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September 27, 2002

## SUITABILITY PETITION

Dockets Management Branch  
HFA-305, Room 1061  
Food and Drug Administration  
5630 Fishers Lane  
Rockville, MD 20852

RE: Suitability Petition

Dear Sir/Madam:

Enclosed are four copies of a suitability petition we are filing on behalf of Highland VetPharma, LLC, St. Louis, MO. The petition requests the Commissioner to permit Highland to file an abbreviated new animal drug application (ANADA) for ivermectin for cats having a different dosage form (molded, chewable tablet) than that of the listed approved new animal drug Heartgard® for Cats (Merial Ltd., NADA 141-078), an extruded chewable tablet.

Please do not hesitate to contact us if additional information is required at this time.

Sincerely,



Mark L. Shepard, M.S.  
Vice President

Enclosure

Cc: Highland VetPharma, LLC

MLS:mlm

H:\Users\COMMON\239\ltr petitions ivermectin for cats.doc

02P.0429

CP1

## **SUITABILITY PETITION**

**Petition Filed By:**

**Highland VetPharma, LLC  
11960 Westline Drive, Suite 180  
St. Louis, Missouri 63146**

**Proposed Product:**

**A Palatable, Chewable Tablet Form  
of Ivermectin for Cats**

**Date:**

**September 27, 2002**



**SUITABILITY PETITION**

The undersigned submits this petition under 512(n)(3) of the Federal Food, Drug, and Cosmetic Act, to request that the Commissioner of Food and Drugs permit Highland VetPharma to file an abbreviated new animal drug application having a dosage form which differs from that of the listed approved new animal drug.

Name: James M. Bausch  
Title: President + COO

9/23/02  
(Date)

1. Action Requested

This action requests the Commissioner to permit the filing of an abbreviated new animal drug application (ANADA) for our proposed product which differs from the approved listed product as follows:

Listed Product (Reference Drug)

Heartgard® (ivermectin) for cats, NADA 141-078, originally approved by the Center for Veterinary Medicine on December 23, 1996, and sponsored by Merial Ltd., is an extruded chewable tablet for use in cats to prevent feline heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the removal and control of adult and immature hookworms (*Ancylostoma tubaeforme* and *Ancylostoma braziliense*). It is offered in two formulations containing ivermectin at levels of 55 mcg and 165 mcg, respectively. Heartgard® for Cats is administered at monthly intervals at the recommended minimum dose of 24 mcg ivermectin per kg of body weight.

Proposed Product

The proposed product is a molded (form-filled) chewable tablet, also to be offered in two formulations containing the same levels of ivermectin as the approved listed product, which will be indicated for use in cats for the same claims and will utilize the same oral dosage directions as the listed

product. The proposed tablets are packaged in blister packs of six tablets each.

II. Statement of Grounds

Change of dosage form is one of the five specified variances from the listed product which can be considered under a suitability petition pursuant to section 512 (n)(3) of the Federal Food, Drug, and Cosmetic Act (FFD&C Act), as amended. The proposed product differs from the listed product in dosage form. The listed product is an extruded chewable tablet, whereas the proposed product is a molded chewable tablet produced by a method whereby the actual tablet blister is used as the mold for the finished dosage form.

The approval of this petition and the ultimate approval of an abbreviated new animal drug application for a molded palatable, chewable tablet form of ivermectin would provide the cat owner with an alternative to the listed product which is also readily administered, and is also accepted by the cat as a "treat", similar to the listed product. In addition, due to its unique vegetable oil-based formulation, the proposed product is less likely than the listed product to produce fragments of chewables in the cat's feces.

The legal basis under which this application proceeds is as promulgated in the FFD&C Act which allows the Commissioner to accept a generic drug

application for an animal drug product which differs in dosage form from the listed reference drug product. The dosage form for the proposed generic product described in this petition is similar to that of the listed drug in that both products are oral dosage forms containing the same level of active ingredient. The difference is that this proposed generic product is in a molded, palatable, chewable tablet form whereas the listed drug is an extruded, palatable, chewable tablet.

The petitioner is not aware of any information which would be unfavorable to the granting of the requested action.

### III. Environmental Impact

Highland VetPharma, LLC hereby claims a categorical exclusion from the requirements of preparing an environmental assessment for this action based on 21 CFR 25.30(h). This subparagraph provides for categorical exclusions for actions such as the issuance, amendment, or revocation of procedural or administrative regulations and guidelines, including procedures for submission of applications for product development, testing and investigational use, and approval. To the best of the petitioner's knowledge, no extraordinary circumstances exist which may significantly affect the human environment as discussed under 21 CFR 25.21.

