Date of Approval: June 23, 2005

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-095

DECTOMAX (doramectin) Pour-On

"To add persistent effect periods for *Bovicola (Damalinia) bovis* for 77 days and *Linognathus vituli* for 42 days after treatment"

Sponsored by:
Pfizer, Inc

1. GENERAL INFORMATION

a.	File Number:	NADA 141-095
b.	Sponsor:	Pfizer, Inc 235 East 42d St. New York, NY 10017 Drug Labeler Code: 000069
c.	Established Name:	Doramectin
d.	Proprietary Name:	DECTOMAX Pour-On
e.	Dosage Form:	Solution
f.	How Supplied:	250 mL, 1 liter, 2.5 liter, and 5 liter containers
g.	How Dispensed:	Over-the-Counter (OTC)
h.	Amount of Active Ingredients:	5 mg doramectin/mL
i.	Route of Administration:	Topical
j.	Species/Class:	Beef cattle & Dairy cattle less than 20 months
k.	Recommended Dosage:	Administer 500 mcg doramectin/kg (227 mcg/lb) of body weight. Each mL contains 5 mg of doramectin, sufficient to treat 22 lb (10 kg) of body weight.
l.	Pharmacological Category:	Antiparasitic

m. Indications: For the treatment and control of the following in cattle.

Gastrointestinal Roundworms

Ostertagia ostertagi	Adults and L_4, including inhibited larvae
Ostertagia lyrata	Adults
Haemonchus placei	Adults and L_4
Trichostrongylus axei	Adults and L_4
T. colubriformis	Adults and L_4
Cooperia oncophora[1]	Adults and L_4
C. pectinata	Adults
C. punctata	Adults and L_4
C. surnabada	Adults
Bunostomum phlebotomum	Adults
Oesophagostomum radiatum	Adults and L_4
Trichuris spp.	Adults

[1]Efficacy below 90% was observed against adult *Cooperia oncophora* in some clinical studies

Lungworms	
Dictyocaulus viviparus	Adults and L_4
Eyeworms	
Thelazia gulosa	Adults
Thelazia skrjabini	Adults

Grubs
Hypoderma bovis
H. lineatum

Sucking Lice
Haematopinus eurysternus
Linognathus vituli
Solenopotes capillatus

Biting Lice
Bovicola (Damalinia) bovis

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, Dictyocaulus viviparus, Ostertagia ostertagi,* and *Oesophagostomum radiatum* for 28 days; and *Cooperia punctata* and *Haemonchus placei* for 35 days after treatment.

n. Effect of Supplement: This supplement allows the following additional persistent effect indications. DECTOMAX Pour-On solution has been proved to effectively control infestations and to protect cattle from reinfestation with *Bovicola (Damalinia) bovis* for 77 days and *Linognathus vituli* for 42 days after treatment.

2. EFFECTIVENESS

a. Dose Characterization

Effectiveness studies were presented in the original NADA 141-095 FOI Summary approval dated September 16, 1997, establishing the recommended effective dose of DECTOMAX Pour-On for the treatment and control of internal and external parasites.

b. Substantial Evidence

Two dose confirmation studies, conducted under the same protocol, evaluated the persistent effect of DECTOMAX Pour-On, administered topically at a dose of 500 mcg/kg against infestations of *Linognathus vituli* and *Bovicola (Damalinia) bovis*.

In each study, twenty-four (24) adequately infested mixed-sex beef calves (principals) having at least 5 *B. bovis* and 10 *L. vituli* were randomly and equally assigned to either the DECTOMAX Pour-On vehicle group or the DECTOMAX Pour-On group. From Day -1 to Day 35, the calves were kept in pens by treatment group. From Day 35 to Day 182, all calves were commingled in one pen. On Day 0, DECTOMAX Pour-On or vehicle was applied to the principal calves as indicated by treatment group. Lice counts of 9 predefined body regions were performed on these calves on Day -1 and Day 35. The pre-treatment lice infestations were cleared from the calves treated with DECTOMAX Pour-On by Day 35. To determine the persistent effect of DECTOMAX Pour-On, two seeder calves that were adequately infested with *B. bovis* and *L. vituli* were introduced to the pen where the principal calves were housed on Days 35, 63, 91, 119, and 147. The seeder calves remained in the pen for the duration of the study. Two louse-free sentinel calves were introduced to the pen on Days 35, 56, 77, 98, 119, 140, and 161 to confirm that natural contact transmission of lice was occurring. The sentinel calves were removed from the pen 28 days after entry. Lice counts were done every 7 days from Day 35 through Day 182 on the principal, seeder, and sentinel calves during the period they were in the pen.

