National Registration Authority
For Agricultural & Veterinary Chemicals

Public Release Summary

for

DORAMECTIN

in the product

DECTOMAX
INJECTABLE ENDECTOCIDE

This document is published by the National Registration Authority for Agricultural and Veterinary Chemicals.

For further information, please contact:

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FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent Statutory Authority with responsibility for the assessment and approval of agricultural and veterinary chemical products prior to sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies including the Department of Human Services and Health (Environmental Health and Safety Unit), the Environment Protection Agency (EPA), the National Occupational Health and Safety Commission (Worksafe Australia) and State Departments of Agriculture and Health.

The NRA has a policy of encouraging openness and transparency in its activities and seeking community involvement in decision making. The publication of Public Release Summaries for products containing new active ingredients is a part of that process.

The information and technical data required by the NRA in order to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the document "Requirements for Clearance of Agricultural and Veterinary Chemical Products" which can be obtained from the NRA.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and advisory agencies. The document has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment. Further more detailed technical assessment reports on occupational health and safety, public health considerations and environmental impact are available from the NRA on request.

As a relatively new organization, the NRA would welcome comment on the usefulness of this document and suggestions for further improvement. Comments should be forwarded to The National Registration Manager, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240, Queen Victoria Terrace, Parkes, ACT, 2600.

ABBREVIATIONS AND ACRONYMS

ADI	Acceptable Daily Intake (for humans)
d	Day
EHSU	Environmental Health and Safety Unit (Department of Human Services and Health)
EUP	End Use Product
Fo	Original Parent Generation
h	Hour
HPLC	High Performance Liquid Chromatography
id	Intradermal
ip	Intraperitoneal
im	Intramuscular
iv	Intravenous
in vitro	Outside the living body and in an artificial environment
in vivo	Inside the living body of a plant or animal
kg	Kilogram
L	Litre
LC50	Concentration that kills 50% of the test population of organisms
LD50	Dosage of chemical that kills 50% of the test population of organisms.
m	Metre
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit (a legal limit)
MSDS	Material Safety Data Sheet
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration/Level
NRA	National Registration Authority for Agricultural and Veterinary Chemicals
po	Oral
ppb	parts per billion
ppm	parts per million
s	Second
sc	Subcutaneous
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGAC	Technical Grade Active Constituent
µg	microgram
WHP	Withholding Periods

1. EXECUTIVE SUMMARY

INTRODUCTION

The purpose of this document is to provide a summary of the data reviewed and an outline of regulatory considerations for the proposed clearance and registration of the chemical doramectin for use as an injectable endectocide in beef cattle. The information provided herein is a very brief version, presenting only the conclusions reached by the various expert reviewers after consideration of a large scientific database. All trial data and methods of assessment presented for evaluation were according to accepted scientific principles and of a standard publishable in reputable refereed journals.

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) has completed an assessment of the data submitted by the applicant in support of this use of doramectin and now invites public comment before proceeding to approve this product for use in Australia. The following information is provided for public comment.

EFFICACY AND SAFETY IN TARGET SPECIES.

Following a full assessment of the safety and efficacy data submitted by the applicant, the NRA concludes that doramectin can be approved for use in Australia.

Dose titration studies against individual species of nematodes and arthropod parasites of cattle established the dose of 200 µg/kg as optimal against the least susceptible species. Results of the subsequent Australian and New Zealand clinical trial program, substantiated by data collected in North America and Europe, were found to support the following conclusions and label claims:

A single subcutaneous injection of doramectin, administered to cattle at a dose of 200 µg/kg, is efficacious against the adult stage of *Ostertagia ostertagi, Haemonchus placei, Trichostrongylus axei, T. colubriformis, T. longispicularis, Cooperia oncophora, C. punctata, Bunostomum phlebotomum, Oesophagostomum radiatum, Toxocara vitulorum* and *Dictyocaulus viviparus.*

In addition, a single 200 µg/kg dose is efficacious against fourth stage larvae of *O. ostertagi, H. placei, T. axei, T. colubriformis, C. oncophora, C. punctata, O. radiatum, D. viviparous* and inhibited L4 stages of *O. ostertagia.*

The same dose level is effective in providing long acting control from reinfection by *O. ostertagi* and *H. placei* for up to 21 days, *D. viviparus* for up to 28 days and by *C. oncophora* for up to 14 days.

Against lice, a single 200 µg/kg dose is highly effective against *Linognathus vituli* and aids in the control of *Bovicola bovis.*

The safety of doramectin was demonstrated by an extensive field safety testing program in Australia at 3X the proposed dose, covering a variety of breeds, age groups, climatic and

nutritional conditions and concurrent treatments. These data were fully substantiated by the safe and uneventful use of doramectin in North America and European clinical trials.

