

NET WT. 0.21 OZ. (6.08g)

Distributed by: FARNAM COMPANIES, INC., Omaha, Nebraska 68112, U.S.A.

Syringe Label

Example OTC Ivermectin Paste

Back of Box Label

Lot No & Exp Date ▼

**HBK018
05-2001**

INDICATIONS: Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism. ZIMECTERIN® (ivermectin) Paste provides effective 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*, *Tricodontophorus* spp; **Small Strongyles** including those resistant to some benzimidazole class compounds (adults and fourth-stage larvae) — *Cyathostomum* spp, *Cylicocyclus* spp, *Cylicostephanus* spp, *Cylicodontophorus* spp; **Pinworms** (adults and fourth-stage larvae) — *Oxyuris equi*; **Ascarids** (adults and third- and fourth-stage larvae) — *Parascaris equorum*; **Hairworms** (adults) — *Trichostrongylus axei*; **Large-mouth Stomach Worms** (adults) — *Habronema muscae*; **Bots** (oral and gastric stages) — *Gastrophilus* spp; **Lungworms** (adults and fourth-stage larvae) — *Dicyocaulus amfii*; **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.

DOSAGE AND ADMINISTRATION: 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 that 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.

PARASITE CONTROL PROGRAM: All horses should be included in a regular parasite control program with particular attention being paid to mares, foals and yearlings. Foals should be treated initially at 6 to 8 weeks of age, and routine treatment repeated as appropriate. Consult your veterinarian for a control program to meet your specific needs. ZIMECTERIN (ivermectin) Paste effectively controls gastrointestinal nematodes and bots of horses. Regular treatment will reduce the chances of verminous arteritis caused by *S. vulgaris*.

PRODUCT ADVANTAGES: Broad-spectrum Control — ZIMECTERIN Paste kills important internal parasites, including bots and the arterial stages of *Strongylus vulgaris*, with a single dose. ZIMECTERIN Paste is

a potent anti-parasitic agent that is neither a benzimidazole nor an organo-phosphate.
Safety — ZIMECTERIN (ivermectin) Paste may be used in horses of all ages, including mares at any stage of pregnancy. Stallions may be treated without adversely affecting their fertility.



83855

Distributed by:
FARNAM COMPANIES, INC.
Omaha, Nebraska 68112 U.S.A.



U.S. Pat. 4,199,569
Made in U.S.A.

ZIMECTERIN REG TM FARNAM COMPANIES, Inc.
ZIMECTERIN® (ivermectin) Paste 1.87%

Side of Box Labels

most likely the result of microfilariae dying in large numbers. Symptomatic treatment may be advisable. Consult your veterinarian should any such reactions occur. Healing of summer sores involving extensive tissue changes may require other appropriate therapy in conjunction with treatment with ZIMECTERIN (ivermectin) Paste. Reinfection, and measures taken to prevent it, should also be considered. Consult your veterinarian if the condition does not improve.

NOTE TO USER: Swelling and itching reactions after treatment with ZIMECTERIN Paste have occurred in horses carrying heavy infections of neck threadworm (*Onchocerca* sp) microfilariae. These reactions were rare.
ZIMECTERIN (ivermectin) Paste syringe in an approved landfill or by incineration.
Ivermectin and excreted ivermectin residues may adversely affect aquatic organisms. Do not contaminate ground or surface water. Dispose of the

CAUTION: ZIMECTERIN® (ivermectin) Paste has been formulated specifically for use in horses only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result. Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes. Keep this and all drugs out of the reach of children.

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

top of box label



FOR ORAL USE IN HORSES ONLY
ZIMECTERIN®
(ivermectin) **Paste 1.87%**
ANTHELMINTIC AND BOTICIDE
Contents will treat up to 1250 lb body weight
Net Wt 0.21 oz (6.08 g)



Product 70961



Product 41284

ivomec®

(ivermectin)

Premix for Swine Type A Medicated Article Antiparasitic



ACTIVE DRUG INGREDIENT

Ivermectin... 0.6%

INGREDIENTS

Ground Corn Cob

SEE DIRECTIONS ON BACK PANEL

TO BE USED ONLY IN THE MANUFACTURE OF SWINE FEEDS

Important: Must be diluted in feed before use

MERCK AGVET DIVISION

Merck & Co., Inc.

Kenilworth, NJ 07033-0001, 0001 U.S.A.

MADE IN THE NETHERLANDS



IVOME[®]C Premix for Swine

(ivermectin)

Type A Medicated Article

INDICATIONS

For the treatment and control of gastrointestinal roundworms (*Ascaris suum*, adults and fourth-stage larvae; *Ascarops strongylina*, adults; *Hyostrongylus rubidus*, adults and fourth-stage larvae; *Oesophagostomum* spp., adults and fourth-stage larvae), kidneyworms (*Stephanurus dentatus*, adults and fourth-stage lar-

vae), lungworms (*Metastrongylus* spp., adults), lice (*Haematopinus suis*) and mange mites (*Sarcoptes scabiei* var. *suis*) when incorporated into complete swine feeds at the level listed in the table below. Follow mixing directions when preparing complete feeds.

DOSAGE AND ADMINISTRATION

Add IVOME[®]C Premix to starter, grower and finisher feeds at 300 g per ton to supply 1.8 g ivermectin per ton (2 ppm) of feed. Use this Type C Medicated Feed as

the only feed for 7 consecutive days. This provides approximately 100 mcg ivermectin per kg of body-weight per day.

MIXING DIRECTIONS

Required amount of IVOME[®]C Premix (Type A) Medicated Article 0.6% to medicate one ton of complete (Type C) Medicated Feed

Required level of ivermectin per ton of complete (Type C) Medicated Feed

300 g

1.8 g

IVOME[®]C Premix should be thoroughly and evenly mixed in the feed in accordance with good manufacturing practices for medicated feeds. Dispersion of ivermectin in the feed is enhanced by diluting 1 part ivermectin Type A Medicated Article with 14 parts of finely ground feed ingredients to provide an intermediate premix. Ten lb of this intermediate premix is used to provide 1.8 g ivermectin in one ton of complete Type C Medicated Feed.

on which they feed. Do not permit water runoff from swine production sites to enter lakes, streams, or ponds. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

WARNING: WITHDRAW 5 days before slaughter.

RECOMMENDED TREATMENT PROGRAM:

To reduce natural sources for reinfection, it is recommended that a parasite control program with IVOME[®]C Premix should begin with treatment of all growing pigs on the premises for 7 consecutive days. Where an all-in all-out system is not possible, all growing pigs being transferred between facilities where reinfection may occur and all incoming pigs should be treated with IVOME[®]C Premix for Swine for 7 consecutive days.

Keep this and all drugs out of the reach of children.

CAUTION: • IVOME[®]C Premix for Swine has been formulated specifically for use in swine **only**. This product should not be used for other animal species.

Pigs exposed to contaminated premises, soil or pasture may need retreatment if reinfection occurs.

- Not to be fed to swine that weigh more than 220 lbs.
- Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

NOTE: (1) Since the effect of ivermectin on mange mites is not immediate, avoid contact between treated pigs and mange free pigs for approximately one week after completion of treatment. Exposure of treated pigs to mange infested pigs or contaminated premises may result in re-infestation

ENVIRONMENTAL SAFETY:

Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms

(2) Louse eggs are unaffected by ivermectin and may require up to three weeks to hatch. Louse infestations developing from hatching eggs may require retreatment.

*IVOME[®]C and Pig Head Logo are registered trademarks of Merck & Co., Inc., Whitehouse Station, NJ 08889

LOT AND EXP DATE

(Pyrantel Tartrate)

EQUI AID CW 48

TYPE A MEDICATED ARTICLE

Equine Anthelmintic

Mixing and Use Directions

Equi Aid CW is to be administered on a continuous basis either as a top dress or mixed in the horse's daily grain ration at the rate of 1.2 mg/lb (2.64 mg/kg) body weight daily. The duration of administration is for the period during which the animal is at risk of exposure to internal parasites.

Foals may be treated at such time when consistent intake of grain mix is occurring. This is generally between two and three months of age.

Equi Aid CW may be used in mares at any stage of pregnancy or lactation. Stallion fertility is not affected by the use of Equi Aid CW.

TYPICAL MIXING DIRECTIONS TO DELIVER 1.2 mg/lb (2.64 mg/kg)

lb of medicated grain mix per 100 lb of body weight	lb of Equi Aid CW 48	lb of non-medicated feed	Resulting concentration g/ton
2.00	2.5	1,997.5	120
1.50	3.3	1,996.7	160
1.00	5.0	1,995.0	240
0.50	10.0	1,990.0	480
0.20	25.0	1,975.0	12,000
lb of medicated top-dress per 100 lb of body weight			
0.04	125.0	1,875.0	6,000
0.025	200.0	1,800.0	9,600
0.02	250.0	1,750.0	12,000

Warning: NOT FOR USE IN HORSES INTENDED FOR FOOD.

CAUTION: CONSULT YOUR VETERINARIAN BEFORE USING IN SEVERELY DEBILITATED ANIMALS AND FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT AND CONTROL OF PARASITISM. DO NOT MIX IN FEEDS CONTAINING BENTONITE.

ANADA 200-168, APPROVED BY FDA

CWA50 BL 7H1

EQUI AID CW[®] 48

(Pyrantel Tartrate)

EQUI AID CW 48

Type A Medicated Article

EQUINE ANTHELMINTIC

ACTIVE DRUG INGREDIENT: Pyrantel Tartrate..... 10.6% (48 grams per pound)

INGREDIENTS: Brewers dried yeast, brewers dried grains, and silicon dioxide.

INDICATIONS FOR USE:

For the prevention of *Strongylus vulgaris* larval infections in horses.

For control of the following parasites in horses:

LARGE STRONGYLES (adults) *S. vulgaris*, *S. edentatus*, *Triodontophorus* spp.

SMALL STRONGYLES (adult and fourth-stage larvae) *Cyathostomum* spp., *Cylicocycylus* spp., *Cylicostephanus* spp., *Cylicodontophorus* spp., *Poteriostomum* spp.

