DATE OF APPROVAL LETTER:

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-095

DECTOMAX® (doramectin)

Pour-On

"...for treatment and control of *Trichostrongylus axei* (L_4)"

"…control infection and to protect cattle from reinfection with *Haemonchus placei* for 35 days after treatment"

Sponsored by:

Pfizer, Inc.

I. GENERAL INFORMATION: NADA NO. 141-095

Sponsor: Pfizer, Inc
235 East 42nd Street
New York, New York 10017

Established Name: doramectin

Trade Name: DECTOMAX® (doramectin) Pour-On

Marketing Status: over-the-counter (OTC)

Effect of Supplement: New indications for therapeutic efficacy against *Trichostrongylus axei* (L_4) and persistent efficacy for 35 days against *Haemonchus placei*.

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
	Haemonchus placei	Adults and fourth-stage larvae
	Trichostrongylus axei	Adults and fourth stage larvae
	Trichostrongylus colubriformis	Adults and fourth-stage larvae
	Cooperia oncophora	Adults and fourth-stage larvae
	Cooperia punctata	Adults and fourth-stage larvae
	Cooperia pectinata	Adults
	Cooperia surnabada (syn. mcmasteri)	Adults
	Bunostomum phlebotomum	Adults
	Oesophagostomum radiatum	Adults and fourth-stage larvae
	Trichuris spp.	Adults
Lungworms	*Dictyocaulus viviparus*	Adults and fourth-stage larvae
Eyeworms	*Thelazia gulosa*	Adults
	Thelazia skrjabini	Adults
Grubs	*Hypoderma bovis*	
	Hypoderma lineatum	
Lice	Sucking *Haematopinus eurysternus*	Biting *Damalinia bovis*
	Linognathus vituli	
	Solenopotes capillatus	
Mange mites	*Chorioptes bovis*	
	Sarcoptes scabiei	
Horn Flies	*Haematobia irritans*	

Dectomax pour-on solution has been proved to effectively control infections and to protect cattle from reinfection with *Cooperia oncophora* and *Dictyocaulus viviparus* for 21 days, *Ostertagia ostertagi*, *Cooperia punctata,* and *Oesophagostomum radiatum* for 28 days after treatment, and *Haemonchus placei* for 35 days after treatment.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE:

A. Dosage Form: Pour-on solution containing 5 mg doramectin/mL.

B. Route of Administration: DECTOMAX® (doramectin) Pour-On should be applied topically along the mid-line of the back.

C. Approved Dose: 500 mcg doramectin/kg body weight (5 mL/110 lb body weight)

IV. EFFECTIVENESS:

Data demonstrating the effectiveness of DECTOMAX® (doramectin) Pour-On for previously registered indications are discussed in the parent NADA 141-095 FOI Summary (approval date September 16, 1997). Data from the following dose confirmation trials demonstrate that the efficacy of DECTOMAX® (doramectin) Pour-On, administered at the recommended dosage treats and controls *Trichostrongylus axei* (L4) and controls infections and prevents reinfection with *Haemonchus placei* for up to 35 days after treatment.

TRICHOSTRONGYLUS AXEI (L_4) THERAPEUTIC EFFECTIVENESS

SUMMARY

Two dose confirmation studies (1231C-60-93-017, 1231C-60-97-278) were conducted to confirm the effectiveness of doramectin pour-on, administered topically at a dose of 500 mcg/kg, against *Trichostrongylus axei* L_4 infections in cattle.

RESULTS

Results are presented on an individual study basis in the section following (see Tables 4.1 and 4.2).

OVERALL CONCLUSIONS

A single topical application of doramectin pour-on at a dosage of 500 mcg/kg was highly efficacious in reducing *Trichostrongylus axei* L_4 recovered at necropsy from calves artificially infected with infective larvae of *Trichostrongylus axei*.

A. Dose Confirmation Study 1231C-60-93-017

1. Investigator: Dr. L.R. Ballweber
College of Veterinary Medicine
Mississippi State University
Mississippi State, Mississippi

2. General Design:

   a. Purpose: To evaluate the therapeutic efficacy of doramectin pour-on at a dosage of 500 mcg/kg BW against artificially-induced, immature nematode infections in cattle.

   b. Animals: Ten (10) per group. Animals were 5 to 6 months old and weighed 125 to 191 kg at the start of the study.

   c. Controls: Animals in the negative control group (T1) received no medication.

   d. Procedure: On Day 0, calves were weighed and randomly allocated to a non-medicated group or a doramectin-treated group. All calves received infective larvae of *Trichostrongylus axei* on Day 11. On Day 17, animals in the doramectin group (T2) were treated topically with doramectin pour-on at a dose of 500 mcg/kg BW. Animals in group T1 received no medication. Animals were euthanized and necropsied on Days 31 and 32 for determination of worm burdens.

3. Results: The percentage reduction in arithmetic mean nematodes in the doramectin group, compared to the non-medicated group, is summarized in Table 4.1. There were no adverse events observed at any time during the study for any of the doramectin-treated cattle.