For each study, percent efficacy was determined by comparing the geometric mean lice counts of the treated group with those of an untreated control group for each species present in at least six adequately infested control animals at each count day using Abbot's formula. A general linear repeated-measures mixed model was used to analyze log transformed lice counts. The significance for the louse count comparisons was set at $P<0.05$. The persistent effect period was determined at each count day when there was an adequate level of infestation in at least 6 control animals, a statistically significant difference between treated and control animals at $P<0.05$, and 95% efficacy using geometric means for each genus species of parasite. Using these criteria the two studies supported a persistent effect against *Linognathus vituli* for 42 days and *Bovicola* (*Damalinia) bovis* for 77 days after treatment.

The two studies are summarized below.

B.1 Dose Confirmation Study 2039B-60-99-119

1) Investigator: John E. Lloyd, Ph.D.
Jim W. Waggoner, Ph.D., P.A.S.
University of Wyoming
Laramie, Wyoming

2) General Design:

a. Purpose: To evaluate the persistent efficacy of DECTOMAX Pour-On administered at a dose of 500 mcg/kg body weight to *Bovicola (Damalinia) bovis* and *Linognathus vituli* infested cattle that are housed with untreated calves with *Bovicola (Damalinia) bovis* and *Linognathus vituli* infestations.

b. Animals: Male castrate and female beef cross-bred calves 4 to 10 months old were used. There were twenty-four (24) principal animals weighing 165 to 246 kg at the start of the study (twelve per treatment group). There were ten (10) infested seeder calves weighing 183 to 261 kg and fourteen (14) non-treated non-infested sentinel calves weighing 175 to 231 kg.

c. Infestation: The principal calves were naturally infested with *Bovicola (Damalinia) bovis* and *Linognathus vituli* at the start of the study. Additional louse exposure came by natural transfer from seeder calves introduced into the pen periodically for the duration of the study.

d. Controls: There were twelve (12) animals in the negative control group that received vehicle.

e. Treatment Regimen: The principal calves were given a single administration of 1 mL/10 kg body weight of vehicle or doramectin (500 mcg doramectin/kg body weight) on Day 0.

f. Study Duration: 182 days

g. Primary Variable: The density of louse populations was assessed by summing the lice counts within pre-defined areas of examination on 9 body regions on Days -1, 35, 42, 49, 56, 70, 77, 84, 91, 98, 105, 112, 119, 126, 133, 140, 147, 154, 161, 168, 175, and 182.

3) Results: There was an adequate level of infestation of *Bovicola (Damalinia) bovis* in the 12 vehicle control calves throughout the study. For *Linognathus vituli*, the infestation was adequate through Day 42. On Day 35 the treatment was 100% effective against *Bovicola (Damalinia) bovis* and *Linognathus vituli*. The period of persistent effect demonstrated against *Bovicola (Damalinia) bovis* was 98 days and against *Linognathus vituli* was 42 days. The results are summarized in Table 2.1 for *Bovicola (Damalinia) bovis* and Table 2.2 for *Linognathus vituli*.

Table 2.1 Study 2039B-60-99-119 – Persistent Efficacy (based on Geometric Means) of DECTOMAX Pour-On Against *Bovicola (Damalinia) bovis*

Day of Study	Geometric Mean Lice Counts: Vehicle Control	Geometric Mean Lice Counts: DECTOMAX Pour-On	P-value[a]	% Efficacy[b]
-1	13.3	12.4	-	-
35	27.3	0	-	100.0
42	30.8	0.7	0.0001	97.7
49	30.4	0.1	0.0001	99.8
56	33.3	0.3	0.0001	99.2
63	48.1	0.7	0.0001	98.6
70	43.2	0.7	0.0001	98.4
77	36.3	0.7	0.0001	98.2
84	36.1	0.2	0.0001	99.6
91	34.3	0.2	0.0001	99.3
98	39.8	1.2	0.0001	97.1
105	50.2	2.6	0.0001	94.8
112	47.4	2.8	0.0001	94.1
119	74.9	3.3	0.0001	95.6
126	58.4	6.8	0.0001	88.4
133	44.7	8.1	0.0001	81.8
140	44.3	9.0	0.0008	79.8
147	45.6	13.3	0.0072	70.7
154	47.4	32.6	0.2991	31.4
161	49.8	44.7	0.7689	10.1
168	39.5	49.8	0.6148	-
175	27.3	45.6	0.1689	-
182	28.6	44.5	0.1733	-