EVALUATION OF TOXICOLOGY

Doramectin, the active ingredient of Dectomax Injectable Endectocide, caused reddening of the skin and reddening and swelling of the conjunctivae of the eyes in rabbits. No skin sensitisation has been observed. Dectomax formulation was not a skin sensitiser.

Upon repeated oral administration of rats and dogs with doramectin, the main toxic effects were generalised signs of nervous dysfunction. Some liver toxicity was observed at higher doses. The compound had no effect on fertility or reproductive function in rats, and was not toxic to genetic material (DNA). There was however an increase in death of embryos and impairment of foetal development in mice and rats. Foetal malformations such as cleft palate and deformed forepaws were increased in rabbits but only at doses associated with toxicity to the maternal animals, which is consistent with other members of this class of compound.

Conclusion: Based on an assessment of the toxicology and the potential dietary intake of residues, it was considered that there should be no adverse effects on human health from the use of Dectomax Injectable Endectocide.

The Acceptable Daily Intake (ADI) in Australia is 0.05µg/kg/day (3µg/60kg person /day).

ENVIRONMENTAL SAFETY

Environmental exposure to doramectin will principally involve the soil, as the drug will be excreted largely unchanged in cattle dung and sorbs strongly to soils. Laboratory and field studies indicate that doramectin degrades at a moderate rate in soils and also that accumulation, bioaccumulation and leaching are unlikely to occur.

The ecotoxicological profile of doramectin is typical of the avermectins, being characterised by low to moderate acute toxicity to birds, mammals, earthworms, and terrestrial and aquatic flora, and very high toxicity to aquatic organisms and non-target insects. The proposed use of doramectin is not expected to lead to significant aquatic exposure. In addition, the product label contains specific instructions to avoid release of any product into rivers or streams.

The main concern is for beneficial dung breeding invertebrates such as dung beetles. Other avermectins have been shown to disrupt populations of these organisms for up to 8 weeks after treatment. However, field studies provided by the company indicated successful colonization of dung pats from treated cattle at 28 days after treatment, and a modeling exercise revealed no significant depletion of dung beetles populations over the breeding season. Agricultural authorities in some States advise that restrictions on use of doramectin to protect dung beetle breeding fauna are not warranted as there is no evidence of a problem with currently used avermectins in the field, but concede that this has not been tested. To help resolve these conflicting views, the company is conducting further studies in this area.

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OCCUPATIONAL HEALTH AND SAFETY

Doramectin has been classified by Worksafe Australia as a hazardous substance. Australian chemical industry workers do not handle doramectin. The product is imported final-packed ready for end users.

End users may experience some skin contact with the product in routine use. It is not a skin irritant or sensitiser. Agricultural workers should not suffer any adverse health effects following short term or long term use of the product. Use of personal protective equipment is not required, but the product safety directions do instruct users to avoid skin contact.

Dectomax Injectable Endectocide for Cattle can be used safely in accordance with the control measures specified on the product label and in the MSDS.

POTENTIAL FOR CHEMICAL RESIDUES IN FOOD

Doramectin is formulated as a subcutaneous injection and is given to cattle at a dose rate of 0.2 mg/kg body weight. On average, animals are dosed two or three times per year.

Appropriate residue and metabolism studies were provided in accordance with the Requirements for Clearance of Agricultural and Veterinary Chemical Products to support the use of Doramectin in cattle. Two Australian trials were conducted at Armidale, NSW.

The residue data and use pattern indicate that a meat withholding period of 49 days is appropriate. The residue and metabolism data show that under Good Agricultural Practice the proposed MRLs should not be exceeded and consumption of meat from treated animals is unlikely to result in the ingestion of residues exceeding the established Acceptable Daily Intake (ADI).

The following consequential additions have been recommended for the MRL Standard:

TABLE 1

Compound	Food	MRL (mg/kg)
ADD:		
Doramectin		
	Cattle fat	0.02
	Cattle meat	*0.005
	Cattle, Edible offal of	0.02

NOTE: "*" indicates that the MRL has been set at or about the limit of analytical determination

and

TABLE 3

Compound	Residue
ADD:	
Doramectin	Doramectin

IMPLICATIONS FOR TRADE

The ADI, MRLs and WHP as now proposed in Australia are conservative compared with those adopted elsewhere. The MRL has been set at the level of quantitation. Because of this, the maximum potential residue levels in animal products from Australia are very low. If used according to label directions and under good agricultural practices, violative residues in commodities traded overseas are unlikely to occur.

Dectomax has been discussed with Producer and Exporter Industry groups. Consistent with registrations for other macrocyclic lactones, an ESI has not been proposed at this time.

7. OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Doramectin has been classified for health effects by Worksafe Australia, according to the NOHSC Approved Criteria for Classifying Hazardous Substances, as a hazardous substance.

Australian chemical industry workers do not handle doramectin. The product is imported final-packed ready for users.

Transport workers, storepersons and retailers will handle the product. They may come into contact with the product if the packaging is breached accidentally. The product Material Safety Data Sheet (MSDS) contains sufficient information to enable these workers to cope with spills.