PINWORMS (adult and fourth-stage larvae) *Oxyuris equi*

ASCARIDS (adult and fourth-stage larvae) *Parascaris equorum*.

WARNING: DO NOT USE IN HORSES INTENDED FOR FOOD.
FOR USE IN THE MANUFACTURING OF EQUINE FEEDS ONLY

CAUTION: Certain components of animal feeds, including medicated premixes, possess properties that may be a potential health hazard or a source of personal discomfort to certain individuals who are exposed to them. Human exposure should, therefore, be minimized by observing the general industry standards for occupational health and safety.

Precautions such as the following should be considered: dust masks or respirators and protective clothing should be worn. Dust arresting equipment and adequate ventilation should be utilized; personal hygiene should be observed; wash before eating or leaving a work site; be alert for signs of allergic reactions - seek prompt medical treatment if such reactions are suspected.

SEE BACK OF PACKAGE FOR FURTHER USE DIRECTIONS
STORE IN A DRY COOL PLACE

Net Weight 50 pounds

Distributed by



Phoenix, AZ

(PYRANTEL TARTRATE)
EQUI AID CW[®] 48

CWA50-FL 7H1

NDC 0009-0547-01

Net Weight 40 Pounds (18 kg)
(4.627gal [17.5 L])

MGA[®] 500

Liquid Premix

(Type A Medicated Article)

**Heifers Fed in Confinement for Slaughter:
For Increased Rate of Weight Gain, Improved Feed Efficiency
and Suppression of Estrus (Heat).**

**Heifers Intended for Breeding:
For Suppression of Estrus (Heat).**

Each Pound Contains:

Active Drug Ingredient:

Melengestrol Acetate 500 mg
(as melengestrol acetate and its propylene glycol ketal)

Inactive Ingredient:

Propylene Glycol, U.S.P. 99.89%

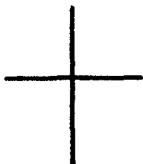
Caution: For manufacturing, processing, or repacking. To be mixed with feed prior to animal use. Use only as directed. Excessive contact with skin should be avoided. Destroy empty container. Do not reuse.

Store at room temperature

NADA #39-402, Approved by FDA

813 931 107γ

Pharmacia & Upjohn Company • Kalamazoo, MI 49001, USA



MGA 500
CCS# 0547-01
813 931 107 gamma
EDP# 692017
8.75 x 7.125"
Black

MGA 500
CCS# 0547-01
813 931 107 gamma
EDP# 692017
8.75 x 7.125"
PMS 2915

NDC 0009-0547-01

MGA[®] 500 Liquid Premix (Type A Medicated Article)

Heifers Fed in Confinement for Slaughter: For Increased Rate of Weight Gain, Improved Feed Efficiency and Suppression of Estrus (Heat).

Heifers Intended for Breeding: For Suppression of Estrus (Heat).

DIRECTIONS FOR USE:

Heifers Fed in Confinement for Slaughter:

MGA 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in liquid Type C medicated feed which must be fed at 0.5 to 2.0 pounds per head daily to provide 0.25 to 0.5 mg of melengestrol acetate per head per day. Average daily intakes approximating the middle of this range provide the most optimal and economical improvements in rate of gain and feed utilization. Constant daily intakes of 0.35 to 0.50 mg per head per day give a high degree of estrus suppression. Levels of 0.25 to 0.35 mg provide a lower but still effective degree of estrus suppression.

Heifers Intended for Breeding:

MGA 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in the supplement to provide 0.5 mg of melengestrol acetate per head per day.

Not for human use. Restricted Drug—Use Only As Directed (California)

CAUTION: Not effective in steers and spayed heifers.

Heifers Fed in Confinement for Slaughter:

Withdrawal periods of three to five days or more should be avoided to prevent the possibility that the heifers may come into estrus (heat) at loading time.

Heifers Intended for Breeding:

Do not exceed 24 days of feeding of melengestrol acetate to heifers intended for breeding. A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

MIXING DIRECTIONS:

Liquid Type B and C medicated feeds containing melengestrol acetate must have a pH of 4.0 to 8.0 and their labels must bear appropriate mixing directions. Mixing directions for liquid Type B or C feeds stored in recirculation tank systems are: "Recirculate immediately prior to use for no less than 10 minutes, moving not less than 1 percent of the tank contents from the bottom of the tank to the top. Recirculate daily, as directed in this paragraph even when the Type B (or C) feed is not used." Mixing directions for liquid Type B and C feeds stored in mechanical, air or other agitation-type tank systems are: "Agitate immediately prior to use for not less than 10 minutes, creating a turbulence at the bottom of the tank that is visible at the top. Agitate daily, as directed in this paragraph, even when the Type B (or C) feed is not used."

Intermediate premixes should not be made from MGA 500 Liquid Premix (Type A Medicated Article) except as a part of a continuous mixing operation to make a complete liquid Type B or Type C medicated feed.

Thoroughly mix 0.5 to 4 pounds of MGA 500 Liquid Premix (Type A Medicated Article) per ton of a non-medicated feed to prepare a Type C medicated feed containing 0.25 to 2.0 grams of melengestrol acetate per ton. The following Table may be used as a guide in determining the amount of MGA 500 Liquid Premix (Type A Medicated Article) to be added to prepare a ton of Type C medicated feed.

Amount of Type C Feed Fed (lb/head/day)	Melengestrol Acetate (mg/head/day)	MGA 500 Liquid Premix Per Ton of Type C Feed		Amount of Type C Feed Fed (lb/head/day)	Melengestrol Acetate (mg/head/day)	MGA 500 Liquid Premix Per Ton of Type C Feed	
		When Added by Weight (lb)	When Added by Volume (mL)			When Added by Weight (lb)	When Added by Volume (mL)
0.5	0.25	2.00	876	1.5	0.25	0.66	289
0.5	0.30	2.40	1051	1.5	0.30	0.80	350
0.5	0.35	2.80	1226	1.5	0.35	0.93	407
0.5	0.40	3.20	1402	1.5	0.40	1.07	469
0.5	0.45	3.60	1577	1.5	0.45	1.20	526
0.5	0.50	4.00	1752	1.5	0.50	1.33	582
1.0	0.25	1.00	438	2.0	0.25	0.50	219
1.0	0.30	1.20	526	2.0	0.30	0.60	263
1.0	0.35	1.40	613	2.0	0.35	0.70	307
1.0	0.40	1.60	701	2.0	0.40	0.80	350
1.0	0.45	1.80	788	2.0	0.45	0.90	394
1.0	0.50	2.00	876	2.0	0.50	1.00	438

Type B medicated feed containing 4 to 10 grams melengestrol acetate per ton may be manufactured by thoroughly mixing 8 to 20 lbs of MGA 500 Liquid Premix with 1992 to 1980 lbs of non-medicated feed. Labeling for such Type B feed shall contain directions for manufacturing Type C medicated feeds containing 0.25 to 2.0 grams melengestrol acetate per ton (0.125 to 1.0 mg/lb). The Type C medicated feed, containing melengestrol acetate, must be top dressed on grain or roughage or mixed with a complete ration at the rate of 0.5 to 2.0 pounds per head per day.

Good manufacturing practice regulations must be adhered to in manufacturing feeds containing MGA 500.

Pharmacia & Upjohn Company • Kalamazoo, MI 49001, USA

813 925 006 ε



MGA 500 Liquid Premix
 CCS# 0547-01
 EDP# 692017
 CODE# 813 925 006ε (epsilon)
 8.75" X 7.125"
 Draw # PD1480
 BLACK

I NO. 51227-0001

CONTROL NO.
EXPIRES**BOVATEC® 20 LIQUID**

brand of lasalocid

Type A Medicated Article. (Medicated Premix)

CATTLE:
FOR IMPROVED FEED EFFICIENCY AND INCREASED RATE OF WEIGHT GAIN WHEN USED IN MEDICATED FEEDS FOR CATTLE FED IN CONFINEMENT FOR SLAUGHTER.

FOR INCREASED RATE OF WEIGHT GAIN WHEN USED IN MEDICATED FEEDS FOR PASTURE CATTLE (SLAUGHTER, STOCKER, FEEDER CATTLE, AND DAIRY AND BEEF REPLACEMENT HEIFERS).

FOR CONTROL OF COCCIDIOSIS CAUSED BY *Eimeria bovis* AND *E. zuernii* IN CATTLE UP TO 800 POUNDS.**SHEEP:**
FOR PREVENTION OF COCCIDIOSIS CAUSED BY *Eimeria ovina*, *E. crandallis*, *E. ovinoidalis* (*E. ninakohlyakimovae*), *E. parva*, AND *E. intricata* IN SHEEP MAINTAINED IN CONFINEMENT.

Each pound contains 90.7 grams (20%) of lasalocid (as lasalocid sodium activity) in a carrier suitable for incorporation in liquid feed supplements.

IMPORTANT: MUST BE THOROUGHLY MIXED IN FEEDS BEFORE USE.

DO NOT FEED UNDILUTED.

See side panels for use directions.



Net Wt. 50 Lbs. (22.68 Kg)

Roche Vitamins Inc.
Parsippany, New Jersey 07054

XPL0037087

NADA 96-298, APPROVED BY FDA.

MADE IN U.S.A.

