Approval Date: July 18, 1997

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 141-061

B. Sponsor

Pfizer, Inc.
235 East 42nd Street
New York, New York 10017

C. Proprietary Name

Dectomax® Injectable Solution

D. Established Name

doramectin 1% injectable solution

E. Dosage Form

DECTOMAX Injectable Solution is a sterile 1% solution containing 10 mg doramectin/mL.

F. ROUTE OF ADMINISTRATION:

DECTOMAX Injectable Solution may be administered by subcutaneous or intramuscular injection.

G. APPROVED DOSAGES:

DECTOMAX Injectable Solution may be administered by subcutaneous or intramuscular injection.

H. Dispensing Status

OTC

I. Indication

For the treatment and control of the following nematode and arthropod parasites 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 viviparous	Adults and fourth-stage larvae

Eyeworms

Thelazia spp.	Adults

Grubs

Hypoderma bovis
Hypoderma lineatum

Lice

Haematopinus eurysternus
Linognathus vituli
Solenopotes capillatus

Mange mites

Psoroptes bovis
Sarcoptes scabiei

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

J. Effect of Supplement

New claims for persistent control of gastrointestinal roundworms and lungworms in cattle.

II. EFFECTIVENESS

Data demonstrating the effectiveness of DECTOMAX Injectable Solution for previously approved indications are discussed in the parent NADA 141-061 FOI Summary (approval date July 30, 1996). Data from the following dose confirmation trials demonstrate that DECTOMAX Injectable Solution given at the recommended dosage protects cattle against infection or reinfection with *Cooperia punctata* and *Dictyocaulus viviparus* for 28 days after treatment.

A. Dose Confirmation

Study No. 1231C-60-95-198

1. Type of study: Dose confirmation of persistent efficacy against artificially-induced infections of nematodes in cattle.

2. Investigator:

   Dr. Edward G. Johnson
   Johnson Research
   Parma, Idaho

3. General design:

   a. Purpose: To evaluate the persistent efficacy of doramectin against *Dictyocaulus viviparus* and *Cooperia punctata*.

   b. Animals: Forty-two (42) Holstein calves (10 per group, with 2 larval viability monitors). Animals were approximately 3-6 months old and weighed 75 to 200 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. One thousand *Cooperia punctata* larvae and 50 *Dictyocaulus viviparus* larvae were administered daily. The larval viability monitors were administered 2,000 and 30,000 *D. viviparus* and *C. punctata*, respectively on Day 28.

   e. Dosage form: The dosage form was the approved formulation of injectable solution containing 10 mg doramectin per mL.

   f. Route of administration: Subcutaneous injection

   g. Dose: 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.

   h. Test duration: 42 to 43 days after Groups T1 and T2 were treated.

   i. 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 *Cooperia punctata* and *Dictyocaulus viviparus* larvae were administered to all groups.

4. Results –The mean worm counts for each group, number of infected animals in parentheses, and percent efficacy are given:

	D. viviparus	***C. punctata***	***C. oncophora***	***O. radiatum***
T1 Saline Control	12 (10)	349 (10)	442 (10)	276 (10)
T2 Doramectin 28 days	0 100%	18 (3) 94%	110 (8) 75%	9 (4) 97%
T3 Doramectin 21 days	0.1 (1) 99%	0 100%	6 (1) 98%	2 (1) 99%
T 4 Doramectin 14 days	0.1 (1) 99%	0 100%	0 100%	0 100%

5. Statistical methods: 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) x 100 = Percentage Efficacy

6. Conclusion: This study is adequate to establish a level of persistent efficacy for *Dictyocaulus viviparus, Cooperia punctata*, *and Oesophagostomum radiatum* for 28 days and for *Cooperia oncophora* for 21 days.

7. Adverse reactions: Nine animals, representing all treatment groups and the monitors developed and were treated for pneumonia during the study. One doramectin-treated animal exhibited salivation at 1 hour post-treatment.

Study No. 1231C-60-95-215

1. Type of study: Dose confirmation of persistent efficacy against artificially-induced infections of nematodes in cattle.

2. Investigator:

   Dr. Bert Stromberg
   St. Paul, Minnesota

3. General design:

   a. Purpose: To evaluate the persistent efficacy of doramectin against *Dictyocaulus viviparus* and *Cooperia punctata*.

   b. Animals: Forty-two (42) Simmental and Simmental-cross calves (10 per group, with 2 larval viability monitors). Animals were approximately 2-6 months old and weighed 110 to 200 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: Saline was administered to the controls.

d. Infection: Infective larvae were given to each animal daily, starting on Day 14 after treatment through Day 28. One thousand *Cooperia punctata* larvae and 50 *Dictyocaulus viviparus* larvae were administered daily. The larval viability monitors were administered 2,000 and 30,000 *D. viviparus* and *C. punctata*, respectively on Day 28.

e. Dosage form: The dosage form was the approved formulation of the injectable solution containing 10 mg doramectin per mL.

f. Route of administration: Subcutaneous injection

g. Dose: 1 mL/110 lb body weight (200 mcg ivermectin/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.

h. Test duration: 42 to 45 days after Groups T1 and T2 were treated.

i. Pertinent variables measured: Worm counts were determined at necropsy which was 42 to 45 days after Groups T1 and T2 received treatment, 14 to 17 days after the last *Cooperia punctata* and *Dictyocaulus viviparus* larvae were administered to all groups.