Agricultural workers should not suffer any adverse health effects following short term or long term use of the product.

End users may experience some skin contact with the product routine use. It is not a skin irritant or sensitiser. Use of personal protective equipment is not required, but the product safety directions do instruct users to avoid skin contact.

End users can also minimize the possibility of skin contact by maintaining injection equipment.

Self injection by end users is possible, but exposure to significant amounts of doramectin is unlikely to occur by this route.

Workers are unlikely to inhale any vapours from the product.

There are no occupational health and safety concerns for workers re-handling treated animals.

Dectomax Injectable Endectocide for Cattle can be used safely in accordance with the control measures specified on the product label and in the MSDS.

8. EVALUATION FOR POTENTIAL CHEMICAL RESIDUES IN FOOD

RESIDUE EVALUATION

This document provides evaluation of the data provided by the applicant to support establishment of the MRLs for doramectin in meat and offal of cattle.

The application proposes use of a 1% doramectin preparation as an injectable antiparasitic for treatment of endoparasites and ectoparasites in/on cattle at an application rate of 1 mL/50 kg bw (200 µg ai/kg) by subcutaneous injection.

The compound has also been known as UK, 67-994. Its CAS Registry Number is 117704-25-3 and chemical name, CAS: 25-cyclohexyl-5-O-demethyl-25-de(1-methylpropyl)avermectin A1a.

Metabolic studies

Reference: Study No 1535N 60 89-010; Experiments done in 1989, Report 1992/USA

12 Cattle, 186-222 kg body weight (bw), were given a single subcutaneous injection of tritium-labelled Doramectin at 200 µg/kg in commercial formulation. Plasma and excreta were collected for 14 days. Animals were slaughtered at 21, 28 or 35 days, collecting injection site and bile. Analysis was by scintillation counting and unchanged drug by HPLC.

Plasma levels reached a maximum of 0.084 mg/L at days 1-3 and declined to 0.015-0.020 mg/L by day 14 (calculated from tritium values). Actual Doramectin levels were slightly lower. By day 14 an average of 87% of dose was recovered from faeces.

The dose was rapidly absorbed - less than 1% remained at injection sites at days 21 and 28, except for one animal which was 1.05 mg/kg. At day 35, injection sites (4 animals) were less than 0.02 mg/kg.

Reference: Study No: CM-92-01; "The Comparative Metabolism of T-Doramectin in cattle, dog and rat." Report 1992/USA.

Metabolism in cattle, dogs and rats appears similar. Residues consist mostly of unchanged Doramectin with a des-methyl derivative being the only significant metabolite.

Analytical methodology

Reference: Report AHDM-92-01 "An HPLC Assay for the Detection of Doramectin in Cattle Liver and Fat". Method is also applicable to other tissues.

The detection and quantitation of doramectin at the ng/g level is based on its extraction from tissue homogenates and subsequent conversion to a chemically stable aromatic fluorescent derivative. The conversion of doramectin can be carried out in the presence of a fixed quantity of internal standard which is similar in structure differing only in the presence of the hydroxyl group at the C23 position and the saturation of the C22-C23 bond. A calibration curve is obtained from either the weighted least squares linear regression analysis of HPLC peak height ratios of doramectin or doramectin peak height (dependent variable) and nominal fortification levels (independent variable). The limit of determination is 1 µg/kg.

Residue definition

The major residue is unchanged parent compound.

The residue definition is: Doramectin

Residue trials

Reports 5.4-5.6 were previously submitted and reviewed, and have some relevance to assessment of the current submission.

Reference: Study Nos: 2539A-14-92-190 & 2539A-14-92-110; 1 992-93 at Armidale, NSW.

Cattle, 175-216 kg bw, were given a single subcutaneous injection of Doramectin in commercial formulation at 200 µg/kg. Tissues were collected at slaughter at 35, 42 and 49 days. Analysis was by HPLC with a limit of determination of 0.001 mg/kg. Maximum residues of Doramectin (mg/kg) were as shown in the following table.

W days	Liver	Kidney	Fat	Injection site	Muscle
35	0.037	0.007	0.035	NA	0.004
42	0.013	0.003	0.017	0.23	0.002
49	0.005	0.003	0.007	0.69	0.001

Injection site data was provided as a separate report. The maximum figures are actually outliers. At 42 days the other five samples were 0.002-0.088 mg/kg while at 49 days the second figure was 0.083 mg/kg and the others 0.002-0.004 mg/kg. Label instructions clearly define high in the neck as the site of injection. This area is trimmed at slaughter.

Reference: Study No: 2539A-14-92-109; 1992-93 at Armidale, NSW.