IV. Economic Impact

An economic impact statement pertaining to (1) Cost (and price) increases to industry, government, and consumers; (2) productivity of wage earners, businesses, or government; (3) competition; (4) supplies of important materials, products, or services; (5) employment; and (6) energy supply or demand has not been prepared for this petition. Highland VetPharma will provide such an analysis if so requested by the Commissioner.

V. Identification of Single Listed Reference Drug

NADA NO.	NAME OF DRUG	COMPANY	APPROVAL DATE
141-078	Heartgard® for Cats	Merial Ltd.	12/23/96

VI. Labeling

Differences between the proposed generic product labeling and the listed reference product labeling:

I. Box Label (Note: The small sized box is used as illustration; identical respective changes are also made for the other box size.)

A. Side and End Panels

1. Brandname is different
2. Bar code is different (end panel)

B. Front Panel

1. "Highland VetPharma" replaces "Merck"

2. The product brand name is changed to "Brandname."
3. The product number is changed.
4. The patent number is different
5. All other information will change to reflect sponsorship by Highland VetPharma.

## II. Package Insert

### A. Front Panel

1. The bar code and corresponding number is changed.
2. The brand name is changed to "Brandname" throughout.

### B. Back Panel

1. The brand name is changed throughout.
2. Under Safety:
  - a. In the first sentence of the first paragraph, "Heartgard for Cats" is changed to "ivermectin in cats."
  - b. In the second sentence, "Heartgard for Cats" is changed to "ivermectin."
  - c. In the last sentence, "Heartgard for Cats" is changed to "ivermectin."

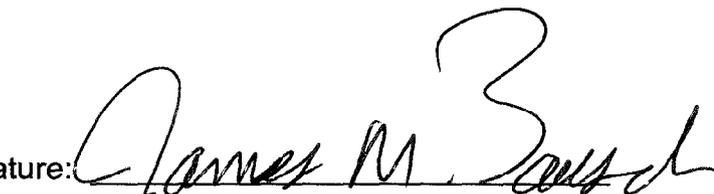
3. In the remainder of the rear insert panel, all information is changed to reflect sponsorship by Highland VetPharma.

The following pages provide copies of the proposed generic product labeling and the reference drug labeling.

VII. Certification

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to this petition.

Signature:



Name of Petitioner: Highland Vet Pharma, LLC

Mailing Address: 11960 Westline Industrial Drive, Ste. 180  
St. Louis, MO 63146

Telephone Number: (314) 205-9666

**PROPOSED GENERIC PRODUCT LABELING**

<b>Brandname</b> (ivermectin) Chewables <b>for Cats</b>	Lot Exp ▼	Box Top  Up to 5 lb 6 Chewables
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HIGHLAND VETPHARMA	Package Front
<b>Brandname™ for Cats</b> (ivermectin) <b>Chewables</b>	
Administer once a month to prevent heartworm disease and to remove and control infections of hookworms in cats.	
Recommended for cats <b>up to 5 lb</b> body weight.	
Contains 6 Chewables/Each chewable contains 55 mcg of ivermectin.	
Product XXXXX	
<b>Caution:</b> Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.	
Store at controlled room temperature of 59° - 86°F (15° - 30° C). Protect product from light.	
<b>Keep this and all drugs out of the reach of children.</b>	
Manufactured for: Highland VetPharma, St. Louis, MO 63146	

	Package Back
Brandname is a trademark of: Highland VetPharma, St. Louis, MO 63146 Pat. No. X,XXX,XXX	

Brandname™ **for Cats** Box End  
(ivermectin)   
Chewables 332155

Brandname™ **for Cats** Box Side 1  
(ivermectin) **up to 5 lb**  
Chewables **6 Chewables**

Brandname™ **for Cats** Box Side 2  
(ivermectin) **up to 5 lb**  
Chewables **6 Chewables**



PACKAGE INSERT

BARCODE  
1 8646 584985 6

Highland VetPharma

1 8646 584985 6

---

**BRANDNAME**

(ivermectin)

---

**Chewables**

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

**INDICATIONS:** For use in cats to prevent feline heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the removal and control of adult and immature hookworms (*Ancylostoma tubaeforme* and *A. braziliense*).