USE DIRECTIONS:**A. FEEDLOT CATTLE BEING FED IN CONFINEMENT FOR SLAUGHTER — FOR IMPROVED FEED EFFICIENCY AND INCREASED RATE OF WEIGHT GAIN AND FOR CONTROL OF COCCIDIOSIS CAUSED BY *Eimeria bovis* AND *E. zuernii*.****SHEEP — FOR PREVENTION OF COCCIDIOSIS CAUSED BY *Eimeria ovina*, *E. crandallis*, *E. ovinoidalis* (*E. ninakohlyakimovae*), *E. parva*, AND *E. intricata* IN SHEEP MAINTAINED IN CONFINEMENT.****FEEDING DIRECTIONS:****FOR IMPROVED FEED EFFICIENCY IN CATTLE:**
Feed continuously at the rate of not less than 10 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 100 mg nor more than 360 mg per head per day.**FOR IMPROVED FEED EFFICIENCY AND INCREASED RATE OF WEIGHT GAIN IN CATTLE:**
Feed continuously at the rate of not less than 25 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 250 mg nor more than 360 mg per head per day.**FOR CONTROL OF COCCIDIOSIS IN CATTLE:**
Feed continuously at the rate of 30 grams of lasalocid per ton of total ration (90% dry matter) to provide an intake of 1 mg of lasalocid per 2.2 pounds of body weight per day in cattle up to 800 pounds (maximum 360 mg per day).**FOR PREVENTION OF COCCIDIOSIS IN SHEEP:**
Feed continuously at the rate of not less than 20 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 15 mg nor more than 70 mg per head per day depending on body weight.**B. PASTURE CATTLE (SLAUGHTER, STOCKER, FEEDER CATTLE, AND DAIRY AND BEEF REPLACEMENT HEIFERS) — FOR INCREASED RATE OF WEIGHT GAIN AND FOR CONTROL OF COCCIDIOSIS CAUSED BY *Eimeria bovis* AND *E. zuernii*.****FEEDING DIRECTIONS:****FOR INCREASED RATE OF WEIGHT GAIN:**
Feed at the rate of not less than 60 mg nor more than 200 mg per head per day. **Hand-fed:** The drug must be contained in at least one pound of feed. **Self-fed:** All medicated, self-fed supplements require a FD 1900.**FOR CONTROL OF COCCIDIOSIS:**
Hand feed continuously at the rate of 1 mg of lasalocid per 2.2 pounds of body weight per day in cattle up to 800 pounds (maximum 360 mg per day).**MIXING DIRECTIONS — for incorporation into liquid feed supplements:**

- (1) Agitate Bovatec® 20 Liquid before use.
- (2) Supplements with suspending agent(s) should be in a pH range of 4 - 8 and maintain positional stability for up to three months with a viscosity not less than 300 cps.
- (3) Conventional liquid supplements should be in a pH range of 4 - 8. Ten minute recirculation required daily and prior to use.

TAKE TIME



OBSERVE LABEL DIRECTIONS

The following is provided as a guide in determining the quantity of Bovatec 20 Liquid (Type A medicated article) to be added in preparing liquid feed supplements (LFS). Preparation of intermediate liquid premix is not recommended.

LFS TO BE FED UNDILUTED

As a Type C Medicated Feed — Hand-Fed or Top Dressed

Amount of LFS to be fed (Lb/Head/Day)	To achieve a lasalocid intake of (Mg/Head/Day)	Bovatec 20 Liquid per Ton LFS	
		Pounds	Fluid Ounce*
0.5	15	0.67	9.8
0.5	60	2.85	39.2
0.5	70	3.09	45.7
0.5	100	4.41	65.3
0.5	200	8.83	130.6
0.5	360	15.88	235.0
1.0	15	.34	4.9
1.0	60	1.33	19.6
1.0	70	1.55	22.9
1.0	100	2.21	32.7
1.0	200	4.41	65.3
1.0	360	7.94	117.5

LFS TO BE DILUTED

As a Type B Medicated Feed — Mixed into a Feed

Amount of LFS to be added to final feed (Lb/Ton)	Lasalocid in final feed (Gram/Ton)	Bovatec 20 Liquid per Ton LFS	
		Pounds	Fluid Ounce*
100	10	2.21	32.7
100	20	4.42	65.3
100	25	5.52	81.6
100	30	6.62	97.9
150	10	1.48	21.8
150	20	2.96	43.6
150	25	3.68	54.4
150	30	4.42	65.3
200	10	1.11	16.4
200	20	2.21	32.7
200	25	2.76	40.8
200	30	3.31	49.0

*6.13 gm lasalocid per fluid ounce (Bovatec 20 Liquid specific gravity is 1.035)

NOTE: Coccidiosis may occur when young pasture cattle are co-mingled with adult cattle passing coccidial oocysts. CAUTION: Do not allow horses or other equines access to premixes or supplements containing lasalocid, as ingestion may be fatal. The safety of lasalocid in unapproved species has not been established. Feeding undiluted or mixing errors resulting in excessive concentrations of lasalocid could be fatal to cattle and sheep.

WARNING: When mixing and handling lasalocid liquid premix, use protective clothing and impervious gloves. Avoid contact with eyes. Operators should wash thoroughly with soap and water after handling. A withdrawal period has not been established for this product in pre-ruminating calves. DO NOT USE IN CALVES TO BE PROCESSED FOR VEAL.

Safe-Guard® Dewormer 20% Type A Medicated Article

NDC 12799-472-00

ACTIVE DRUG INGREDIENT: Fenbendazole 200 grams per kilogram (90.7 grams per pound). INERT INGREDIENTS: Roughage Products or Roughage Products and Calcium Carbonate; and Mineral Oil or Soybean Oil.

CATTLE: Dairy and Beef Cattle SWINE: Growing pigs, gilts, pregnant sows, and boars Zoo and Wildlife Animals

FOR THE REMOVAL AND CONTROL OF:

Lungworms: (*Dictyocaulus viviparus*).
Stomach worms: Barberpole worms (*Haemonchus contortus*), brown stomach worms (*Ostertagia ostertagi*), small stomach worms (*Trichostrongylus axei*).
Intestinal worms: Hookworms (*Bunostomum phlebotomum*), thread-necked intestinal worms (*Nematodirus helvetianus*), small intestinal worms (*Cooperia punctata* & *C. oncophora*).
Bankrupt worms: (*Trichostrongylus colubriformis*).
Nodular worms: (*Oesophagostomum radiatum*).

DOSAGE REGIMEN

5 mg fenbendazole per kg body weight in a one (1) day treatment (2.27 mg fenbendazole per pound).

EXAMPLE OF MIXING AND FEEDING RATES FOR SAFE-GUARD® 20% TYPE A MEDICATED ARTICLE

For a one (1) day treatment, mix the following quantities of SAFE-GUARD® 20% Type A Medicated Article into the daily ration according to body weight and number of cattle per pen.

Amount of SAFE-GUARD® 20% Type A Medicated Article for:

Body Weight	10 Cattle		20 Cattle		100 Cattle		
	lbs.	kg	g	lbs.	g	lbs.	
200	90.7	23	0.05	46	0.10	230	0.5
400	181.4	46	0.10	92	0.20	460	1.0
600	272.2	69	0.15	138	0.30	690	1.5
800	362.9	92	0.20	184	0.40	920	2.0
1000	453.6	114	0.25	228	0.50	1140	2.5
1400	635.0	160	0.35	320	0.70	1600	3.5

Feed as the sole ration for one (1) day. No prior withdrawal of feed or water necessary. When feed containing SAFE-GUARD® has been fed for 1 day and blended according to the above rates based on weight and number of cattle treated, a total intake of 2.27 mg fenbendazole per pound of body weight is assured. Cattle feed containing SAFE-GUARD® can be fed pelleted or as meal.

Under conditions of continued exposure to parasites, retreatment may be needed after 4-6 weeks.

GENERAL MIXING DIRECTIONS

It is recommended that SAFE-GUARD® 20% Type A Medicated Article be diluted before addition to the final feed. A dilution of one part of SAFE-GUARD® 20% Type A Medicated Article and nine parts of grain carrier is the suggested working premix. The working premix is then blended with the complete feed mixture. Thoroughly mix both working premix and complete feed to ensure complete and uniform distribution of the SAFE-GUARD® 20% Type A Medicated Article.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN. NOT FOR USE IN HUMANS. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, obtain an MSDS, or for assistance contact Hoechst Roussel Vet National Service Center at 1-800-247-4838.

RESIDUE WARNING: Cattle must not be slaughtered within 13 days following last treatment. There are no known contraindications to the use of the drug in cattle. For dairy cattle, there is no milk withdrawal period.

FOR THE REMOVAL AND CONTROL OF:

Lungworms: (*Metastrongylus apri*, *Metastrongylus pudendotectus*).
Gastrointestinal worms: Adult and larvae (L₃, L₄ stages, liver, lung, intestinal forms) large roundworms (*Ascaris suum*); nodular worms (*Oesophagostomum dentatum*, *O. quadrispinulatum*); small stomach worms (*Hyostromylus rubidus*); whipworms, adult and larvae (L₂, L₃, L₄ stages - intestinal mucosal forms, (*Trichuris suis*).
Kidney worms: Adult and larvae (*Stephanurus dentatus*).

DOSAGE REGIMEN

9 mg fenbendazole per kg body weight (4.08 mg fenbendazole per pound) to be fed as the sole ration over a period of 3 to 12 days.

EXAMPLE OF MIXING AND FEEDING RATES FOR SAFE-GUARD® 20% TYPE A MEDICATED ARTICLE

Average daily feed consumption		Amount of SAFE-GUARD® 20% Type A Medicated Article added to each ton of swine feed based on weight and average feed consumption.					
		Treatment Period					
Pig. Wt. (lbs.)	lbs. of Feed	3 Days		6 Days		12 Days	
		lbs.	Grams	lbs.	Grams	lbs.	Grams
30	2.25	0.40	182	0.20	91	0.10	46
50	3.20	0.47	213	0.24	107	0.12	54
75	4.25	0.53	241	0.27	121	0.14	61
100	5.30	0.57	258	0.29	129	0.15	65
150	6.80	0.66	301	0.33	151	0.17	76
200	8.00	0.75	341	0.38	171	0.19	86

Feed as the sole ration for three (3) to twelve (12) consecutive days. No prior withdrawal of feed or water necessary. When feed containing SAFE-GUARD® has been blended according to the above rates based on pig weight and average daily feed consumption, and is then fed for 3-12 days, a total intake of 9 mg fenbendazole per kilogram body weight (4.08 mg fenbendazole per pound) is assured. Swine feeds containing SAFE-GUARD® can be fed pelleted or as meal.

