Approval Date October 5, 2007

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-437

NOROMECTIN (ivermectin)
Injection for Cattle and Swine

Indications for use: For the treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs, sucking lice, and mange mites in cattle; for the treatment and control of gastrointestinal roundworms, lungworms, lice, and mange mites in swine; for the treatment and control of warbles (*Oedemagena tarandi)* in reindeer; and for the treatment and control of grubs (*Hypoderma bovis)* in American bison.

Sponsored by:

Norbrook Laboratories, Ltd.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-437
b. Sponsor:	Norbrook Laboratories, Ltd. Station Works Newry BT35 6JP Northern Ireland Drug Labeler Code: 055529
US Agent:	Norbrook, Inc. Bill Zollers, Ph.D. Directory of Regulatory Affairs – USA & Canada 9733 Loiret Boulevard Lenexa, KS 66219
c. Established Name:	Ivermectin
d. Proprietary Name:	NOROMECTIN Injection for Cattle and Swine
e. Dosage Form:	Sterile solution
f. How Supplied:	50 mL rubber-capped bottle; 100 mL, 250 mL, and 500 mL rubber-capped bottles designed for use with automatic syringe equipment.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	10 mg/mL
i. Route of Administration:	Injection
j. Species/Class:	Cattle (exception: not approved for use in lactating dairy cattle and pre-ruminant calves); Swine; Reindeer; American Bison
k. Recommended Dosage:	Cattle: 1 mL per 110 lbs (50 kg) body weight, or 200 mcg/kg, given subcutaneously under the loose skin in front of or behind the shoulder, with a maximum of 10 mL per injection site.

Swine: 1 mL per 75 lbs body weight, or 300 mcg/kg, given subcutaneously under the skin immediately behind the ear.

Reindeer: 200 mcg/kg body weight, subcutaneously. Follow use directions for cattle as described under Administration.

American Bison: 200 mcg/kg body weight, subcutaneously. Follow use directions for cattle as described under Administration.

l. Pharmacological Category: Parasiticide

m. Indications: Cattle: NOROMECTIN Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, grubs, sucking lice, and mange mites in cattle:

<u>Gastrointestinal Roundworms (adults and fourth-stage larvae):</u>
Ostertagia ostertagi (including inhibited *O. ostertagi*)
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
Cooperia oncophora
C. punctata
C. pectinata
Oesophagostomum radiatum
Bunostomum phlebotomum
Nematodirus helvetianus (adults only)
N. spathiger (adults only)

<u>Lungworms (adults and fourth-stage larvae):</u>
Dictyocaulus viviparus

<u>Cattle Grubs (parasitic stages):</u>
Hypoderma bovis
H. lineatum

Sucking Lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

Mites (scabies):
Psoroptes ovis (syn. *P. communis* var. *bovis*)
Sarcoptes scabiei var. *bovis*

Persistent Activity
Ivermectin injection has been proved to effectively control infections and to protect cattle from reinfection with *Dictyocaulus viviparus* and *Oesophagostomum radiatum* for 28 days after treatment; *Ostertagia ostertagi, Trichostrongylus axei,* and *Cooperia punctata* for 21 days after treatment; *Haemonchus placei* and *Cooperia oncophora* for 14 days after treatment..

Swine: NOROMECTIN Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, lice, and mange mites in swine:

Gastrointestinal Roundworms:
Large roundworm, *Ascaris suum*
(adults and fourth-stage larvae)
Red stomach worm, *Hyostrongylus rubidus*
(adults and fourth-stage larvae)
Nodular worm, *Oesophagostomum* spp.
(adults and fourth-stage larvae)
Threadworm, *Strongyloides ransomi*
(adults)

Somatic Roundworm Larvae:
Threadworm, *Strongyloides ransomi*
(somatic larvae). Sows must be treated at least seven days before farrowing to prevent infection in piglets.

Lungworms:
Metastrongylus spp.(adults)

Lice:
Haematopinus suis

Mange mites:
Sarcoptes scabiei var. *suis*

Special Minor Use:

NOROMECTIN Injection is indicated for the effective treatment and control of warbles (*Oedemagena tarandi*) in reindeer. Follow use directions for cattle as described under Administration

NOROMECTIN Injection is indicated for the effective treatment and control of grubs (*Hypoderma bovis*) in American bison. Follow use directions for cattle as described under Administration.

n. Pioneer Product: IVOMEC Injection for Cattle and Swine; ivermectin; NADA 128-409; Merial Ltd.

o. Effect of Supplement: This supplement provides for extension of persistent effect indications as claimed by the pioneer sponsor. Specifically, the package insert has been revised as follows: Persistent activity against *Oesophagostomum radiatum* changed from 14 to 28 days and that of *Trichostrongylus axei* and *Cooperia punctato* from 14 to 21 days.

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 is required to show that 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 Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Norbrook Laboratories, Ltd. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product NOROMECTIN Injection for Cattle and Swine (ivermectin). The generic product is administered as a sterile solution, contains the same active ingredients 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 Injection for Cattle and Swine (ivermectin), the subject of Merial, Ltd., NADA 128-409, was approved on February 13, 1984.

3. HUMAN SAFETY:

- **Tolerances for Residues:**

  The tolerance established for the pioneer product applies to the generic product. Tolerances of 100 parts per billion (ppb) and 10 ppb are established for 22, 23-dihydroavermectin B_1a (marker residue) residues in the liver (target tissue) and muscle, respectively, of cattle under 21 CFR 556.344. A tolerance of 20 parts per billion (ppb) is established for 22, 23-dihydroavermectin B_1a residues in the liver and muscle of swine under 21 CFR 556.344. Tolerances of 15 parts per billion (ppb) are established for 22, 23-dihydroavermectin B_1a residues in the liver of reindeer and American bison 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:**

  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  The withdrawal time of 35 days has been established for ivermectin in cattle, 18 days withdrawal has been established in swine, 56 days in reindeer, and 56 days in American bison (21 CFR 522.1192). Withdrawal periods for milk and for pre-ruminating calves have not been established.

- **Regulatory Method for Residues:**

  The analytical methods for detection of ivermectin in tissues are HPLC methods with fluorescence detection. The methods are found on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that the injectable product NOROMECTIN Injection for Cattle and Swine, 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:

Generic Labeling for ANADA 200-437:
NOROMECTIN Injection for Cattle and Swine (ivermectin) – container and carton label – 50 mL, 100 mL, 250 mL, 500 mL; insert

Pioneer Labeling for NADA 128-409:
IVOMEC Injection for Cattle and Swine (ivermectin) – container and carton label – 50 mL, 200 mL, 500 mL; insert