Approval Date: December 19, 1997

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 128-409

B. Sponsor

Merial Limited
2100 Ronson Road
Iselin, New Jersey 08830-3800

C. Proprietary Name

IVOMEC® Injection for Cattle and Swine

D. Established Name

ivermectin

E. Dosage Form

IVOMEC Injection is a sterile 1% solution available in 50, 200, 500, and 1000 mL plastic containers

This FREEDOM OF INFORMATION SUMMARY references data in Public Master File (PMF) 5059, 61 FR 4442, February 6, 1996, in support of the supplemental new animal drug application. The data were generated by:

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F. Dispensing Status

OTC

G. Dosage Regimen

200 g ivermectin/kg body weight (1 mL/110 lb body weight)

H. Route of Administration

IVOMEC Injection should be administered by subcutaneous injection.

I. Indication

CATTLE: Ivomec injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, sucking lice, and mange mites:

Gastrointestinal Roundworms (adults and 4th stage larvae):

- *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)

Lungworms (adults and fourth-stage larvae):

- *Dictyocaulus viviparus*

Cattle Grubs (parasitic stages):

- *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

- IVOMEC Injection has been proved to effectively control infections and to protect cattle from re-infection with *Dictyocaulus viviparus* and *Ostertagia ostertagi* for 21 days after treatment; *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrongylus axei*, *Cooperia punctata* and *Cooperia oncophora* for 14 days after treatment.

- SWINE: Ivomec Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, lice, and mange mites:

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*

- *REINDEER*: For the treatment and control of warbles (*Oedemagena tarandi*)
- Additional indications contained in this supplemental NADA are for the treatment and control of grubs (*Hypoderma bovis*) in American bison.

J. Effect of Supplement

New claim for the treatment and control of grubs (*Hypoderma bovis*) in American bison.

II. EFFECTIVENESS

Effectiveness data from PMF 5059, 61 FR 4442, February 6, 1996, demonstrated that ivermectin injection, when administered subcutaneously at a dose of 200 g/kg body weight, was efficacious in treating and controlling grubs (*Hypoderma bovis*) in American bison.

III. TARGET ANIMAL SAFETY

Target animal safety data from PMF 5059, 61 FR 4442, February 6, 1996, demonstrated that based on clinical observation and evaluation of hematology, serum chemistry, and gross pathology, American bison treated with ivermectin at a dosage of 1000 g/kg body weight (5X the optimal dose) were not adversely affected by the elevated level of the drug. The data demonstrate that ivermectin injection, when administered subcutaneously at a dosage of 200 g/kg body weight, is safe to American bison.

IV. HUMAN FOOD SAFETY

The target tissue (liver) and marker residue (22,23-dihydroavermectin B1a) for ivermectin residues in cattle were applied to the American bison because a residue depletion study submitted under PMF 5059, 61 FR 4442, February 6, 1996, had results showing similarity of residues in the liver and fat of American bison to residues in the liver and fat of reindeer, therefore, the tolerance assigned to reindeer (15 ppb) was used

for American bison in calculating the withdrawal time. The withdrawal time was calculated to be 56 days.

V. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA comply with the requirements of section 512 of the Act and demonstrate that ivermectin injection, when used under the proposed conditions of use, is safe and effective for the treatment and control of grubs (*Hypoderma bovis*) in American bison.

Based on a tissue residue study in American bison, the similarity of those data to the residues in reindeer, and the current tolerance of 100 ppb for the marker residue (22, 23-dihydro-avermectin B_{1a}) of ivermectin in cattle (21 CFR 556.344), a 56-day withdrawal period is assigned for American bison treated with ivermectin at the recommended dose.

The original approval of ivermectin injection was as an over-the-counter drug. Accurate diagnosis of the need to treat for grub (*Hypoderma bovis*) infestations in American bison, which is the new species to be added to the label, can be made with a reasonable degree of certainty by the layman. Adequate directions for use have been written for the layman, and the conditions for use prescribed on the labeling are likely to be followed in practice. Therefore, the Center for Veterinary Medicine (CVM) has concluded that this product shall retain over-the-counter marketing status.

Under the Center's supplemental approval policy 21 CFR 514.106(b)(2)(vii), this is a Category II change. The approval of this change did not require a reevaluation of the safety or effectiveness data in the parent application.