GENERAL MIXING DIRECTIONS

It is recommended that SAFE-GUARD® 20% Type A Medicated Article be diluted before addition to the final feed. A dilution of one part of SAFE-GUARD® 20% Type A Medicated Article and nine parts of grain carrier is the suggested working premix. The working premix is then blended with the complete feed mixture. Thoroughly mix both working premix and complete feed to ensure complete and uniform distribution of the SAFE-GUARD® 20% Type A Medicated Article.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN. NOT FOR USE IN HUMANS. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, obtain an MSDS, or for assistance contact Hoechst Roussel Vet National Service Center at 1-800-247-4838.

RESIDUE WARNING: There is no pre-slaughter withdrawal period as SAFE-GUARD® can be fed to day of slaughter.

FOR THE REMOVAL AND CONTROL OF:

Internal parasites in hoofed zoo and wildlife animals (see dosage section for specific parasites, animal species and required doses).

DOSE/DOSAGE REGIMENS:

Host Animal	Recommended Treatment for	mg Fenbendazole/kg Body Wt./Day x Days of Treatment
Bighorn Sheep (<i>Ovis canadensis canadensis</i>)	lungworms: (<i>Protostrongylus</i> spp.)	10 mg x 3
Feral Swine (<i>Sus scrofa</i>)	kidney worms: (<i>Stephanurus dentatus</i>), roundworms: (<i>Ascaris suum</i>), nodular worms: (<i>Oesophagostomum dentatum</i>)	3 mg x 3
Ruminants - subfamily antilopinae: Persian gazelles (<i>Gazella subgutturosa subgutturosa</i>) Addra gazelle (<i>Gazella dama ruficollis</i>) Stenderhorn Gazelle (<i>Gazella leptoceros</i>) Kenya impala (<i>Aepyceros melampus rendilis</i>) Roosevelt's gazelle (<i>Gazella granti roosevelti</i>) Indian blackbuck (<i>Antelope cervicapra</i>) Mhorri gazelle (<i>Gazella dama mhorri</i>) Thomson's gazelles (<i>Gazella thomsoni thomsoni</i>)	small stomach worms: (<i>Trichostrongylus</i> spp.), thread-necked intestinal worms: (<i>Nematodirus</i> spp.), barberpole worms: (<i>Haemonchus</i> spp.), whipworms: (<i>Trichuris</i> spp.)	2.5 mg x 3
Ruminants - subfamily hippotraginae: Addax (<i>Addax nasomaculatus</i>) Angolan roan antelope (<i>Hippotragus equinus cottoni</i>) Fringed-ear oryx (<i>Oryx gazella callotis</i>) Arabian oryx (<i>Oryx leucoryx</i>)		
Ruminants - subfamily caprinae: Armenian mouflon (<i>Ovis orientalis gmelini</i>) Russian saiga (<i>Saiga tatarica</i>)		

It is recommended that the user exercise judgmental expertise as needed for retreatment within six (6) weeks. This would depend upon the conditions of continued exposure to parasites, condition of treated animals, and ambient temperatures.

GENERAL MIXING DIRECTIONS:

SAFE-GUARD® 20% Type A Medicated Article must be mixed according to directions and at correct concentrations based upon the species to be treated. It is recommended that SAFE-GUARD® 20% Type A Medicated Article be diluted before addition to the final feed. The correct proportions of premix and feed ingredients should be established for blending into the complete feed. This premix and feed ingredient combination should be thoroughly and uniformly mixed with the complete feed.

SAFE-GUARD® 20% Type A Medicated Article can be fed to adult and young animals either in a mash or pelleted feed. No prior withdrawal of feed or water is necessary.

WARNING: KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN. NOT FOR USE IN HUMANS. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, obtain an MSDS, or for assistance contact Hoechst Roussel Vet National Service Center at 1-800-247-4838.

RESIDUE WARNING: Do not use 14 days before or during the hunting season.

ANIMAL SAFETY: No contraindications for the use of fenbendazole in a zoo environment have been established. Administration to breeding and pregnant ruminants at 2 to 22 times the recommended dose has had no apparent adverse effect.

MUST BE MIXED BEFORE FEEDING ACCORDING TO DIRECTIONS AND PERMITTED CLAIMS

FOR USE IN MANUFACTURED FEEDS ONLY

CONSULT YOUR VETERINARIAN FOR ASSISTANCE IN THE DIAGNOSIS, TREATMENT, AND CONTROL OF PARASITISM

Net Weight 25 pounds (11.34 kg)

Safe-Guard REG TM
Hoechst Celanese Corporation
Distributed by:

Hoechst

Hoechst Roussel Vet
A member of the Hoechst Group
30 Independence Blvd., Warren, NJ 07059
Approved FDA NADA 131-675



TAKE TIME



OBSERVE LABEL DIRECTIONS

584730-598

[Code of Federal Regulations]
[Title 21, Volume 1, Parts 1 to 99]
[Revised as of April 1, 1999]
From the U.S. Government Printing Office via GPO Access
[CITE: 21CFR25.33]

[Page 240-241]

TITLE 21--FOOD AND DRUGS

PART 25--ENVIRONMENTAL IMPACT CONSIDERATIONS--Table of Contents

Subpart C--Categorical Exclusions

Sec. 25.33 Animal drugs.

The classes of actions listed in this section are categorically excluded and, therefore, ordinarily do not require the preparation of an EA or an EIS:

(a) Action on an NADA, abbreviated application, or a supplement to such applications, if the action does not increase the use of the drug. Actions to which this categorical exclusion applies may include:

(1) An animal drug to be marketed under the same conditions of approval as a previously approved animal drug;

(2) A combination of previously approved animal drugs;

(3) A new premix or other formulation of a previously approved animal drug;

(4) Changes specified in Sec. 514.8 (a)(5), (a)(6), or (d) of this chapter;

(5) A change of sponsor;

(6) A previously approved animal drug to be contained in medicated feed blocks under Sec. 510.455 of this chapter or as a liquid feed supplement under Sec. 558.5 of this chapter; or

(7) Approval of a drug for use in animal feeds if such drug has been approved under Sec. 514.2 or 514.9 of this chapter for other uses.

(b) [Reserved]

(c) Action on an NADA, abbreviated application, or a supplement to such applications, for substances that occur naturally in the environment when the action does not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment.

[[Page 241]]

(d) Action on an NADA, abbreviated application, or a supplement to such applications, for:

(1) Drugs intended for use in nonfood animals;

(2) Anesthetics, both local and general, that are individually administered;

(3) Nonsystemic topical and ophthalmic animal drugs;

(4) Drugs for minor species, including wildlife and endangered species, when the drug has been previously approved for use in another or the same species where similar animal management practices are used; and

(5) Drugs intended for use under prescription or veterinarian's order for therapeutic use in terrestrial species.

(e) Action on an INAD.

(f) Action on an application submitted under section 512(m) of the act.

(g) Withdrawal of approval of an NADA or an abbreviated NADA.

(h) Withdrawal of approval of a food additive petition that reduces or eliminates animal feed uses of a food additive.

Liquid Chromatographic Determination of Ivermectin in Feed

PVM 1:1996

Abstract

An analytical method for determining ivermectin in feed at 0.50–3 ppm is presented. The method is based on liquid chromatographic measurement after sample preparation by adsorption chromatography on alumina and solid-phase extraction. Two complete, final, finished medicated feeds and the corresponding control feeds used in their preparation were analyzed. Recoveries from feeds fortified at 50–150% of the 2 ppm ivermectin use concentration also were determined. Mean recoveries from replicate analyses ranged from 90 to 100%, and coefficients of variation (CVs) were less than 4.5%. No significant interferences were found in control feeds. The pooled distribution of individual analytical results ($n = 100$) gave a mean recovery of 100%, a recovery range of 90–111%, and an overall CV of 5.5%. Resolution of the total variance into its 2 components gave a within-laboratory CV of 4.1% and a between-laboratory CV of 3.4%. There was no significant difference in recoveries among laboratories, days, concentrations, and feed base or between fortified and medicated feeds ($P > 0.2$).

Method Authors

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Peer Laboratories

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Hazleton Laboratories, PO Box 7545, Madison, WI 53707

Office of the Indiana State Chemist, Purdue University, 1154 Biochemistry Building, West Lafayette, IN 47907

Reviewers

John O'Rangers and Mary Leadbetter, U.S. Food and Drug Administration, Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855

Standard Reference Material

Ivermectin liquid reference standard (available from Merck & Co., Inc., West Point, PA).

1. Summary of Results of Verification Study

1.1 Summary of Submitting Laboratory's Data

- 1.1.1 *Matrixes.*—Complete swine feeds including grain products (containing crude protein, $\geq 16\%$; crude fat, $\geq 3\%$; and crude fiber, $\leq 7\%$), plant protein products, animal protein, animal fat, and a mixture of numerous vitamins and minerals.
- 1.1.2 *Study design.*—Six 10 g samples of drug-free feed were supplemented with ivermectin at 25–150% of the nominal 2 ppm in ivermectin-medicated feed. Each sample was analyzed once.

Two complete medicated feeds were formulated with ivermectin at 1.5 and 3 ppm. These concentrations were selected to bracket the nominal medication concentration of 2 ppm ivermectin in feed. Each feed was extracted with methanol, and 8 portions of the extracts were carried separately through the complete analytical procedure.

1.2 Summary of Peer Laboratory Data

See Table 1 for summary of peer laboratory data.

- 1.2.1 *Matrixes.*—Two medicated feeds prepared with 2 commercial mixers from 2 different base feeds were analyzed: a wheat-based feed mixed in a horizontal ribbon mixer and a corn-based ration mixed with a vertical mixer.
- 1.2.2 *Study design.*—Each of the 2 samples, both prepared to contain 2 ppm ivermectin, was analyzed 5 times by each of 4 laboratories: 4 laboratories \times 2 feeds \times 5 replicates = 40 data points.

2. Safety Precautions

Acetonitrile is extremely flammable and is harmful if inhaled or absorbed through skin. Methanol is extremely flammable and is harmful if inhaled or absorbed through skin. Concentrated phosphoric acid is corrosive. Transfers involving these compounds should be made in a fume hood.