**DOSAGE:** BRANDNAME for cats should be administered orally at monthly intervals at the recommended minimum dose level of 24 mcg of ivermectin per kilogram (10.9 mcg/lb) of body weight. The recommended dosing schedule for prevention of feline heartworm disease and control of hookworms is as follows:

Cat Weight Lb	BRANDNAME for Cats Chewables per month	Ivermectin Content
Up to 5	1	55 mcg
5 to 15	1	165 mcg

For cats over 15 lb., use the appropriate combination of chewables. BRANDNAME for Cats is recommended for use in cats 6 weeks of age and older.

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. BRANDNAME can be offered to the cat by hand or may be added to a small amount of cat food. If manual dosing is required, the chewable should be broken into pieces for administration. Food should be routinely available during the day of treatment administration. If cats are fasted, or if the chewable is not broken into pieces for manual dosing, then reduced absorption may result. A relationship between reduced absorption and reduced efficacy has not been established.

Care should be taken to see that the cat consumes the complete dose. Treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing with a new chewable is recommended. Fragments of chewables have

occasionally been observed in the feces of some cats; efficacy of the product was not adversely affected.

BRANDNAME for Cats should be given at monthly intervals when mosquitoes potentially carrying infective heartworm larvae are active. The initial dose must be given within a month (30 days) after the cat's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the cat's last exposure to mosquitoes. For optimal performance, BRANDNAME for Cats must be given once a month on or about the same date. If treatment is delayed, whether by a few days or many, immediate treatment with BRANDNAME for Cats and resumption of the recommended dosing regimen will minimize the opportunity for development of adult heartworm.

It is recommended that cats should be tested for existing heartworm infection prior to starting treatment with BRANDNAME (ivermectin) for Cats. Cats already infected with adult heartworms can safely be given BRANDNAME for Cats monthly to prevent further infections.

Monthly treatment with BRANDNAME for Cats also provides effective removal and control of adult and immature hookworms (*A. tubaeforme* and *A. braziliense*).

**SAFETY:** In clinical studies involving more than 3000 doses of ivermectin in cats, observations reported within 24 hours of treatment included vomiting of  $\leq 0.3\%$  and diarrhea in  $\leq 0.2\%$  of the doses administered. There were no statistical differences between ivermectin and the product vehicle (control) for these observations.

A wide margin of safety was demonstrated in clinical trials at the recommended dose level in cats and kittens 6 weeks of age and older and in laboratory studies in cats with circulating microfilariae of *D. immitis*. A wide margin of safety has also been demonstrated at 3 times the recommended dose in pregnant or breeding queens and breeding toms. No adverse effects were observed in either male or female cats or their offspring in breeding studies. A 30-fold safety margin over the minimum recommended dosage was established in a single dose tolerance study. In growing kittens dosed monthly for 8 consecutive doses, one cat given 5 times the market dose vomited and a second cat in this group experienced diarrhea within 24 hours of the initial treatment. In clinical trials, many commonly used flea control products, anthelmintics, vaccines, antibiotics and steroid preparations were administered with ivermectin without incident.

**Keep this and all drugs out of the reach of children.** In case of ingestion by humans, clients should be advised to contact a physician immediately.

**STABILITY:** BRANDNAME Chewables for Cats are stable 2 years when stored below 30°C and protected from light.

Store at controlled room temperature of 59°F - 86°F (15° - 30°C). Protect product from light.

**HOW SUPPLIED:** BRANDNAME is available in two dosage strengths (See DOSAGE section) for cats of different weights. Each strength comes in a convenient carton of 6 chewables, packed 10 cartons per tray.

**Highland VetPharma**  
St. Louis, MO 63146, U.S.A.

U.S. Pat. X,XXX,XXX  
Printed in U.S.A.

November 2002

**REFERENCE PRODUCT LABELING**

Heartgard™  
(ivermectin)  
Chewables for Cats

Lot & Exp ▼

DBD068  
FEB 99

up to 5 lb  
6 Chewables



Heartgard™  
(ivermectin)  
Chewables

for Cats

up to 5 lb  
6 Chewables

# Heartgard™ for Cats (ivermectin)

## Chewables

Convenience Pack

Administer once a month to prevent heartworm disease  
and to remove and control infections of hookworms in cats.

Recommended for cats **up to 5 lb** bodyweight.

Contains 6 Chewables / Each chewable contains 55 mcg of ivermectin.