Cattle were given a subcutaneous injection of doramectin in commercial formulation at 300µg/kg (1.5x recommended). Tissues were collected at slaughter at 14 and 49 days. Analysis was by HPLC with a limit of determination of 0.001 mg/kg. Maximum residues of doramectin were in liver (0.35 mg/kg, 14 days; 0.006 mg/kg, 49 days) and fat (0.36 mg/kg, 14 days: 0.004 mg/kg, 49 days)

Reference: Study No: 1531N-60-90-049; 1991/USA

Cattle were given a single subcutaneous injection of doramectin, in dose vehicle at 200 µg/kg. Tissues were collected at slaughter at 14, 21, 28 and 35 days. Analysis was by HPLC with limit of determination of 0.0025 mg/kg. Maximum residues of doramectin (mg/kg) were:

W days	Liver	Kidney	Fat	Muscle	Injection site
14	0.11	0.025	0.32	0.016	1.5
21	0.069	0.020	0.38	0.015	3.1
28	0.045	0.014	0.14	0.007	0.82
35	0.021	0.008	0.090	0.006	2.4

Reference: Study Nos 1531E-60-87-040 & 1534E-60-87-001; 1987/USA

Female cattle, approx. 135 kg bw, were given a subcutaneous injection of 200 µg/kg of 0.25% aqueous micelle solution of doramectin. Plasma and tissues were collected at intervals to 35 days. Analysis was by HPLC with a limit of determination of 0.001 mg/kg. Maximum residues were in liver and fat but no residues were detected at 35 days.

Reference: Study Nos 1535B-60-88-005 and -006; 1988/USA

Holstein cattle, approx. 130 kg bw, were given a subcutaneous injection of 200 µg/kg of 0.25% aqueous micelle solution. Doramectin was tritium-labelled. Plasma and tissues were collected at intervals to 28 days. Analysis was by HPLC with a limit of determination of 0.001 mg/kg and also by combustion and scintillation counting. 1% of the dose was cleared in the urine and 85% in faeces in 7 days. Maximum residues of doramectin were in liver and fat with levels at 28 days, being 0.005 and 0.006 mg/kg.

Reference: Study No 1535N-60-89-009

Cattle were given a subcutaneous injection of 200 µg/kg of tritium-labelled doramectin in commercial formulation. Tissues were collected at 21, 28 and 35 days. Analysis was by HPLC with a limit of determination of 0.001 mg/kg and also by combustion and scintillation counting. At 35 days doramectin was detected only in liver (means 0.005 mg/kg) and maximum tritium levels were in liver and fat equivalent to 0.020 and 0.022 mg/kg.

Withholding period statements

Recommended label statements are:

MEAT - DO NOT USE LESS THAN 49 DAYS BEFORE SLAUGHTER FOR HUMAN CONSUMPTION

ANIMALS MUST NOT BE REPEAT TREATED WITHIN 5 WEEKS OF A PREVIOUS TREATMENT

MILK - DO NOT USE DURING LACTATION OR LESS THAN 60 DAYS BEFORE CALVING WHEN MILK OR MILK PRODUCTS ARE TO BE USED FOR HUMAN CONSUMPTION

Dietary Intake

Dietary intake calculations indicate that the theoretical maximum daily intake of doramectin from cattle meat, fat and offal does not exceed the doramectin ADI, and is thus safe for human consumption.

9. IMPLICATIONS FOR TRADE

The export commodities associated with Dectomax use are meat and offals of cattle, and cattle milk by-products

The countries principally involved in trade of these commodities with Australia are : Japan, USA, Korea, Taiwan, Canada, United Kingdom, Indonesia, Philippines, Hong Kong and Singapore.

The following tables illustrate the value and tonnage of these export commodities in each market:

EXPORTS OF BEEF
1995 Calendar Year

	$A '000	Tonnes
Japan	1558387	335806
USA	515173	226195
Korea, Republic	172614	66200
Taiwan	111104	31516
Canada	80977	33727
United Kingdom	44000	6871
Indonesia	31251	10916
Philippines	31174	16082
Hong Kong	22177	5564
Singapore	20192	5986
TOTAL TOP 10	2587049	738863
TOTAL REST	127470	54905
ALL COUNTRIES	2714519	793768

EXPORTS OF OFFAL
1995 Calendar year

	$ '000	Tonnes
Japan	64079	14526
Malaysia	8260	5691
Korea	7949	2581
Indonesia	6917	4630
USA	6708	3641
Hong Kong	6595	3650
South Africa	6501	5459
U.K.	6009	2597
Russian Federation	5561	4602
France	4747	1244
TOTAL TOP 10	123326	48621
TOTAL REST	19539	11734
TOTAL COUNTRIES	142865	60355

EXPORTS OF MILK & MILK PRODUCTS 1995 Calendar Year		
	$A '000	**Tonnes**
Philippines	205718	93560
Jordan	170379	55507
Malaysia	151187	61243
Japan	110641	48475
Thailand	104734	39789
Singapore	97444	54731
Taiwan	73635	30532
Seychelles	68764	19144
Hong Kong	45368	34446
Indonesia	37047	19300
TOTAL TOP 10	1064917	456727
TOTAL REST	419346	158875
ALL COUNTRIES	1484263	615602

Source: Australian Bureau of Statistics, Feb 1996.