3. Scope

This peer-verified method specifies a liquid chromatographic (LC) method for determining ivermectin in medicated feed at concentrations ranging from 1.0 to 3.0 ppm.

4. References

- (1) Fink, D.W. (1994) *J. AOAC Int.* **77**, 1353–1358
- (2) Campbell, W.C. (Ed.) (1989) *Ivermectin and Abamectin*. Springer-Verlaag, New York, NY
- (3) Fink, D.W. (1988) in *Analytical Profiles of Drug Substances*, Vol. 17, K. Florey (Ed.), Academic Press, San Diego, CA, pp 155–184
- (4) Alva-Valdes, R., Wallace, D.H., Foster, A.G., Ericsson, G.F., & Wooden, J.W. (1989) *Am. J. Vet. Res.* **50**, 1392–1395
- (5) Doherty, S.J., Fox, A., & Fink, D.W. (1990) *J. Assoc. Off. Anal. Chem.* **73**, 931–934
- (6) Fox, A., & Fink, D.W. (1985) *Analyst* **110**, 259–261
- (7) Oehler, D.D., & Miller, J.A. (1989) *J. Assoc. Off. Anal. Chem.* **72**, 59
- (8) Youden, W.J., & Steiner, E.H. (1975) *Statistical Manual of the AOAC*, AOAC, Arlington, VA, p. 16

5. Definitions

For the purposes of this peer-verified method, the following definition applies: Ivermectin concentration in the medicated feed is the total of the H₂B_{1a} (5-O-demethyl-22,23-dihydroavermectin A_{1a}) and H₂B_{1b} [5-O-demethyl-25-de(1-methylpropyl)-22,23-dihydro-25-(1-methylethyl)avermectin A_{1a}] components determined by the procedure specified in this method. The ivermectin content is expressed in micrograms per gram (parts per million) of medicated feed.

6. Principle

Ivermectin is extracted from feed into methanol, and the extract is pretreated by conventional gravity-fed adsorption chromatography on alumina (activity III). The analyte is further separated from feed interferences by sequential solid-phase extraction (SPE) with Sep-Pak C₁₈ and silica cartridges. The drug is recovered in mobile phase for direct measurement by reversed-phase LC on a Burdick & Jackson OD5 column with photometric detection at 245 nm. Typically, 8–12 feeds can be analyzed per day.

7. Standard Solutions

7.1.1 Ivermectin standard solution, 0.42 µg/mL.—Weigh equivalent of 30 mg ivermectin as liquid reference standard (Merck & Co., West Point, PA) and dilute to 100 mL with methanol. Dilute 7.0 mL portion of this stock solution to 100 mL with methanol. Further dilute 2.0 mL portion of this intermediate solution to 100 mL with methanol to prepare working standard solution for processing. Stock solution is

stable for 1 week if refrigerated at 5°C. Make subsequent dilutions fresh daily.

7.1.2 Internal standard solution, 0.18 µg/mL.—Prepare an internal standard stock solution of 22,23-dihydroavermectin B_{1a} δ² isomer (Merck & Co., West Point, PA) of ca 10 µg/mL in acetonitrile. This internal standard stock solution is stable for at least 4 months if refrigerated. Dilute 7.0 mL of this internal standard solution to 200 mL with acetonitrile. This internal standard solution is stable for at least 2 months if refrigerated at 5°C. Dilute 50 mL of this stock solution with 50 mL water. Allow to come to room temperature before using. Make the diluted solution fresh daily.

8. Reagents

- 8.1.1 Mobile phase.**—Acetonitrile–methanol–water (53 + 35 + 7). Deaerate this solution with either vacuum or an ultrasonic bath. (Solvents obtained from Fisher Chemical, Optima, LC grade; water, LC grade).
- 8.1.2 Alumina.**—Reagent grade neutral alumina suitable for chromatographic adsorption (Brockman activity I) brought to activity III by addition of 6% water (i.e., 30 mL distilled water added to 500 g alumina). Mix well and allow to equilibrate overnight before using.

9. Apparatus

- 9.1.1 Liquid chromatograph.**—A typical configuration consists of Waters Model 510 pump, Shimadzu Model SIL-9A injector, LDC Model 3000 UV detector, and Spectra-Physics Model SP 4270 integrator or equivalent modules. The system is operated at a detector wavelength of 245 nm (0.1 absorption unit fullscale) and at a flow rate of ca 1.0 mL/min (flow rate is adjusted to attain baseline resolution (*R_s*) between H₂B_{1a} and H₂B_{1b} of 1.5). Injections are made with a Shimadzu injector set to 100 µL volume, and the system is operated at a column temperature of 30°C.
- 9.1.2 Chromatographic column.**—Burdick and Jackson OD5, 25 cm × 4.6 mm id. Other columns (C₁₈ and similarly end-capped) having the same dimensions and giving similar resolution are acceptable alternatives.
- 9.1.3 SPE cartridges.**—Silica Sep-Pak and C₁₈ Sep-Pak (Waters), parts 51900 and 51910, respectively.

10. Preparation of Alumina Adsorption Column

The column should be 10–14 mm id glass tubing, 30–40 cm high, with a 3.5 cm long tapered end having an opening of 4–5 mm id. Insert a small plug of glass wool in the lower end of the column and compress the plug firmly with a rod so that it is ca 4–5 mm thick. Add 5 g (or enough) alumina to clean, dry

column to achieve a height of 5–6 cm. Pack by gently tapping the sides of the tube. Prepare separate columns for each sample.

11. Sample Preparation and Extraction

Grind 1 kg feed in a micromill so that the feed passes through a 8–15 mesh (2.38–1.29 mm) screen. Mix well. Accurately weigh a sample of ground feed expected to contain 0.04 mg ivermectin (e.g., 20 ± 0.5 g feed is expected to contain 2 ppm of the drug) and transfer to a 200 mL wide-mouth amber glass bottle for extraction. Add 100.0 mL methanol, tighten cap, place bottle in ultrasonic bath (unthermostatted) with the water level near the level of extraction volume for 20 min, and then place bottle on a horizontal reciprocal shaker for 1 h at high speed (240 cycles/min). Transfer ca 40 mL extract to a 50 mL centrifuge tube, and centrifuge for 5 min at 1800–2000 rpm. Transfer ca 20 mL of clear supernatant to top of alumina column and allow liquid to pass through column bed by gravity. Reject first 5 mL of eluate and collect remainder in a clean tube. This eluate is the working purified sample solution. It can be kept overnight if refrigerated.

Pipet 5.00 mL internal standard solution (0.18 $\mu\text{g}/\text{mL}$) into individual 15 mL centrifuge tubes and 2.00 mL working standard or purified sample solution into individual tubes. Prepare as many standards as necessary to accommodate the number of samples being analyzed. Stopper centrifuge tubes and mix on Vortex mixer for 15 s.

12. Solid-Phase Extraction

Remove plunger from a 10 cc plastic disposable syringe with a center line fitting and fit into long end of a Waters silica Sep-Pak as a reservoir. Cut a 200 μL plastic pipet tip to ensure a snug fit in the SPE vacuum manifold. Place short end of silica Sep-Pak into the modified pipet tip. Pipet 5.00 mL acetonitrile into syringe barrel and apply vacuum (5–15 in. Hg) to draw solvent through Sep-Pak. Dry column by holding vacuum (5–15 in. Hg) for 1 min after last portion of solvent exits Sep-Pak. In a similar manner, elute silica Sep-Pak with 5.00 mL methylene chloride (Fisher Chemical, Optima [LC grade]). Dry column by holding vacuum (5–15 in. Hg) for 1 min after last portion of solvent exits Sep-Pak.

Remove syringe barrel assembly from vacuum manifold. Remove silica Sep-Pak and pipet tip from syringe barrel and set aside. Attach syringe barrel to long end of a Waters C_{18} Sep-Pak. Fit another 200 μL pipet tip to vacuum manifold and insert short end of C_{18} Sep-Pak into it. Pipet 5.0 mL methylene chloride into syringe barrel to prewash cartridge. Apply vacuum (5–15 in. Hg) to draw solvent through and dry for 1 min after last portion of solvent exits Sep-Pak. Pipet 5.0 mL acetonitrile–water (1 + 1) into syringe barrel and draw a minimum vacuum. Do not allow columns to dry.

Pour solutions from centrifuge tubes prepared under **Sample Preparation and Extraction** into individual reservoirs attached to C_{18} Sep-Pak and apply vacuum (5–15 in. Hg) to

system to allow sample and standard to enter Sep-Pak. Maintain vacuum for ca 15 s after last portion of solvent exits Sep-Pak. Rinse walls of 15 mL centrifuge tubes with 2.0 mL acetonitrile–water (1 + 1) and add this to respective reservoir. Elute through column by applying maximum vacuum. To dry column, maintain vacuum for ca 1 min after last portion of solvent exits Sep-Pak.

Place reservoir and C_{18} Sep-Pak assembly onto pretreated silica Sep-Pak with another 200 μL pipet tip trimmed to fit. Elute ivermectin onto silica phase with 10.0 mL methylene chloride–acetonitrile (9 + 1). Maintain vacuum for ca 1 min after last portion of solvent exits silica Sep-Pak. Remove C_{18} Sep-Pak from assembly and discard. Refit syringe barrel to silica Sep-Pak and remove this assembly from vacuum manifold. Elute analytes from silica Sep-Pak with 4.00 mL acetonitrile by replacing syringe plunger and applying enough pressure to collect eluant in a culture tube (13 mm id, 100 mm long) in ca 45 s. Place culture tubes on an analytical evaporator (such as an N-evap) and remove solvent with stream of nitrogen or air in a 50°C water bath. Dissolve sample residue and standard in 2.00 mL mobile phase and mix on a Vortex mixer for 20 s. Multiple standard preparations may be combined for autosampling. These solutions can be kept overnight if refrigerated.

12.1 Determination

Use final solutions of sample and standard directly for LC injections. Inject standard, followed by 2 or 3 samples, and then repeat injection of standard.