   Table 4.1: Percent efficacy of doramectin pour-on solution administered topically at 500 mcg/kg

Parasite	Arithmetic Mean Worm Counts		% Efficacy
	Non-medicated	Doramectin	
Trichostrongylus axei L4	640	0	100

4. Data analysis: Total *Trichostrongylus axei* L_4 burdens for each animal were estimated from the number of fourth-stage larval parasites found in the abomasum at necropsy.

   Arithmetic mean nematode counts were calculated for each nematode species. These were used to estimate the percentage efficacy for the treated group compared to the non-medicated group using the following formula:

   [(Arithmetic mean number of worms in non-medicated cattle) - (Arithmetic mean number of worms in doramectin-treated cattle)] ÷ [Arithmetic mean number of worms in non-medicated cattle] X 100 = Percentage Efficacy

5. Conclusion: A single application of doramectin pour-on administered to cattle at a dose of 500 mcg/kg BW was effective against induced *Trichostrongylus axei* L4 infection in cattle.

B. Dose Confirmation Study 1231C-60-97-278

1. Investigator: Edward G. Johnson
   24007 Highway 20/26
   Parma, Idaho

2. General Design:

   a. Purpose: To evaluate the therapeutic efficacy of doramectin pour-on at a dosage of 500 mcg/kg BW against artificially-induced infections of immature stages of *Trichostrongylus axei* infections in cattle.

   b. Animals: Ten (10) per group. Animals were 3 to 6 months old and weighed 119 to 217 kg at the start of the study.

   c. Controls: Animals in the control group (T1) received saline.

   d. Procedure: Calves were randomly allocated to a non-medicated group or a doramectin-treated group. All calves received infective larvae of *Trichostrongylus axei* on Day 0. On Day 10, calves were weighed and animals in the doramectin group (T2) were treated topically with doramectin pour-on at a dose of 500 mcg/kg BW. Animals in group T1 received saline at a dose of 1 mL/10 kg BW. Animals were euthanized and necropsied on Day 21 for determination of worm burdens.

3. Results: The percentage reduction in arithmetic mean nematodes in the doramectin group, compared to the non-medicated group, is summarized in Table 4.2. There were no adverse events observed at any time during the study for any of the doramectin-treated cattle.

Table 4.2. Percent efficacy of doramectin pour-on solution administered topically at 500 mcg/kg

Parasite	Arithmetic Mean Worm Counts	% Efficacy

	Non-medicated	Doramectin	
Trichostrongylus axei L4	5490	0	100

4. Data analysis: Arithmetic mean worm counts were calculated for worm species. These were used to estimate the percentage efficacy for the treated group compared to the non-medicated group, using the following formula:

   [(Arithmetic mean number of nematodes in non-medicated cattle) - (Arithmetic mean number of nematodes in doramectin-treated cattle)] ÷ [Arithmetic mean number of nematodes in non-medicated cattle] X 100 = Percentage Efficacy

5. Conclusion: A single application of doramectin pour-on administered to cattle at a dose of 500 mcg/kg BW was effective against induced *Trichostrongylus axei* L4 infection in cattle.

PERSISTENT EFFICACY - *HAEMONCHUS PLACEI*

SUMMARY

Two dose confirmation studies (1231C-60-95-199, 1231C-60-97-277) were conducted to evaluate the persistent efficacy of doramectin pour-on, administered topically at a dose of 500 mcg/kg against artificial infections of nematodes.

RESULTS

Results are presented on an individual study basis in the section following (see Tables 4.3 and 4.4).

OVERALL CONCLUSIONS

A single topical application of doramectin pour-on at a dosage of 500 mcg/ provided persistent efficacy against challenge infections of *Haemonchus placei* for up to 35 days after treatment. No significant adverse reaction to treatment was observed in either study.

A. Dose Confirmation Study 1231C-60-95-199

1. Investigator: Edward G. Johnson
   24007 Highway 20/26
   Parma, Idaho

2. General Design:

a. Purpose: To evaluate the persistent efficacy of doramectin pour-on, administered topically at a dosage of 500 mcg/kg BW against artificially induced nematode infections.

b. Animals: Ten (10) per group. Animals were 4 to 6 months old and weighed 127 to 251 kg at the start of the study.

c. Controls: Animals in the negative control group (T1) received saline.

d. Procedure: Forty-two (42) animals were weighed and randomly allotted to a saline-treated group (T1, 10 animals) or to one of three doramectin-treated groups (T2 to T4, 10 animals each) on Day 0. No physical contact was permitted between groups. On Day 0, animals in Groups T1 and T2 were treated topically with saline (1 mL/10 kg BW) or doramectin pour-on (500 mcg/kg BW), respectively. Groups T3 and T4 were treated with doramectin pour-on in an identical manner on Days 7 and 14, respectively.

   All animals in Groups T1 to T4 were challenged daily on Days 14 to 35 with infective *Haemonchus placei* larvae (1995 mixed strain isolated in Louisiana and Idaho). Animals from Groups T1 to T4 were euthanized and necropsied on Days 49 and 50 for determination of worm counts.