Overseas Registrations and Use Patterns.

Worm burdens are dependent on stocking rates, weather conducive to survival of worm larvae on pasture and the nutritional status of cattle. Thus the time of use of this product will vary across Australia, but will principally be associated with winter infestations from autumn pickups and spring infestations associated with rising temperatures and increased rainfall. The frequency of treatment is expected to be higher in younger animals, with a dose at weaning and probably another 8 weeks later. As the animal's resistance against worms develops, retreatment intervals should lengthen considerably.

The dose rate is the same in all 34 countries where the product is registered. The dose is 1 mL per 50 kg bodyweight given by injection under the skin high on the neck. In a few countries, the intramuscular route is also approved.

The withholding period in Australia is 49 days where a minimum retreatment interval of 5 weeks has been established. In a number of European countries, the frequency of use is higher because of higher stocking rates and the need for sheltering during winter. However, most European countries, including the UK, have a registered withholding period of 42 days, without the requirement for a minimum retreatment interval.

Codex MRLs

Of most significance is the comparison between MRLs proposed in Australia and those proposed by the International Joint Expert Committee on Food Additives (JECFA). Internationally accepted MRLs, as recommended by JECFA and adopted by the Codex Alimentarius (CODEX) have increased in importance under the terms of the General Agreement on Tariffs and Trade (GATT). For doramectin, JECFA has recommended MRLs of .1 ppm in liver, .03 ppm in kidney, .01 ppm in muscle and .15 ppm in fat, considerably

above those proposed in Australia (meat at .005ppm, fat at .02 ppm and edible offal at .02ppm.) The JECFA MRLs will be published by mid-1996 .

Australian MRLs And Permitted Residue Levels In Importing Countries.

Australian MRLs are meat at .005ppm, fat at .02 ppm and edible offal at .02 ppm. The Acceptable Daily Intake (ADI) in Australia is .05µg/kg/day (3µg/60kg person /day).

A number of countries importing Australian beef, principally Japan, Canada, Taiwan and Korea, do not have established MRLs for doramectin. Japan already has an established MRL for doramectin in swine at .03ppm for all tissues. The same level is likely to apply to future cattle approvals. Approval is pending in Taiwan and Korea. Taiwan will not establish a formal MRL. Korea will establish an MRL, and it is likely to be consistent with that established by JECFA.

The USA has approved a target tissue (liver) tolerance level of .1 ppm and a withholding period of 35 days, based on an ADI of 45µg/60kg/day.

Registration is pending in Canada. Canada receives beef from the US under the North American Free Trade Agreement and therefore accepts US tolerance levels in traded produce.

The MRLs in European countries are .015 ppm for liver (the target tissue) and .025ppm for fat, based on an ADI of 12µg/60kg/day.

New Zealand has MRLs set for liver at .01 ppm, muscle at .015 ppm and fat at .02 ppm, with Dectomax licensed there since July 1994.

An MRL has not been set for milk but studies in dairy cattle have shown that when used according to label directions, no detectable levels of doramectin will be present.

Limit of Quantitation

The limit of quantitation for the method currently available in Australia is .005ppm. This is the same as the level set for the Australian meat MRL. As the method is available to other countries, a similar limit of quantitation could apply. However, with all complex methods of analysis, familiarity with the method is necessary to obtain this level consistently.

Risks to Trade

Theoretical trade risks are identified for importing countries where they have not set any tolerance levels for residues in food commodities, usually because they have not yet registered the product.

The product is not registered in Japan although an application for registration is in progress. Japan has not yet set an MRL in cattle. A product containing doramectin is registered for use in swine with a tolerance level of 0.03 ppm. Under GATT however, it is expected that the World Trade Organization will rule that all MRLs must be consistent with safe public health standards. Where applicable, MRLs adopted by the World Health Organization through CODEX will be used as a basis for such rulings. The Joint Expert Committee on Food Additives is in the process of recommending tolerance levels for doramectin of 0.01 ppm for

muscle, 0.03 ppm for kidney, 0.1 ppm for liver and 0.15 ppm for fat, meaning that Australian tolerance levels should be acceptable to all importing countries. Japan has been taking carcasses and offals from beef exporting countries, including Australia, where macrocyclic lactones (avermectins) have been registered for many years with no reported residue crises associated with lack of an MRL.

Although the product is not registered in the US, an application for registration is in progress and the food safety section of the application has been approved. A tolerance level of 0.1 ppm has been approved for liver as the indicator target tissue. Also, a 35 day slaughter withholding period has been approved on the same use pattern as in Australia, indicating tolerance of higher residue levels than would result from the Australian use.