13. Calculations

Measure peak heights, obtain mean peak height ratio for standard, and determine ivermectin with the following formula:

$$\text{Ivermectin, ppm} = \frac{R_x}{R_s} \times C_s \times \frac{100}{M}$$

where R_x is peak height ratio of sample, that is, $(\text{H}_2\text{B}_{1a} + \text{H}_2\text{B}_{1b})/\text{internal standard}$; R_s is mean peak height ratio of standard, that is, $(\text{H}_2\text{B}_{1a} + \text{H}_2\text{B}_{1b})/\text{internal standard}$ (for each standard); C_s is concentration of ivermectin standard solution ($\mu\text{g}/\text{mL}$); and M is weight of feed sample (g).

14. Test Results Report

Ivermectin concentrations are reported in units of parts per million (ppm), calculated to 2 significant figures.

15. Quality Assurance

All aspects of the interlaboratory study were conducted in full compliance with U.S. Food and Drug Administration Good Laboratory Practices regulations as set forth in 21 CFR 58.35 (b)(6)(7). Reports have been reviewed by a quality assurance unit. Quality assurance documentation has been received and is on file from each of the commercial analytical service laboratories participating in the interlaboratory study.

15.1.1 Critical control points.—Baseline resolution between $H_{2B_{1a}}$ and $H_{2B_{1B}}$; resolution separation (R_s) = 1.5.

15.1.2 Analysis of control samples.—Results of the analyses of control feeds should be <0.05 ppm ivermectin (limit of quantitation).

16. Report of Submitting Laboratory

16.1 Experimental Design

Method accuracy over a 6-fold concentration range in the feed was obtained with six 10 g feed samples. A standard ivermectin solution of known concentration was added to each sample at 25–150% of the nominal 2 ppm ivermectin found in medicated feed. Each sample was analyzed by the method.

Two complete medicated feeds formulated with ivermectin were each extracted with methanol, and 8 portions of these extracts were carried separately through the complete analytical procedure. This experimental design resolves feed mixing variance from precision estimates to give a direct measure of analytical precision.

16.2 Results and Discussion

Average recovery over the concentration range 0.50–3 ppm ivermectin was $98 \pm 2\%$. The standard deviation obtained from the 3 ppm feed, 0.006, is twice that obtained from the feed with lower ivermectin concentration. This result indicates that the precision of the method is indeed constant over this concentration range and is therefore $\pm 2\%$ (coefficient of variation; CV) at the 2 ppm level in medicated feed (Table 2).

16.2.1 Precision: Repeatability.—The mean of 4 individual laboratory CVs gives an estimate of the within-laboratory repeatability CV (RSD) of 4.1%.

Reproducibility.—Resolution of the total variance into its 2 components gives a measure of the between-laboratory reproducibility CV (RSD) by difference of 3.4%.

16.2.2 Accuracy.—Application of this procedure over the concentration range 0.50–3.0 ppm ivermectin in feed gives an accuracy of $\pm 2\%$ mean relative error at the 2 ppm level (Table 3).

16.2.3 Recovery.—Mean recoveries from feeds fortified at 50–150% of the 2 ppm ivermectin use concentration ranged from 90 to 110%. All individual within-laboratory CVs were less than 4.5%.

16.2.4 Limit of quantitation.—The limit of quantitation corresponding to an uncertainty of $\pm 30\%$ in the measured value at the 99% confidence level is 0.05 ppm.

16.2.5 Other validation parameters.—There is no significant difference in recoveries among laboratories, days, concentrations, and feed base or between fortified and medicated feeds ($P > 0.2$).

Table 1. Analyses of finished complete medicated feeds mixed with 2 ppm ivermectin

Sample	Ivermectin, ppm			
	A	B	C	D
Corn-based feed	1.9	1.8	2.0	2.1
	1.9	1.8	2.0	2.1
	1.9	1.8	2.0	2.1
	1.9	1.8	1.9	2.0
	1.9	1.8	2.1	2.0
Average, ppm	1.9	1.8	2.0	2.1
Recovery, %	95	90	100	105
CV, %	0	0	3.5	2.6
Wheat-based feed	2.0	1.9	2.0	2.0
	2.0	1.9	2.0	1.9
	1.9	1.9	2.0	2.0
	1.8	2.0	2.0	2.0
	1.9	2.0	2.0	2.0
Average, ppm	1.9	1.9	2.0	2.0
Recovery, %	95	95	100	100
CV, %	4.4	2.8	0	2.2

Table 2. Precision of method for determining ivermectin in feed at 2 ppm

Replicate	Ivermectin found, ppm	
	Feed A (1.5 ppm ivermectin added)	Feed B (3 ppm ivermectin added)
1	1.55	2.95
2	1.49	2.89
3	1.53	2.94
4	1.51	2.90
5	1.52	2.91
6	1.57	2.88
7	1.55	2.97
8	1.57	2.77
Average, ppm	1.54	2.90
SD	0.03	0.06
CV, %	1.9	2.1

Table 3. Accuracy of method for determining ivermectin in feed at 2 ppm

Ivermectin added to feed, ppm	Proportion of ivermectin added to 2 ppm, %	Ivermectin found, ppm	Recovery, %
0.50	25	0.47	94
0.99	50	0.99	100
1.49	75	1.46	98
1.99	100	1.98	99
2.49	125	2.49	100
2.98	149	2.89	97
Average			98 ± 2

Chapter 7 Section 7.0 - Suitability Petition Actions

1989

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
89P-0191 Fermenta Animal Health Co.	Request to reconsider proposal to substitute sulfathiazole for sulfamethazine in a Type A medicated feed article for use in feed for beef cattle.	Denied 12/06/1989
89P-0191 Fermenta Animal Health Co.	Request to substitute sulfathiazole for sulfamethazine in a Type A medicated feed article for use in feed for beef cattle.	Denied 07/13/1989
89P-0446 Boehringer Ingelheim Animal Health, Inc.	Request to differ the dosage form and strength in a Type A medicated feed article.	Approved 12/29/1989

1990

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
89P-0509 Cheminex Laboratories, Inc.	Request to change dosage form in NADA 131-918 (Tribrissen 400 Oral Paste) from paste to a powder mixed with feed.	Approved 01/24/1990
90P-0051/CP1 Beecham Laboratories	Request to change Nemex Tabs from two tablet strengths, 22.7 and 113.5 mg/tablet to four tablet strengths, 22.7, 45.4, 90.8, and 136.2 mg/tablet.	Approved 03/21/1990
90P-0073/CP1 A. L. Laboratories	Request to revoke approval of petition 89P-0446/CP approved in 1989 for Boehringer Ingelheim Animal Health, Inc.	Denied 04/12/1990
90P-0181/CP1 American Cyanamid	Request permission to file ANADA for change of dosage form of CSP500 and CSP250 Type A medicated feed articles containing chlortetracycline, sulfathiazole and penicillin.	Approved 07/31/1990
90P-0213/CP1 Micrel Limited, Inc.	Request permission to file an ANADA containing a change in dosage form to provide microencapsulation (microspheres) of the active ingredient in an injectable form of RALGRO (NADA 038-233).	Denied 08/21/1990
90P-0213/PRC1 Micrel Limited, Inc.	Request reconsideration of 90P-0213/CP1.	Denied 08/21/1990

1991

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
90P-0434/CP Sanofi Health, Inc.	Request permission to substitute a different salt form of one active ingredient in a lincomycin spectinomycin combination. Pioneer product is NADA 046-109.	*Approved 02/27/1991
91P-0048/CP Sanofi Animal Health, Inc.	Request permission to change the dosage form for Sulfaquinoxaline sodium solution. The pioneer NADA is 006-677.	Denied
91P-0071/CP1 Fermenta Animal Health Co.	Request permission to change the strength for oxytetracycline injection. The pioneer is NADA 113-232.	Approved 12/02/1991
91P-0071/CP1 Fermenta Animal Health Co.	Request permission to change strength of oxytetracycline in a generic product referencing NADA 113-232. *Note: The original approval of this petition was revised to require labeling changes of the generic product to be consistent with that of the pioneer product. See 91P-0285/CP1 for details.	See note*
91P-0277/CP1 The Upjohn Co.	Request permission to file an ANADA for a different dosage form of neomycin soluble powder. *The petition was approved but the applicant may not file an ANADA until the pioneer product has been DESI finalized and approved.	Approved* 09/03/1992
91P-0285/CP1 Pfizer, Inc.	Request that FDA require bioequivalence testing of generic oxytetracycline animal drug products referencing Pfizer's Liquamycin LA-200. The petition also requested that FDA deny Fermenta Animal Health Company's ANADA for an oxytetracycline product. Pfizer pointed out that the Fermenta ANADA does not contain tissue residue studies for calculation of a withdrawal period. *Note: Six points raised in the petition were addressed. The Agency agreed that demonstration of in vivo bioequivalence between the Fermenta and Pfizer formulations is essential to the approval of Fermenta's ANADA. The Agency did not agree that tissue residue studies necessarily would be required. The pharmacokinetic profiles of both formulations will be evaluated to determine bioequivalence and could be used in lieu of a tissue residue study in assigning a withdrawal period. The Agency agreed that bioequivalence studies would be required in more than one species but it does not intend to require demonstration of bioequivalence in all classes of animals within a species. Bioequivalence studies in the Fermenta ANADA will be required in swine and in one class of adult ruminating nonlactating cattle. The Agency agreed that the Fermenta product, although a different strength, must be labeled to deliver the same dose of oxytetracycline base to the animal. The Agency retracted a statement made in approving the Fermenta suitability petition requesting that the generic product be labeled at 9.3 mg/lb of body weight. Fermenta will be instructed to label their generic product at 9 mg/lb of body weight. The Agency pointed out that although different salts of oxytetracycline are used in the manufacture of the two products, the finished form of active ingredient in both cases is magnesium chelated oxytetracycline. Some technical issues regarding labeling and notification of the patent holder were also addressed in the Agency's response.	See note* 12/02/1991
91P-0316/CP1 Vet-A-Mix Animal Health	Request permission to file an ANADA for a different strength of sulfamethazine oblets. The pioneer is NADA 122-271.	Approved 09/11/1991