3. Results: The percentage reduction in geometric mean nematodes in the doramectin group, compared to the non-medicated group, is summarized in Table 4.3. There were no adverse events observed at any time during the study for any of the doramectin-treated cattle.

   Table 4.3: Geometric Mean *Haemonchus placei* Nematode Counts and Percent Efficacy

Treatment	Group Size	Persistence Interval	Mean Worm Counts	% Efficacy
T1 - Saline	10	--	106	--
T2 - Doramectin	10	35 days	3	97.4
T3 - Doramectin	10	28 days	0	100
T4 - Doramectin	10	21 days	0	100

4. Data analysis: Nematode percentage efficacy was calculated using the following formula:

[(Geometric mean number of worms in non-medicated cattle) - (Geometric mean number of worms in doramectin-treated cattle)] ÷ [Geometric mean number of worms in non-medicated cattle] X 100 = Percentage Efficacy

5. Conclusion: A single application of doramectin pour-on administered to cattle topically at a dose of 500 mcg/kg BW provided persistent efficacy against challenge infections of *Haemonchus placei* for 35 days.

B. Dose Confirmation Study 1231C-60-97-277

1. Investigator: Edward G. Johnson
24007 Highway 20/26
Parma, Idaho

2. General Design:

a. Purpose: To evaluate the persistent efficacy of doramectin pour-on, administered topically at a dosage of 500 mcg/kg BW against artificially induced nematode infections.

b. Animals: Ten (10) per group. Animals were 5 to 6 months old and weighed 113 to 263 kg at the start of the study.

c. Controls: Animals in the control group (T1) received saline.

d. Procedure: Forty-two (42) animals were weighed and randomly allotted to a saline-treated group (T1, 10 animals), to one of three doramectin-treated groups (T2 to T4, 10 animals each), or as larval monitors (2 animals) on Day 0. No physical contact was permitted between groups.

On Day 0, animals in Groups T1 and T2 were treated topically with saline (1 mL/10 kg BW) or doramectin pour-on (500 mcg/kg BW), respectively. Groups T3 and T4 were treated with doramectin pour-on in an identical manner on Days 7 and 14, respectively.

All animals in Groups T1 to T4 were challenged daily on Days 21 to 35 with infective *Haemonchus placei* larvae (1997 strain isolated in Mississippi). The two larval viability monitor animals were challenged on Day 35, to confirm the viability of the inoculum at the end of the infection phase of the study. Animals from Groups T1 to T4, and larval monitor animals were euthanized and necropsied on Day 49 for determination of worm counts.

3. Results: The percentage reduction in geometric mean nematodes in the doramectin group, compared to the non-medicated group, is summarized in table

4.4. There were no adverse events observed at any time during the study for any of the doramectin-treated cattle.

Table 4.4. Geometric Mean *Haemonchus placei* Nematode Counts and Percent Efficacy

Treatment	Persistence Interval	Mean Worm Counts	% Efficacy
T1 - Saline	--	368	--
T2 - Doramectin	35 days	4	98.9
T3 - Doramectin	28 days	10	97.2
T4 - Doramectin	21 days	1	99.6

4. Data analysis: Geometric mean worm counts were calculated for worm counts. These were used to estimate the percentage efficacy for the treated group compared to the non-medicated group, using the following formula:

   [(Geometric mean number of nematodes in non-medicated cattle) - (Geometric mean number of nematodes in doramectin-treated cattle)] ÷ [Geometric mean number of nematodes in non-medicated cattle] X 100 = Percentage Efficacy

5. Conclusion: A single application of doramectin pour-on administered to cattle topically at a dose of 500 mcg/kg BW provided persistent efficacy against challenge infections of *Haemonchus placei* for 35 days.

V. ANIMAL SAFETY:

As discussed in the parent NADA 141-095 FOI Summary (approval date Sept. 16, 1997).

VI. HUMAN SAFETY

As discussed in the parent NADA 141-095 FOI Summary (approval date Sept. 16, 1997) and supplemental approval FOI Summary (dated October 25, 1998).

VII. AGENCY CONCLUSIONS

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® (doramectin) Pour-On, is safe and effective for the treatment and control of *Trichostrongylus axei* (L_4) in cattle and to control infections and to protect cattle from re-infection with *Haemonchus placei* for 35 days after treatment, when administered topically at a dose of 500 mcg/kg bodyweight.

There are no changes to the codified tolerances for doramectin in cattle or to the established preslaughter withdrawal time of 45 days.

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)(ii) of the FFDCA, this approval for food producing animals qualifies for THREE 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.

DECTOMAX® (doramectin) Pour-On is under U.S. patent number 5,089,480, which expires on July 30, 2010.

VIII. APPROVED PRODUCT LABELING (attached)

A. Facsimile label - 250 mL, 1 liter, 2.5 liter, and 5 liter containers

B. Facsimile package insert.

C. Box carton – 250 mL size