In the EU, the product is registered in most member States including the UK. Here, tolerance levels of 0.015 ppm for liver and 0.025 ppm for fat have been set for these indicator target tissues. Also, member states have individually set a withholding period between 42-50 days (see table following) on the same or a more frequent use pattern than in Australia, indicating tolerance of residue levels consistent with or higher than would result from the proposed Australian use.

Withholding Period	**European Country**
35 days	Algeria, Turkey
42 days	United Kingdom, Ireland , France, Greece, Italy, Portugal, Spain, Austria, Switzerland, Norway,
49 days	Sweden
50 days	Germany
75 days	Netherlands (under appeal)

In other countries to which Australia exports cattle meat and/or offal, either there is no legislation regarding MRLs for food residues or the countries seem willing to accept the CODEX tolerance levels (MRLs) or the US safe limits (MRLs), both of which mean Australian commodity produce would be acceptable. These countries have been taking carcasses and offals from beef exporting countries where macrocyclic lactones (avermectins) have been registered for many years with no reported residue crises associated with lack of an MRL.

Conclusion

The ADI, MRLs and WHP as now proposed in Australia are conservative compared with those adopted elsewhere. The MRL for meat has been set at the level of quantitation. Because of this, the maximum potential residue levels in animal products from Australia are very low. If used according to label directions and under good agricultural practices, violative residues in commodities traded overseas are unlikely to occur.

Dectomax has been discussed with Producer and Exporter Industry groups. Consistent with registrations for other macrocyclic lactones, an ESI has not been proposed at this time.

IMMEDIATE CONTAINER (Bottle) **25/1/96**
LAB0015

CAUTION

USE STRICTLY AS DIRECTED
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING
FOR ANIMAL TREATMENT ONLY

DECTOMAX*

Injectable endectocide

Active Constituent: DORAMECTIN 10 mg/mL

For the treatment and control of doramectin sensitive internal and external parasites of cattle.

50mL/200mL/500 mL

Pfizer Animal Health

*Trademark

IMMEDIATE CONTAINER (Bottle)
Left Panel
LAB0015

READ OUTER CONTAINER ZIP SEAL LABEL BEFORE USING THIS PRODUCT

DIRECTIONS FOR USE
Do not use during lactation or less than 60 days before calving when milk or milk products are to be used for human consumption.
Animals must not be repeat-treated within 5 weeks of a previous treatment

DOSE: 1mL per 50 kg bodyweight by subcutaneous injection (under the skin).

NOT TO BE USED FOR ANY PURPOSE OR IN ANY MANNER CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.

Worm parasites may develop resistance to any anthelmintic. If this is suspected please contact your local veterinary practitioner or advise the manufacturer.

WITHHOLDING PERIODS:
MEAT- DO NOT USE LESS THAN 49 DAYS BEFORE SLAUGHTER FOR HUMAN CONSUMPTION.
MILK- DO NOT USE DURING LACTATION OR LESS THAN 60 DAYS BEFORE CALVING WHEN MILK OR MILK PRODUCTS ARE TO BE USED FOR HUMAN CONSUMPTION.

SAFETY DIRECTIONS: Product is poisonous if swallowed. Avoid contact with eyes, skin and clothing.

FIRST AID: If poisoning occurs contact a doctor or Poisons Information Center. If swallowed and if more than 15 minutes from a hospital induce vomiting, preferably using Ipecac Syrup APF. If skin contact occurs remove contaminated clothing and wash skin thoroughly.

DISPOSAL: Empty containers should be disposed of by burying at a depth of 500mm at a licensed/approved disposal site or in waste ground away from water courses.

NRA:46128/01
STORAGE: Store below 30°C (Room Temperature).

Batch No. Exp. date

PM ____

Pfizer Animal Health
A division of Pfizer Pty. Limited
Wharf Road
West Ryde NSW 2114

*Trademark

Zip Seal Label (Plastic container)
(Top Panel) Left Section
LAB0015

CAUTION

USE STRICTLY AS DIRECTED
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING
FOR ANIMAL TREATMENT ONLY

DECTOMAX*

Injectable endectocide

Active Constituent: DORAMECTIN 10 mg/mL

For the treatment and control of internal and external parasites of cattle

50mL/200mL/500 mL

Pfizer Animal Health

*Trademark

PM_____

Zip Seal Label (Plastic container)
(Top Panel) Central Section
LAB0015

Dectomax Injectable Endectocide is for the treatment and control of doramectin sensitive internal and external parasites of cattle, providing sustained protection against reinfection by Small Brown Stomach Worm, Small Intestinal Worm, Barber's Pole Worm and Lungworm

DIRECTIONS FOR USE

READ ZIP SEAL LABEL BOOKLET BEFORE USING THIS PRODUCT

Do not use during lactation or less than 60 days before calving when milk or milk products are to be used for human consumption.
Animals must not be repeat-treated within 5 weeks of a previous treatment

DOSE: 1 mL per 50 kg bodyweight
Administer Dectomax by subcutaneous injection (under the skin) into the neck region and preferably high up behind the ear. Use the dose rate, according to the weight of the animal, given in the tables in the booklet The dose rate should be based on the heaviest member in the weight range. Cattle should be weighed with either scales or a weighband. Check accuracy of injection equipment regularly

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WITHHOLDING PERIODS:
MEAT- DO NOT USE LESS THAN 49 DAYS BEFORE SLAUGHTER FOR HUMAN CONSUMPTION.
MILK- DO NOT USE DURING LACTATION OR LESS THAN 60 DAYS BEFORE CALVING WHEN MILK OR MILK PRODUCTS ARE TO BE USED FOR HUMAN CONSUMPTION.

