Date of Approval Letter: February 1, 1999

# FREEDOM OF INFORMATION SUMMARY

## SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

## NADA 141-061

DECTOMAX® (doramectin)
1% Injectable Solution for Cattle and Swine

"...effectively controls infections and protects cattle from reinfection with *Haemonchus placei* for 14 days after treatment."

Sponsored by:

Pfizer, Inc.

## I. GENERAL INFORMATION

| | |
|---|---|
| NADA Number: | 141-061 |
| Sponsor: | Pfizer, Inc. 235 East 42nd Street<br>New York, New York 10017 |
| Established Name: | doramectin |
| Trade Name: | DECTOMAX® 1% Injectable Solution for Cattle and Swine |
| Marketing Status: | over-the-counter (OTC) |
| Effect of Supplement: | New indication for persistent control of nematodes in cattle adding protection against *Haemonchus placei* for 14 days after treatment. |

## II. INDICATIONS FOR USE: For the treatment and control of the following in cattle.

| | | |
|---|---|---|
| Gastrointestinal roundworms | *Ostertagia ostertagi* | Adults and fourth-stage larvae |
| | *Ostertagia ostertagi* | Inhibited fourth-stage larvae |
| | *Ostertagia lyrata* | Adults and fourth-stage larvae |
| | *Haemonchus placei* | Adults and fourth-stage larvae |
| | *Trichostrongylus axei* | Adults and fourth-stage larvae |
| | *Trichostrongylus colubriformis* | Adults and fourth-stage larvae |
| | *Trichostrongylus longispicularis* | Adults |
| | *Cooperia oncophora* | Adults and fourth-stage larvae |
| | *Cooperia punctata* | Adults and fourth-stage larvae |
| | *Cooperia pectinata* | Adults |
| | *Cooperia surnabada (syn. mcmasteri)* | Adults and fourth-stage larvae |
| | *Bunostomum phlebotomum* | Adults |
| | *Strongyloides papillosus* | Adults |
| | *Oesophagostomum radiatum* | Adults and fourth-stage larvae |
| | *Trichuris* spp. | Adults |
| Lungworms | *Dictyocaulus viviparus* | Adults and fourth-stage larvae |
| Eyeworms | *Thelazia* spp. | Adults |
| Grubs | *Hypoderma bovis*<br>*Hypoderma lineatum* | |
| Lice | *Haematopinus eurysternus*<br>*Linognathus vituli*<br>*Solenopotes capillatus* | |
| Mange mites | *Psoroptes bovis*<br>*Sarcoptes scabiei* | |

Dectomax injectable solution has been proved to effectively control infections and to protect cattle from reinfection with *Cooperia oncophora* and *Haemonchus placei* for 14 days; *Ostertagia ostertagi* for 21 days; and *Cooperia punctata, Oesophagostomum radiatum,* and *Dictyocaulus viviparus* for 28 days after treatment.

## III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

A. Dosage Form: DECTOMAX® 1% Injectable Solution for Cattle and Swine is a sterile solution containing 10 mg doramectin/mL.

B. Route of Administration: DECTOMAX® 1% Injectable Solution for Cattle and Swine may be administered by subcutaneous or intramuscular injection.

C. Approved Dose: 200 mcg doramectin/kg body weight (1 mL/110 lb body weigh)

## IV. EFFECTIVENESS

Data demonstrating the effectiveness of DECTOMAX® 1% Injectable Solution for Cattle and Swine of previously approved indications are discussed in the parent NADA 141-061 FOI Summaries (original approval dated July 30, 1996, supplemental approvals dated July 18, 1997, September 18, 1997, and October 25, 1998). Data from the following dose confirmation trials demonstrate that DECTOMAX® 1% Injectable Solution administered at the recommended dosage protects cattle against infection or reinfection with *Haemonchus placei* for 14 days after treatment.

Note: Nematode percentage efficacies were calculated using the following formula:

[Arithmetic mean number of nematodes in control cattle) - (Arithmetic mean number of nematodes in doramectin-treated cattle)] ÷ (Arithmetic mean number of nematodes in control cattle) × 100 = Percent Effectiveness

A. Dose Confirmation: Study No. 1231C-60-95-198

1. Investigator: Dr. T.A. Yazwinski, University of Arkansas, Fayettville, Arkansas

2. General design:

   a. Purpose: To evaluate the persistent efficacy of doramectin against artificially induced infections of *Haemonchus placei*.

   b. Animals: Forty-two (42) Holstein calves (10 per group, with 2 larval viability monitors). Animals were approximately 2-6 months old and weighed 81 to 211 kg at the start of the study. All animals were treated with fenbendazole during the acclimation period to eliminate any existing infections as confirmed by negative fecal egg counts done on Day -1.

   c. Controls: Control animals received saline.

   d. Infection: Infective larvae were given to each animal daily, starting on Day 14 after treatment through Day 28. Three hundred *Haemonchus placei* larvae were administered daily. The larval viability monitors were given 10,000 *Haemonchus placei* larvae on Day 28.

e. Test article administration: The approved formulation of injectable solution containing 10 mg doramectin per mL was administered by subcutaneous injection. 1 mL/110 lb body weight (200 mcg doramectin/kg body weight) was given once to each animal in three groups. Groups T1 and T2 were treated with saline and doramectin, respectively, on Day 0. Group T3 was treated with doramectin on Day 7, and Group T4 was treated with doramectin on Day 14.

f. Pertinent variables measured: Worm counts were determined at necropsy which was 42 to 43 days after Groups T1 and T2 received treatment, 14 to 15 days after the last *Haemonchus placei* larvae were administered to all groups.