Net Wt. 3.0055

Store at controlled room temperature of 59° - 86°F (15° - 30°C)  
Protect product from light.

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

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



up to 5 lb  
6 Chewables

for Cats

Heartgard™  
(ivermectin)  
Chewables

Heartgard™  
(ivermectin)  
Chewables for Cats



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HEARTGARD is a trademark of Merck & Co., Inc., Whitehouse Station, N.J., U.S.A.  
Merck AgVet Division, Merck & Co., Inc., Whitehouse Station, N.J., U.S.A.  
Pat. No. 4,199,569

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00088135



08924302



8924302

# Heartgard™ for Cats (ivermectin)

## Chewables

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

**INDICATIONS:** For use in cats to prevent feline heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection, and for the removal and control of adult and immature hookworms (*Ancylostoma tubaeforme* and *A. braziliense*).

**DOSAGE:** HEARTGARD for Cats should be administered orally at monthly intervals at the recommended minimum dose level of 24 mcg of ivermectin per kg (10.9 mcg/lb.) of body weight. The recommended dosage schedule for prevention of feline heartworm disease and control of hookworms is as follows:

Cat Weight lb	HEARTGARD for Cats Chewables per month	Ivermectin content
up to 5	1	55 mcg
5 to 15	1	165 mcg

For cats over 15 lb., use the appropriate combination of chewables.

HEARTGARD for Cats is recommended for use in cats 6 weeks of age and older.

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. HEARTGARD for Cats can be offered to the cat by hand or may be added to a small amount of cat food. If manual dosing is required, the chewable should be broken into pieces for administration. Food should be routinely available during the day of treatment administration. If cats are fasted, or if the chewable is not broken into pieces for manual dosing, then reduced absorption may result. A relationship between reduced absorption and reduced efficacy has not been established.

Care should be taken to see that the cat consumes the complete dose. Treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing with a new chewable is recommended. Fragments of chewables have occasionally been observed in the feces of some cats, efficacy of the product was not adversely affected.

HEARTGARD for Cats should be given at monthly intervals when mosquitoes potentially carrying infective heartworm larvae are active. The initial dose must be given within a month (30 days) after the cat's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the cat's last exposure to mosquitoes. For optimal performance, HEARTGARD for Cats must be given once a month on or about the same date. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD for Cats and resumption of the recommended dosing regimen will minimize the opportunity for development of adult heartworm.

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

It is recommended that cats should be tested for existing heartworm infection prior to starting treatment with HEARTGARD™ (ivermectin) for Cats. Cats already infected with adult heartworms can safely be given HEARTGARD for Cats monthly to prevent further infections.

Monthly treatment with HEARTGARD for Cats also provides effective removal and control of adult and immature hookworms (*A. tubaeforme* and *A. braziliense*).

**SAFETY:** In the clinical studies involving more than 3000 doses of HEARTGARD for Cats, observations reported within 24 hours of treatment included vomiting in  $\leq 0.3\%$  and diarrhea in  $\leq 0.2\%$  of the doses administered. There were no statistical differences between HEARTGARD for Cats and the product vehicle (control) for these observations

A wide margin of safety was demonstrated in clinical trials at the recommended dose level in cats and kittens 6 weeks of age and older and in laboratory studies in cats with circulating microfilariae of *D. immitis*. A wide margin of safety has also been demonstrated at 3 times the recommended dose in pregnant or breeding queens and breeding toms. No adverse effects were observed in either male or female cats or their offspring in breeding studies. A 30-fold safety margin over the minimum recommended dosage was established in a single dose tolerance study. In growing kittens dosed monthly for 8 consecutive doses, one cat given 5 times the market dose vomited and a second cat in this group experienced diarrhea within 24 hours of the initial treatment. In clinical trials, many commonly used flea control products, anthelmintics, vaccines, antibiotics and steroid preparations were administered with HEARTGARD for Cats without incident.

**Keep this and all drugs out of the reach of children.** In case of ingestion by humans, clients should be advised to contact a physician immediately.

**STABILITY:** HEARTGARD Chewables for Cats are stable for 2 years when stored below 30°C and protected from light.

Store at controlled room temperature of 59°- 86°F (15°- 30°C).

**HOW SUPPLIED:** HEARTGARD for Cats is available in two dosage strengths (see DOSAGE section) for cats of different weights. Each strength comes in a convenient carton of 6 chewables, packed 10 cartons per tray.



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