SAFETY DIRECTIONS
Product is poisonous if swallowed. Avoid contact with eyes, skin and clothing.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Center. If swallowed and if more than 15 minutes from a hospital induce vomiting, preferably using Ipecac Syrup APF. If skin contact occurs remove contaminated clothing and wash skin thoroughly.

Additional information is listed in the Material Safety Data Sheet.

NRA:46128/01

STORAGE
Store below 30°C (Room temperature).

BATCH No: EXPIRY DATE:

Pfizer Animal Health
A division of Pfizer Pty. Limited
Wharf Road
West Ryde NSW 2114

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CAUTION
USE STRICTLY AS DIRECTED
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING
FOR ANIMAL TREATMENT ONLY

INTRODUCTION

Dectomax Injectable Endectocide is a broad spectrum parasiticide for cattle of all ages. Dectomax is highly effective in killing internal and external parasites that can cause disease and limit production potential.. The active constituent in Dectomax (doramectin) is a member of the macrocyclic lactone family of chemicals and was discovered and patented by Pfizer.

FEATURES

[√] Highly effective parasite control.
[√] Sustained protection against reinfection by Small Brown Stomach Worm, Small Intestinal Worm, Barbers Pole Worm and Lungworm
[√] Non-irritant formulation.
[√] Broad spectrum of activity.
[√] Wide margin of safety in all ages of stock, including young calves.

PRODUCT DESCRIPTION

Dectomax is a colourless to pale yellow, sterile solution which is packed in ready to use coloured ultra violet light resistant glass bottles. It is formulated to deliver the recommended dosage at a rate of 1mL for every 50 kg of body weight (200 ug doramectin per kg of body weight) when administered by subcutaneous injection.

HOW DECTOMAX WORKS

The primary mode of action of the active constituent in Dectomax (doramectin) is to inhibit the electrical activity that controls nerve cells in nematodes (worms) and muscle cells in arthropods (lice) causing paralysis and death of the parasite.

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PARASITES WHICH DECTOMAX IS EFFECTIVE AGAINST

Dectomax has a broad spectrum of activity. It was highly effective in the treatment and control of the following species in Australian trials:

Adult and immature Gastro-Intestinal Roundworms

Ostertagia ostertagi (including inhibited larvae) - Small brown stomach worm
Haemonchus placei - Barber's pole worm
Trichostrongylus axei - Stomach hair worm
T. colubriformis - Black scour worm
T. longispicularis [1]
Cooperia oncophora - Small intestinal worm
C. punctata
Bunostomum phlebotomum [1] - Hook worm
Oesophagostomum radiatum - Nodule worm
Toxocara vitulorum [1] - Round worm

[1] adults only

Adult and immature Lungworm

Dictyocaulus viviparus

Sucking Lice

Linognathus vituli

Biting Lice

Effective as an aid in the control of biting louse (*Bovicola bovis*).

Sustained protection

Australian trials also demonstrated the following levels of sustained protection against reinfection from four common and important worm species.

Species	Period of protection following treatment
Ostertagia ostertagi	Up to 21 days
Cooperia oncophora	Up to 14 days
Haemonchus placei	Up to 21 days
Dictyocaulus viviparus	Up to 28 days

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SAFETY OF DECTOMAX

During extensive field trials, Dectomax was proven to have a wide margin of safety when administered to cattle of all ages, including young calves. The product has also been specially formulated to minimize the risk of injection site pain after administration.

DIRECTIONS FOR USE

Do not use during lactation or less than 60 days before calving when milk or milk products are to be used for human consumption.

Animals must not be repeat-treated within 5 weeks of a previous treatment

To avoid tissue residues, take care to estimate the weights and dosages in young animals

Administer Dectomax by subcutaneous injection (under the skin) into the neck region and preferably high up behind the ear. Use the dose rate, according to the weight of the animal, given in the tables below. The dose rate should be based on the heaviest member in the weight range (given under the heading "weight (kg)"). Cattle should be weighed with either scales or a weighband.

