Date of Approval: May 7, 2007

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-299

IVER-ON
(ivermectin)

Pour-on for Cattle

Parasiticide

The effect of the supplement is the addition of CVM requested changes to the Environmental Safety, Disposal statement, and Residue Information and the addition of claims that are no longer protected by three years marketing exclusivity that expired on November 24, 2006, specifically: *Dictyocaulus viviparus* for 28 days, *Cooperia surnabada* for 14 days, and *Damalinia bovis* for 56 days after treatment. Also, the persistent activity periods are extended for the following: *Oesophagostomum radiatum* from 14 days to 28 days and *Cooperia punctata* and *Trichostrongylus axei* from 14 to 21 days after treatment.

Sponsored by:

Med-Pharmex, Inc.

1. GENERAL INFORMATION:

a. ANADA Number:	ANADA 200-299
b. Sponsor:	Med-Pharmex, Inc. 2727 Thompson Creek Rd. Pomona, CA 91767-1861 Drug Labeler Code: 054925
c. Established Name:	Ivermectin
d. Proprietary Name:	IVER-ON
e. Dosage Form:	Pour-On
f. How Supplied:	8.5 fl. oz/250 mL bottle, 33.8 fl. oz/1 L with a squeeze-measure-pour system, 84.5 fl oz/2.5 L, and 169 fl oz/5 L collapsible packs intended for use with appropriate automatic dosing equipment.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	Each milliliter (mL) of solution contains 5 milligrams (mg) of ivermectin
i. Route of Administration:	Topical
j. Species/Class:	Cattle
k. Recommended Dosage:	500 mcg/kg (1 mL for each 22 lb. of bodyweight)
l. Pharmacological Category:	Parasiticide
m. Indications:	Ivermectin Pour-On applied at the recommended dose level of 500 mcg/kg is indicated for the effective control of these parasites.

Gastrointestinal Roundworms
Ostertagia ostertagi (adults and L4)
(including inhibited stage)
Haemonchus placei (adults and L4)
Trichostrongylus axei (adults and L4)
T. colubriformis (adults and L4)
Cooperia oncophora (adults and L4)
Cooperia punctata (adults and L4)
Cooperia surnabada (adults and L4)
Strongyloides papillosus (adults)
Oesophagostomum radiatum (adults and L4)
Trichuris spp. (adults)

Lungworms
Dictyocaulus viviparus (adults and L4)

Cattle Grubs (parasitic stages)
Hypoderma bovis
H. lineatum

Mites
Sarcoptes scabiei var. *bovis*

Lice
Linognathus vituli
Haematopinus eurysternus
Damalinia bovis
Solenopotes capillatus

Horn Flies
Haematobia irritans

Persistent Activity:
Ivermectin Pour-On has been proven to effectively control infections and protect cattle from re-infection with *Oesophagostomum radiatum* and *Dictyocaulus viviparus* for 28 days after treatment; *Cooperia punctata* and *Trichostrongylus axei* for 21 days after treatment; *Ostertagia ostertagi, Haemonchus placei, Cooperia oncophora* and *Cooperia surnabada* for 14 days after treatment; *Damalinia bovis* for 56 days after treatment.

n. Pioneer Product:	IVOMEC Pour-on for Cattle; ivermectin; NADA 140-841; Merial Ltd.
o. Effect of Supplement:	The effect of the supplement is the addition of CVM requested changes to the Environmental Safety, Disposal statement, and Residue Information portions of the labeling and the addition of claims that are no longer protected by three years marketing exclusivity that expired on November 24, 2006, specifically: *Dictyocaulus viviparus* for 28 days, *Cooperia surnabada* for 14 days, and *Damalinia bovis* for 56 days after treatment. Also, the persistent activity periods are extended for the following: *Oesophagostomum radiatum* from 14 days to 28 days and *Cooperia punctata* and *Trichostrongylus axei* from 14 to 21 days after treatment.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guidance, revised October 9, 2002).

Based on the formulation characteristics of the generic product, Med-Pharmex, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product IVER-ON (ivermectin) Pour-on for Cattle. The generic product is administered as a pour on, contains similar active ingredient in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product IVOMEC (ivermectin) Pour-on for Cattle, the subject of Merial Ltd., NADA 140-841, was approved on December 4, 1990.

3. HUMAN SAFETY:

Refer to the FOI Summary for more details.

- **Tolerances for Residues:**
  The tolerance established for the pioneer product applies to the generic product. A tolerance of 100 parts per billion (ppb) and 10 ppb is established for 22, 23-dihydroavermectin B_1a (marker residue) residues in the liver and muscle, respectively, of cattle under 21 CFR 556.344. The Acceptable Daily Intake (ADI) for total residues of ivermectin is 1 microgram per kilogram of body weight per day.

- **Withdrawal Times:**
  Under the CVM Bioequivalence Guidelines, when a generic product is granted a waiver of the *in vivo* bioequivalence testing, the withdrawal period established for the pioneer product is also assigned to the generic product.

  For this reason, a withdrawal period of 48 days has been established for IVER-ON (ivermectin) Pour-On for Cattle (21 CFR 524.1193).

- **Regulatory Method for Residues:**
  The analytical methods for the determination of ivermectin in tissues are HPLC methods with fluorescence detection. These methods are found on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

4. AGENCY CONCLUSIONS:

This ANADA filed under section 512(b)(2) of the Federal, Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that IVER-ON Pour-on for Cattle, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

<u>Generic Labeling for ANADA 200-299:</u>
Package Insert
Container Labels – Front and Back and Carton Labels
8.5 fl. oz/250 mL bottle
33.8 fl. oz/1 L Container
84.5 fl. oz/2.5 L Collapsible pack
169 fl. oz/5 L Collapsible pack

Pioneer Labeling for NADA 140-841:

250 mL Container: Container Labels, Label Insert, Label Outsert, and Carton Labels

1 L Container: Container Labels, Label Insert, Label Outsert, and Carton Labels

2.5 L Container: Container Labels, Label Outsert, and Carton Labels

5 L Container: Label Outsert

20 L Container: Label Outsert