[a] P-value: Statistical significance at alpha = 0.05

[b] % efficacy = $\frac{\text{Mean no. of lice vehicle-treated group} - \text{Mean no. lice doramectin-treated group}}{\text{Mean no. of lice vehicle-treated group}} \times 100$

Table 2.2 Study 2039B-60-99-119 – Persistent Efficacy (based on Geometric Means) of DECTOMAX Pour-On Against *Linognathus vituli*

Day of Study	Geometric Mean Lice Counts: Vehicle Control	Geometric Mean Lice Counts: DECTOMAX Pour-On	P-value[a]	% Efficacy[b]
-1	34.5	33.9	-	-
35	14.5	0.0	-	100.0
42	10.6	0.0	0.0001	100.0
49	3.8	0.1	0.0001	98.5
56	2.0	0.0	0.0018	100.0
63	1.6	0.0	0.0054	100.0
70	1.3	0.0	0.0166	100.0
77	1.5	0.0	0.0093	100.0
84	1.9	0.0	0.0024	100.0
91	2.3	0.0	0.0006	100.0
98	3.3	0.1	0.0001	98.2
105	4.5	0.0	0.0001	100.0
112	5	0.1	0.0001	97.6
119	3.8	0.1	0.0001	96.7
126	2.3	0.1	0.0021	94.6
133	4.4	0.2	0.0001	96.3
140	2.4	0.2	0.0019	93.3
147	4.5	0.5	0.0002	88.6
154	3.3	0.6	0.0048	81.5
161	4.8	1.3	0.0069	73.5
168	3.3	1.3	0.0735	60.3
175	2.2	2.6	0.7240	-
182	2.2	3.1	0.4724	-

[a] P-value: Statistical significance at alpha = 0.05

[b] % efficacy = $\frac{\text{Mean no. of lice vehicle-treated group – Mean no. lice doramectin-treated group}}{\text{Mean no. of lice vehicle-treated group}} \times 100$

4) Adverse Events: No treatment related health problems were observed during this study.

B.2 Dose Confirmation Study 2039B-60-99-120

1) Investigator: Larry L. Smith, D.V.M.
Research and Development, Inc.
108 Davis Street
Lodi, Wisconsin

2) General Design:

a. Purpose: To evaluate the persistent efficacy of DECTOMAX Pour-On administered at a dose of 500 mcg/kg body weight to *Bovicola (Damalinia) bovis* and *Linognathus vituli* infested cattle that are housed with untreated calves with *Bovicola (Damalinia) bovis* and *Linognathus vituli* infestations.

b. Animals: Male castrate and female beef cross-bred calves 4 to 8 months old were used. There were twenty-four (24) principal animals weighing 119 to 197 kg at the start of the study (twelve per treatment group). There were ten (10) infested seeder calves weighing 129 to 321 kg and fourteen (14) non-treated non-infested sentinel calves weighing 217 to 352 kg.

c. Infestation: The principal calves were naturally infested with *Bovicola (Damalinia) bovis* and *Linognathus vituli* at the start of the study. Additional louse exposure came by natural transfer from seeder calves introduced into the pen periodically for the duration of the study.

d. Controls: There were twelve (12) animals in the negative control group that received vehicle.

e. Treatment Regimen: The principal calves were given a single administration of 1 mL/10 kg body weight of vehicle or doramectin (500 mcg doramectin/kg body weight) on Day 0.

f. Study Duration: 182 days

g. Primary Variable: The density of louse populations was assessed by summing the lice counts within pre-defined areas of examination on 9 body regions on Days -1, 35, 42, 49, 56, 70, 77, 84, 91, 98, 105, 112, 119, 126, 133, 140, 147, 154, 161, 168, 175, and 182.

3) Results: There was an adequate level of infestation of *Bovicola (Damalinia) bovis* in the 12 vehicle control calves throughout the study. For *Linognathus vituli*, the infestation was adequate through Day 154. On Day 35 the treatment was 100% effective against *Bovicola (Damalinia) bovis* and *Linognathus vituli*. The period of persistent effect demonstrated against *Bovicola (Damalinia) bovis* was 77 days and against *Linognathus vituli* was 105 days. The results are summarized in Table 2.3 for *Bovicola (Damalinia) bovis* and Table 2.4 for *Linognathus vituli*.