91P-0421/CP1
 Arthur A. Checci, Inc. Request permission to file an ANADA for a Tolnaftate 1% in an oil base that differs from the pioneer product Tolnaftate 1% cream. The pioneer is NADA 037-502. Prior to making a decision, CVM requested additional information on the formulation of the proposed generic product, including information on a patent and information on the rationale for each ingredient in the formulation. Pending
 01/03/1992

1992

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
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91P-0071/CP1 Fermenta Animal Health Co.	Request permission to label the product in subject ANADA as "OXYJECT 180" instead of "OXYJECT 185" as originally approved.	Acknowledged 06/01/1992
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91P-0255/CP1 Sanofi Animal Health	Request permission to file an ANADA for an oral dosage form for neomycin solution in place of the pioneer's soluble powder form. The pioneer product is NADA 011-315.	Approved 08/04/1992
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91P-0437/CP1 Specialty Biologicals, Inc.	Request permission to file an ANADA for a drug product, Ovagen, that differs from the pioneer (FSH-P) in the method of assay. The pioneer product is NADA 009-505. Submitted in 1991.	Denied 01/22/1992
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91P-0489/CP1 RMS Laboratories, Inc.	Request permission to file an ANADA for a product having a different dosage form than the pioneer, Vetalog Cream (triamcinolone acetonide). The pioneer is NADA 046-146. The proposed product would be a non-aerosol pump spray rather than a cream. Received in 1991.	Approved 02/13/1992
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92P-0057/CP1 The Upjohn Co.	Request permission to file an ANADA for a different dosage form for neomycin sulfate from a soluble powder to a liquid. The pioneer product is NADA 011-315.	Approved 04/03/1992
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92P-0157/CP1 Pfizer, Inc.	Request permission to file an ANADA for a different dosage form for neomycin sulfate from a soluble powder to a Type A medicated article. The pioneer product is NADA 011-315.	Approved 05/12/1992
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92P-0254/CP1 Hill Dermaceuticals, Inc.	Request permission to file an ANADA for the use of a different dosage form and a lesser strength for topical application of fluocinolone acetonide. The pioneer product is NADA 015-152.	Denied 09/02/1992
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92P-0363/CP1 Phoenix Pharmaceutical, Inc.	Request permission to file an ANADA for the use of a different oral dosage form (liquid) and strength for neomycin sulfate. The pioneer product is NADA 011-315.	Approved 10/01/1992
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92P-0366/CP1 The Upjohn Co.	Request permission to file an ANADA for the use of a different oral dosage form (bolus) for neomycin sulfate. The pioneer product is NADA 011-315, and is a soluble powder.	Approved 11/04/1992
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92P-0399/CP1 Sanofi Animal Health,	Request permission to file an ANADA for a different dosage form (bolus) for a neomycin sulfate product. The pioneer product is NADA 011-315, a soluble powder.	Approved 11/23/1992
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Inc.

92P-0402/CP1 Arkansas Microspecialties Co.	Request approval to file an ANADA for the use of a different oral dosage form (liquid) and strength for neomycin sulfate. The pioneer product is NADA 011-315, a soluble powder.	Approved 11/23/1992
92P-0490/CP1 Norbrook Laboratories, Ltd.	Request permission to file an ANADA for an injectable solution containing 300 mg oxytetracycline base per ml. The proposed product brand name is Noromycin LA 300. The pioneer NADA is 113-232.	Denied 04/12/1993
92P-0498/CP1 Fermenta Animal Health	Request permission to change dosage form from a powder to a solution and file an ANADA for neomycin sulfate. The pioneer NADA is 011-315.	Approved 01/29/1993
92P-0511/CP1 Fermenta Animal Health	Request permission to change dosage form from a powder to a bolus and file an ANADA for neomycin sulfate. The pioneer NADA is 011-315.	Approved 01/29/1993

1993

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
93P-0294/CP1 Phoenix Scientific, Inc.	Request permission to file an ANADA for a change in strength of gentamicin sulfate oral solution in a pump dispenser from 4.35 mg/ml to 5.0 mg/ml. The delivery volume would also change from 1.15 ml per pump to 1.0 ml per pump. The pioneer product is NADA 130-464.	Approved 11/03/1993

1994

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
93P-0422/CP1 Wildlife Pharmaceuticals	Request permission to file an ANADA for a change in strength of etorphine hydrochloride parenteral solution from 1 mg/ml to 5 mg/ml. The pioneer product is NADA 095-017.	Denied 02/16/1994
94-0159/CP1 Sanofi Sante Animale, Canada Inc.	Request permission to file an ANADA for a change in strength of the active ingredient, neomycin base, to 56.9% instead of 50% as in the pioneer. The pioneer product is NADA 011-315 sponsored by the Upjohn Co.	Approved 06/29/1994
94P-0039/CP1 Akzo Intervet, Inc.	Request permission to file an ANADA for a change in strength of the implant component of the product. The pioneer product, NADA 134-930, sponsored by Sanofi Animal Health,	Approved 03/21/1994

Inc., is a two component drug consisting of an implant containing 6 mg norgestomet and an injectable solution containing 3 mg norgestomet and 5 mg estradiol valerate per 2 ml. The proposed ANADA would change the strength of the implant from 6 mg to 3 mg of norgestomet. The injectable solution would stay the same.

1995

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
94P-0408/CP1 MacLeod Pharmaceuticals, Inc.	Request permission to file an ANADA for a generic new animal drug containing trimethoprim and sulfadiazine whose strength, dosage form, and inactive ingredient composition differ from the pioneer product. The proposed generic product contains 40 mg/mL trimethoprim and 200 mg/mL sulfadiazine. The trimethoprim in the proposed generic product is in solution whereas the pioneer product is in suspension. The proposed generic product contains an innovative active ingredient, N-methylpyrrolidone. The pioneer product is NADA 106-965 sponsored by Cooper Animal Health.	Denied 01/12/1995
95P-0036/CP1 Norbrook Laboratories Limited	Request permission to file an ANADA (hybrid application) for a generic new animal drug with a dosage form different from the pioneer product. The pioneer product, NADA 055-089, sponsored by Beecham Laboratories, is a powder formulation containing 25 mg amoxicillin per vial for reconstitution with Water for Injection USP, to an oil-based suspension with a nominal concentration of 250 mg amoxicillin base per mL. The Norbrook formulation is an oil-based suspension containing 250 mg amoxicillin base per mL. The pioneer product is indicated for intramuscular or subcutaneous administration, while the generic product will be indicated only for intramuscular administration.	Denied 04/24/1995
95P-0350/CP1 Phoenix Scientific, Inc.	Request permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product only by the addition of 1.5% benzyl alcohol to the formula. The pioneer product is Ivomex 1% Injection, NADA 128-409, sponsored by Merck Research Laboratories.	Not required 01/15/1996

1996

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
96P-0098/CP1 Equi Aid Products, Inc.	Request permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product in two ways: 1) the generic product would be a palatable product to mix with cat food instead of the tablet dosage form of the pioneer product; and 2) pyrantel pamoate would be the only active ingredient instead of pyrantel pamoate and praziquantel. The pioneer product is Drontal Tablets, NADA 141-008, sponsored by Bayer Corp., Agriculture Division, Animal Health.	Denied 04/15/1996
96P-0098/CP1 Equi Aid Products, Inc.	Filed for reconsideration: Request permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product in two ways: 1) the generic product would be a palatable product to mix with cat food instead of the tablet dosage form of the pioneer product; and 2) pyrantel pamoate would be the only active ingredient instead of pyrantel pamoate and praziquantel. The pioneer product is Drontal Tablets, NADA 141-008, sponsored by Bayer Corp., Agriculture Division, Animal Health.	Denied 07/15/1996

1997

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
96P-0438 CP1 Pharmacia & Upjohn	Request permission to file an ANADA for a generic new animal drug which differs from that of the pioneer product only in the formulation and method of oral administration. The product would be formulated as a powder and administered orally once per day in a small amount of palatable feed. The pioneer product is Tribriksen 400 Oral Paste, NADA 131-918, sponsored by Mallinckrodt Veterinary, Inc.	Approved 01/10/1997
97P-0072 CPI VetrePharm Research, Inc.	Request permission to file an ANADA for a generic new animal drug, Butequine TM Paste (phenylbutazone paste) which differs from the pioneer product, Butazolidin Paste, Coopers Animal Health, NADA 116-087 by the following characteristics: Butequine TM Paste: 20 g of phenylbutazone per 60 mL syringe of paste (1g/5g). Butezolidin Paste (pioneer): 12 g of phenylbutazone per 60 g syringe of paste (1g per 5g). The dosage (1-2 g of phenylbutazone/500 lbs body weight) is the same in both products. However, in the generic product, the dosage would be given as 3-6 mL as opposed to 5-10g of the pioneer product.	Approved 04/11/1997