DOSE RATE: 1 mL per 50 kg bodyweight

Weight (kg)	Dose (mL)	Weight (kg)	Dose (mL)
40-50	1	301-350	7
51-75	1.5	351-400	8
76-100	2	401-450	9
101-150	3	451-500	10
151-200	4	501-550	11
201-250	5	551-600	12
251-300	6	601-650	13

Cattle whose weight is in excess of 650 kg should be dosed at 1mL per 50kg bodyweight

Treatment of very young animals (less than 40 kg bodyweight) is generally not warranted

Worm parasites may develop resistance to any anthelmintic. If this is suspected please contact your local veterinary practitioner or advise the manufacturer

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ADMINISTRATION

Before using Dectomax it is important that administration equipment is properly prepared so as to avoid malfunction. Use dry, sterile syringes and needles and aseptic procedures when withdrawing and administering Dectomax. To ensure no problems are experienced the following steps should be taken

1. Remove the protective cap from the Dectomax bottle and sterility the exposed rubber stopper by wiping with disinfectant.
2. Hold the bottle upright and insert the draw off needle firmly into the center of the rubber stopper then push the securing device over the bottle neck.
3. Prime the injector unit before use.

Administer Dectomax subcutaneously into the neck region and preferably high up behind the ear. As an alternative anywhere on the neck where loose skin is present away from valuable carcase muscle is suitable. Animals should be restrained to ensure that treatment can be properly administered. When the temperature of the injectable solution is below 5°C, its viscosity increases and increased effort may be required for injecting. Syringeability can be improved by gently warming the injecting equipment and the product to 15°C.

Caution - To avoid infection leading to carcase damage the following steps should be observed.

(1) Sterility all injection apparatus by boiling. Dry equipment thoroughly before use (Not disposable plastic syringes). Avoid use of strong disinfectants on apparatus. (2) Maintain cleanliness at all times. (3) Keep needles sharp, clean and dry. Replace frequently (4) Use only sterile, dry 16 -18 gauge needles which are 15 mm in length. (5) As far as possible avoid injection of animals during wet weather or under dusty conditions.

DIAGRAM OF APPLICATION SITE

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NOT TO BE USED FOR ANY PURPOSE OR IN ANY MANNER CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.

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MILK- DO NOT USE DURING LACTATION OR LESS THAN 60 DAYS BEFORE CALVING WHEN MILK OR MILK PRODUCTS ARE TO BE USED FOR HUMAN CONSUMPTION.

SAFETY DIRECTIONS
Product is poisonous if swallowed. Avoid contact with eyes, skin and clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. If swallowed and if more than 15 minutes from a hospital induce vomiting, preferably using Ipecac Syrup APF. If skin contact occurs, remove contaminated clothing and wash skin thoroughly.

Additional information is listed in the Material Safety Data Sheet

DISPOSAL: Empty containers should be disposed of by burying at a depth of 500mm at a licensed/approved disposal site or in waste ground away from water courses.

ENVIRONMENTAL SAFETY
If doramectin comes into contact with soil, it readily and tightly binds to it and becomes inactive over time. Doramectin is extremely toxic to aquatic species. Do not contaminate dams, rivers, streams or other waterways with the chemical or used container.

NRA Approval Number: 46128/01

STORAGE
Store below 30°C (Room temperature).

PACKAGING INFORMATION.
Dectomax is available in 50 mL, 200 mL and 500 mL multi-dose packs.

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TREATMENTS PER PACK

As a quick reference, treatments per pack are tabled below.

ANIMAL WEIGHT (kg)	TREATMENTS PER PACK		
	50 mL	200 mL	500 mL
50	50	200	500
100	25	100	250
150	16	66	166
200	12	50	125
250	10	40	100
300	8	33	83
350	7	28	71
400	6	25	62
450	5	22	55
500	5	20	50
550	4	18	45
600	4	16	42
650	3	15	38

(PFIZER LOGO)
***Trademark**
Pfizer Animal Health
A division of Pfizer Pty. Limited
Wharf Rd West Ryde
NSW 2114
TOLL FREE INFORMATION LINE: 008-226655

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FOR ANIMAL TREATMENT ONLY

DECTOMAX*

Injectable endectocide

Active Constituent: DORAMECTIN 10 mg/mL

For the treatment and control of internal and external parasites of cattle

50mL/200mL/500 mL

Pfizer Animal Health

*Trademark

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Dectomax Injectable Endectocide is for the treatment and control of doramectin sensitive internal and external parasites of cattle, providing sustained protection against reinfection by Small Brown Stomach Worm, Small Intestinal Worm, Barbers Pole Worm and Lungworm

DIRECTIONS FOR USE

READ ZIP SEAL LABEL BOOKLET BEFORE USING THIS PRODUCT

Do not use during lactation or less than 60 days before calving when milk or milk products are to be used for human consumption.
Animals must not be repeat-treated within 5 weeks of a previous treatment

DOSE: 1 mL per 50 kg bodyweight
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NRA:46128/01

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BATCH NO: **EXPIRY DATE:**

PM_____

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