3. Results – *Haemonchus placei* was present in adequate numbers for a determination of efficacy.

**Table 4.1.** Arithmetic mean worm counts of *Haemonchus placei* recovered for each group, number of infected animals, and percent efficacy

| | | | | *H. placei* | | |
|---|---|---|---|---|---|---|
| Group | Treatment | Day of Treatment | Persistence Interval | worm count | infected animals | percent efficacy |
| T1 | saline | 0 | - | 2300 | 10 | - |
| T2 | doramectin | 0 | 28 | 610 | 8 | 73.5% |
| T3 | doramectin | 7 | 21 | 483 | 1 | 79.0% |
| T4 | doramectin | 14 | 14 | 180 | 0 | 92.2% |

4. Adverse reactions: No adverse reactions to treatment were observed.

5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Haemonchus placei* for 14 days.

B. Dose Confirmation: Study No. 2239A-60-97-135

1. Investigator: Lora Ballweber, D.V.M., M.S., Mississippi State, Missouri

2. General design:

a. Purpose: To evaluate the persistent efficacy of doramectin against artificially induced infections of *Haemonchus placei.*

b. Animals: Forty-two (42) crossbred beef calves (10 per group, with 2 larval viability monitors). Animals were approximately 2 to 6 months old and weighed 117 to 165 kg at the start of the study. All animals were treated with fenbendazole during the acclimation period to eliminate any existing infections as confirmed by negative fecal egg counts done on Day -1.

c. Infection: Infective larvae were given to each animal daily, starting on Day 14

after treatment through Day 28. Three hundred *Haemonchus placei* larvae were administered daily. The larval viability monitors were given 10,000 *Haemonchus placei* larvae on Day 28.

d. Test article administration: The approved formulation of injectable solution containing 10 mg doramectin per mL was administered by subcutaneous injection. 1 mL/110 lb body weight (200 mcg doramectin/kg body weight) was given once to each animal in three groups. Groups T1 and T2 were treated with saline and doramectin, respectively, on Day 0. Group T3 was treated with doramectin on Day 7 and Group T4 was treated with doramectin on Day 14.

e. Pertinent variables measured: Worm counts were determined at necropsy which was 43 to 44 days after Groups T1 and T2 received treatment, 15 to 16 days after the last *Haemonchus placei* larvae were administered to all groups.

3. Results:

**Table 4.2.** Mean worm counts of *Haemonchus placei* recovered for each group, number of infected animals, and percent efficacy

| Group | Treatment | Day of Treatment | Persistence Interval | Worm Count | Infected Animals | Percent Efficacy |
|---|---|---|---|---|---|---|
| T1 | saline | 0 | 0 | 715 | 10 | - |
| T2 | doramectin | 0 | 28 | 40 | 6 | 94.4% |
| T3 | doramectin | 7 | 21 | 25 | 1 | 96.5% |
| T4 | doramectin | 14 | 14 | 15 | 1 | 97.9% |

4. Adverse reactions: No adverse reactions were observed during these studies.

5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Haemonchus placei* for 28 days.

## V. ANIMAL SAFETY

As discussed in the parent NADA 141-061 FOI Summary (approval date July 30, 1996).

## VI. HUMAN SAFETY

As discussed in the parent NADA 141-061 FOI Summaries (original approval date July 30, 1996, and supplemental approval date October 25, 1998).

## VII. AGENCY CONCLUSION

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 514) to demonstrate that DECTOMAX® 1% Injectable Solution for Cattle and Swine, when used under the proposed conditions of use, is safe and effective to control infections and to protect cattle from reinfection with *Haemonchus placei* for 14 after treatment.

For cattle, tolerances of 0.1 ppm for parent doramectin (marker residue) in liver (target tissue) and 0.3 ppm in muscle are codified at 21 CFR 556.225. The preslaughter withdrawal time is 35 days following one subcutaneous or intramuscular injection of DECTOMAX® 1% Injectable Solution, as specified at 21 CFR 522.770.

The agency has concluded that this product shall retain over-the-counter marketing status because adequate directions for use have been written for the layman and the conditions for use prescribed on the label are likely to be followed in practice.

In accordance with 21 CFR 514.106(b)(2), this is a Category II change which did not require a reevaluation of the safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals qualifies for THREE (3) years of marketing exclusivity beginning on the date of approval because the supplemental application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval of the application and conducted or sponsored by the applicant. The THREE years of marketing exclusivity applies only to the new claim for which the supplemental application is approved.

DECTOMAX® 1% Injectable Solution for Cattle and Swine is under U.S. patent number 5,089,480, which expires on February 18, 2009.

## VIII. APPROVED PRODUCT LABELING (attached)

A. Facsimile label - 500-mL rubber-stoppered, glass vials

B. Facsimile package insert