1998

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
97P-0473/CP1 Macleod Pharmaceuticals, Inc	Request permission to file an ANADA for a generic new animal drug, Unibute Paste (phenylbutazone paste) which differs from the pioneer product, Butazolidin Paste, Mallinckrodt Veterinary, Inc, NADA 116-087 by the following characteristics: Unibute Paste: 20 g of phenylbutazone per 60 g of paste. Butazolidin Paste (pioneer): 12 g of phenylbutazone per 60 g of paste. The dosage (1-2 g of phenylbutazone/500 lbs body weight) is the same in both products.	Approved 01/30/1998
97P-0474/CP1 Macleod Pharmaceuticals, Inc	Request permission to file an ANADA for a generic new animal drug, Uniprim Paste (trimethoprim and sulfadiazine) which differs from the pioneer product, Tribriksen 400 Oral Paste, Mallinckrodt Veterinary, Inc, NADA 131-918 by the following characteristics: Uniprim Paste: 56 g of trimethoprim and 278 mg of sulfadiazine per gram. Uniprim Paste: 67 g of trimethoprim and 333 mg of sulfadiazine per gram. The dosage (1-2 g of phenylbutazone/500 lbs body weight) is the same in both products.	Approved 01/30/1998
98P-0159/CP 1 Phoenix Scientific, Inc.	Request permission to file an ANADA for a generic Ivermectin Chewable Tablet which differs from the pioneer product, Heartgard-30®, Merial Limited NADA 140-886 by the following characteristics: Ivermectin generic is a compressed chewable tablet and Heartgard is an 'extruded' Chewable tablet.	Approved 06/18/1998
98P-0190/CP1 Blue Ridge Pharmaceuticals, Inc.	Request permission to file an ANADA for a generic new animal drug ivermectin/pyrantel pamoate which differs from the pioneer product, Heartgard-30® Plus, Merial Limited, NADA 140-971, by the following characteristic: Ivermectin/pyrantel pamoate generic is a compressed chewable tablet and Heartgard-30® Plus is an 'extruded' tablet.	Approved 06/22/1998
98P-0232/CP1 Virbac, Inc.	Request permission to file an ANADA for a generic new animal drug miconazole nitrate which differs from the pioneer product, Conofite® Lotion 1%, Schering-Plough Animal Health Corporation, NADA 095-184, by the following characteristics: Miconazole 2% is formulated as a leave-on conditioner and Conofite® Lotion 1% is formulated as a topical lotion and a different strength.	Denied 07/08/1998

98P-0580/CP1 Delmarva Laboratories, Inc.	Request permission to file an ANADA for a generic new animal drug clindamycin hydrochloride which differs from the pioneer product, Antirobe® Capsules, Pharmacia & Upjohn Co., NADA 120-161, by the following characteristics: Clindamycin hydrochloride generic is a tablet and Antirobe® is a capsule.	Approved 10/30/1998
98P-0862/CP1 Phoenix Scientific, Inc	Request permission to file an ANADA for a generic new animal drug ivermectin/pyrantel which differs from the pioneer product, Heartgard TM Plus (ivermectin/pyrantel), Merial Limited, NADA 140-971 by the following characteristic: Ivermectin/pyrantel generic is a compressed chewable tablet and Heartgard TM Plus is an 'extruded' chewable tablet.	Approved 12/18/1998
98P-0927/CP1 Heska Corporation	Request permission to file an ANADA for a generic new animal drug ivermectin/pyrantel which differs from the pioneer product, Heartgard TM Plus (ivermectin/pyrantel), Merial Limited, NADA 140-971 by the following characteristic: Ivermectin/pyrantel generic is a compressed chewable tablet and Heartgard TM Plus is an 'extruded' chewable tablet.	Approved 12/18/1998
98P-1037/CP1 Phoenix Scientific, Inc	Request permission to file an ANADA for a generic new animal drug trimethoprim/sulfadiazine which differs from the listed product, trimethoprim/sulfadiazine (Uniprim), Macleod Pharmaceuticals, Inc., ANADA 200-033 by the following characteristic: Trimethoprim/sulfadiazine generic differs in dosage form from the listed product.	Approved 03/03/1999
98P-1196/CP1 Phoenix Scientific, Inc.	Request permission to file an ANADA for a generic new animal drug propofol which differs from the pioneer product, propofol (Rapinivet®) Schering-Plough Animal Health Corp., NADA 141-070, by the following characteristics: Propofol generic differs in concentration and the addition of a preservative from the pioneer product.	Denied 03/26/1999
98P-1231/CP1 Superior Equine Pharmaceuticals, Inc.	Request permission to file an ANADA for a generic new animal drug phenylbutazone which differs from the pioneer product, phenylbutazone, Anthony Products, Co., NADA 049-187 by the following characteristics: Phenylbutazone generic is a powder dosage form where as the pioneer product is a tablet.	Approved 05/03/1999

1999

NUMBER SPONSOR	REASON FOR PETITION	ACTION DATE
99P-0627/CP1 Phoenix Scientific, Inc.	Request permission to file an ANADA for a generic new animal drug clorsulon which differs from the pioneer product, ivermectin/clorsulon (Ivomec® F Injection for Cattle), Merial Ltd, NADA 140-833, by the following characteristics: Clorsulon generic is a single ingredient product where as the pioneer product is a combination product.	Denied 05/27/1999
99P-0794/CP1 Veterinary Research Associates, Inc.	Request permission to file an ANADA for a generic new animal drug propofol which differs from the pioneer product, propofol (PropoFlo™), Abbott Laboratories, NADA 141-098, by the following characteristics: Propofol generic differs in concentration, dosage form, and inactive ingredients from the pioneer product.	Denied 11/05/1999
99P-0923/CP1 Pharmaderm, Div of Altana, Inc.	Request permission to file an ANADA for a generic new animal drug miconazole nitrate which differs from the pioneer product, Conofite® Cream 2%, Schering-Plough Animal Health Corporation, NADA 095-183 by the following characteristics: The generic will provide for a product containing 20 mg miconazole nitrate per gram of cream as opposed to the pioneer product which contains 23 mg miconazole nitrate per gram of cream.	Approved 06/28/1999
99P-2733/CP1 Wildlife Laboratories,	Request permission to file an ANADA for a generic new animal drug, ketamine hydrochloride, which differs from the pioneer product, Vetalar, Fort Dodge Animal Health,	Denied 11/05/1999

Inc.

Div. Of AHP Corp., NADA 045-290 by the following characteristic: the generic product will provide a product containing 200 milligrams per milliliter ketamine hydrochloride whereas the pioneer product contains 100 milligrams per milliliter ketamine hydrochloride.

99P-4167/CP1
A & G Pharmaceuticals,
Inc.

Request permission to file an ANADA for a generic new animal drug, phenylbutazone, which differs from the pioneer product, Phenylbute TM, Phoenix Scientific Inc., NADA 091-818 by the following characteristic: the proposed generic product will have the dosage form of powder, as opposed to the pioneer product which is a tablet.

Filed
09/20/1999

**TRANSCRIPT (3-22-00 by PRM)
2nd GADPTRA policy letter (June 7, 1989)**

II Pre-ANADA Activities

Pre-ANADA activities may include the submission of suitability petitions, request for waivers of in vivo testing, and/or protocols for bioequivalence studies

A. ANADA Suitability Petitions

The filing of a Suitability Petition provides a means by which a firm may request permission to file an ANADA for a product which differs from the approved pioneer product.

The specific variances under the Act for which a Suitability Petition may be submitted are as follows:

1. Change of one ingredient in a combination product or premix
2. Change of a dosage form
3. Change of a strength of an ingredient
4. Change in route of administration
5. Change in use with other animal drugs in animal feed

The required components of the Suitability Petition have been adapted from the Citizen's Petition, as defined in 21 CFR Section 10.30, and are as follows:

1. Identification of Petitioner and appropriate citation of the relevant statutory sections of the Federal Food, Drug, and Cosmetic Act. For ANADA Suitability Petitions, the section is 512 (n) (3).
2. An "Action Requested" section detailing the proposed action that the petitioner is requesting the Agency to take, i.e., for the Commissioner to permit the filing of an ANADA for a proposed product, which differs from the approved pioneer product by the specifically defined characteristics. The proposed product should be identified and characterized.
3. A "Statement of Grounds" section that provides a comprehensive justification for the proposed variance from the pioneer drug product.
4. "Environmental Impact" We have determined that the action of submitting and reviewing the Suitability Petition will not normally be expected to have an environmental impact. Therefore, the Suitability Petition should include a request under 21 CFR 25.24(a)(8) for categorical exclusion from the requirement for an environmental assessment.

5. An "Economic Impact" section is required only when requested by the Commissioner; however, the petitioner should indicate that such an analysis will be provided upon request.
6. A "Certification" section stating that the petitioner has included all information known to him/her which is unfavorable to the petition. The certification must be signed and should contain a mailing address and telephone number.

Additional essential elements of a petition are:

1. Identification of a single listed drug which is the basis of the petition. (Multiple products may be cited to develop a justification in the "Statement of Grounds" section).
2. Inclusion of labeling for the proposed product and labeling of the approved pioneer drug product, noting and explaining all differences.

The Suitability Petition will be approved unless the Secretary finds that:

1. "investigations must be conducted to show the safety and effectiveness, in animals to be treated with the drug, of the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which differ the approved new animal drug, or
2. investigations must be conducted to show the safety for human consumption of any residues in food resulting from proposed active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed which is different from the active ingredients, route of administration, dosage form, strength, or use with other animal drugs in animal feed of the approved new animal drug."

ANADA Suitability Petitions may be filed by submitting 4 copies to:

Dockets Management Branch
HFA -305, Room 4-62
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Telephone inquires and desk copies of Petitions should be directed to

Office of the Associate Director
New Animal Drug Evaluation
Center for Veterinary Medicine
HFV -100, Room 6B-03
Attention: Dr. Melanie Berson
Telephone Number: (301) 443 4500.

B. Request for Waivers of In Vivo Testing

When the proposed product meets specific criteria, a waiver of the requirement for in vivo testing may be requested. If the waiver is granted, the generic product will be considered to be bioequivalent to the reference product. Additionally, if the waiver is granted any withdrawal period established for the reference product will be accepted for the new generic product.

The criteria for waivers include the following:

1. The proposed generic product is a solution intended solely for intravenous injection, and it contains an active drug ingredient or therapeutic moiety combined with the same solvent, in the same concentration as an intravenous solution that is the subject of an approved full new animal drug application.
2. The drug product is a true solution intended for oral administration, contains the same therapeutic moiety in the same concentration as the reference product, and it contains no inactive ingredient that affects the absorption of any active ingredient.
3. The proposed generic product is a topically applied product which is intended for local therapeutic effect.

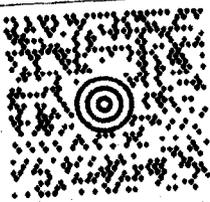
All requests for waivers should be submitted to the Center's Document Control Unit, HFV - 16. They will forward to the Generic Animal Drug Staff for evaluation and issuance of a decision. If the waiver is granted, a copy of the decision letter should be included as part of the subsequent ANADA submission.

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