4. Results – The mean worm counts for each group, number of infected animals in parentheses, and percent efficacy are given:

	D. viviparus	***C. punctata***	***C. pectinata***	***Cooperia* spp.**
T1 Saline Control	12 (9)	815 (10)	85 (8)	1545 (10)
T2 Doramectin 28 days	0 100%	25 (2) 97%	5 (1) 94%	60 (7) 96%
T2 Doramectin 21 days	0 100%	20 (2) 97%	15 (1) 82%	50 (3) 96%
T 4 Doramectin 14 days	0 100%	0 100%	0 100%	10 (2) 99%

5. Statistical methods: Nematode percentage efficacies were calculated 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

6. Conclusion: This study is adequate to establish a level of persistent efficacy for *Dictyocaulus viviparus* and *Cooperia punctata* for 28 days.

7. Adverse reactions: All of the animals exhibited signs of pneumonia and were treated during the course of the study.

Study No. 5232E-03-89-027

1. Type of study: Dose confirmation of persistent efficacy against artificially-induced infections of nematodes in cattle.

2. Investigator:

   C. Hong, Bsc, PhD
   Surrey, UK

3. General design:

   a. Purpose: To evaluate the persistent efficacy of doramectin against *Dictyocaulus viviparus*.

   b. Animals: Forty (40) Fresian-cross calves (10 per group). Animals were approximately 4-6 months old and weighed 95 to 141 kg at the start of the study. The calves were reared indoors and had no existing nematode infections as confirmed by negative fecal egg counts done on Day -15.

   c. Controls: The controls were nonmedicated.

   d. Infection: Calves in Groups T1 and T2 were administered larvae daily from Day 0 to Day 28. Calves in Groups T3 and T4 were administered larvae daily from Day 7 to Day 28. One hundred *Dictyocaulus viviparus* larvae were administered daily.

   e. Dosage form: The dosage form was a prototype of the commercial formulation of the injectable solution containing 10 mg doramectin per mL.

   f. Route of administration: Subcutaneous injection

   g. Dose: 1 mL/110 lb body weight (200 mcg ivermectin/kg body weight) was given once to each animal in two groups. Group T1 was nonmedicated and Group T2 was treated doramectin, on Day 0. Group T3 was nonmedicated and Group T4 was treated with doramectin on Day 7. Group T1 was the control for Group T2 and Group T3 was the

control for Group T4.

h. Test duration: 42 to 43 days after Group T2 was treated.

i. Pertinent variables measured: Worm counts were determined at necropsy which was 42 and 43 days after Group T2 received treatment, 14 to 15 days after the last *Dictyocaulus viviparus* larvae were administered to all groups.

4. Results - The mean worm counts for each group, number of infected animals in parentheses, and percent efficacy are given:

	D. viviparus
T1 Control	382 (10)
T2 Doramectin **28 days**	0.4 (2) 99.9%
T3 Control	354 (10)
T 4 Doramectin **21 days**	0 100%

5. Statistical methods: Nematode percentage efficacies were calculated 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

6. Conclusion: This study is adequate to establish a level of persistent efficacy for *Dictyocaulus viviparus* for 28 days.

7. Adverse reactions: All of the animals were given a prophylactic treatment of Terramycin LA at 1 mL/10 kg on 2 days of the study.

III. TARGET ANIMAL SAFETY

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

IV. HUMAN FOOD SAFETY

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

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 doramectin injectable solution, when used under the proposed conditions of use, is safe and effective for controlling infections and protecting cattle from reinfection with *Cooperia punctata* and *Dictyocaulus viviparus* for 28 days after treatment.

For cattle the tolerance of residues are specified in 21 CFR 556.225. The tolerance of parent doramectin (marker residue) is 100 ppb in liver (target tissue) of cattle. The withdrawal

time is 35 days following one subcutaneous or intramuscular injection of DECTOMAX as specified in 21 CFR 522.770.

The original approval of doramectin injection was as an over-the-counter drug. 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), 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.

Under section 512(c)(2)(F)(iii) 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. The three years of marketing exclusivity applies only to the new claim for controlling infections and protecting cattle from reinfection with Cooperia punctata and Dictyocaulus viviparus for 28 days after treatment for which the supplemental application was approved.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.