Table 2.3 Study 2039B-60-99-120 – Persistent Efficacy (based on Geometric Means) of DECTOMAX Pour-On Against *Bovicola (Damalinia) bovis*

Day of Study	Geometric Mean Lice Counts: Vehicle Control	Geometric Mean Lice Counts: DECTOMAX Pour-On	P-value[a]	% Efficacy[b]
-1	34.7	55.6	-	-
35	210.3	0.0	-	100.0
42	182.3	1.0	0.0001	99.5
49	249.4	1.1	0.0001	99.6
56	230.7	2.2	0.0001	99.0
63	219.3	5.1	0.0001	97.7
70	227.1	6.4	0.0001	97.2
77	202.4	5.5	0.0001	97.3
84	214.0	13.9	0.0001	93.5
91	189.3	19.7	0.0001	89.6
98	197.3	41.6	0.0001	78.9
105	169.1	84.2	0.0302	50.2
112	155.7	115.4	0.4068	25.9
119	142.9	167.7	0.6253	-
126	101.1	151.9	0.1936	-
133	123.6	201.8	0.0791	-
140	82.1	147.3	0.0502	-
147	70.1	122.0	0.0819	-
154	57.1	87.0	0.2821	-
161	28.3	82.3	0.0448	-
168	43.3	63.1	0.3541	-
175	25.7	41.4	0.3295	-
182	20.8	35.8	0.2713	-

[a] P-value: Statistical significance at alpha = 0.05

[b] % efficacy = $\frac{\text{Mean no. of lice vehicle-treated group – Mean no. lice doramectin-treated group}}{\text{Mean no. of lice vehicle-treated group}} \times 100$

Table 2.4 Study 2039B-60-99-120 – Persistent Efficacy (based on Geometric Means) of DECTOMAX Pour-On Against *Linognathus vituli*

Day of Study	Geometric Mean Lice Counts: Vehicle Control	Geometric Mean Lice Counts: DECTOMAX Pour-On	P-value[a]	% Efficacy[b]
-1	122.6	167.7	-	-
35	76.5	0.0	-	100.0
42	50.0	0.0	0.0001	100.0
49	31.3	0.1	0.0001	99.6
56	25.5	0.0	0.0001	100.0
63	19.8	0.1	0.0001	99.7
70	21.0	0.0	0.0001	100.0
77	21.8	0.1	0.0001	99.7
84	14.9	0.1	0.0001	99.2
91	19.6	0.3	0.0001	98.3
98	21.9	0.3	0.0001	98.6
105	15.3	0.4	0.0001	97.4
112	16.2	1.4	0.0001	91.5
119	16.6	2.3	0.0001	86.3
126	15.3	6.6	0.0146	56.6
133	15.3	7.2	0.0269	52.9
140	12.4	7.5	0.1377	39.8
147	10.5	5.7	0.0799	45.9
154	7.0	4.5	0.2335	35.2
161	4.5	7.7	0.1464	-
168	3.1	4.5	0.3595	-
175	2.0	4.6	0.0495	-
182	2.1	4.5	0.0605	-

[a] P-value: Statistical significance at alpha = 0.05

[b] % efficacy = $\frac{\text{Mean no. of lice vehicle-treated group – Mean no. lice doramectin-treated group}}{\text{Mean no. of lice vehicle-treated group}} \times 100$

4) Adverse Events: No treatment related health problems were observed during this study.

3. TARGET ANIMAL SAFETY

No further target animal safety data were required from the original approval as discussed in the parent NADA 141-095 FOI Summary approval dated September 16, 1997.

4. HUMAN SAFETY

No further human food safety data were required from the original approval as discussed in the parent NADA 141-095 FOI Summary approval dated September 16, 1997. There is a 45-day withdrawal period for slaughter, a withdrawal period for milk has not been established, and a withdrawal period has not been established for pre-ruminating calves.

5. 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 21 CFR Part 514 of the implementing regulations. The data demonstrate that DECTOMAX Pour-On for cattle when administered once at 500 mcg doramectin/kg body weight is safe and effective for the following persistent effect periods: *Bovicola* (*Damalinia) bovis* for 77 days and *Linognathus vituli* for 42 days after treatment.

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

In accordance with 21 CFR 514.106(b)(2)(v), this is a Category II change which did not require a reevaluation of safety or effectiveness data in the parent application. Persistence effectiveness studies were submitted to support extended antiparasitic activity against two ectoparasites.

Under Section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval qualifies for THREE years of marketing exclusivity beginning on the date of approval. The three years of marketing exclusivity applies only to the additional persistent effect indications for lice listed above.

DECTOMAX Pour-On is under the following U.S. patent number:

U.S. Patent Number	Date of Expiration
5,089,480	July 30, 2010

6. ATTACHMENTS

Facsimile Labeling is attached as indicated below:

A. 250 mL, 1 liter, 2.5 liter, and 5 liter – bottle label and box carton
B. Package insert for all container sizes