National
Registration
Authority
For Agricultural & Veterinary Chemicals

PUBLIC RELEASE SUMMARY

of the evaluation by the NRA of the new active constituent:

EMAMECTIN

in the product:

PROCLAIM INSECTICIDE

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Foreword

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies, including the Department of Health and Family Services (Chemicals and Non-prescription Drug Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission and State departments of agriculture and environment.

The NRA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for all products containing new active ingredients and for all proposed extensions of use for existing products.

The information and technical data required by the NRA 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 NRA's publications *Ag-Manual: The Requirements Manual for Agricultural Chemicals and Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment. More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library, 22 Brisbane Ave, Barton, ACT.

The NRA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Executive Manager - Registration, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240, Kingston, ACT 2604

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	acceptable daily intake (for humans)
ai	active ingredient
d	Day
DT_{50}	Time for 50% loss, half life
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
h	Hour
HPLC	high pressure liquid chromatography or high performance liquid chromatography
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
IOBC	International Organisation for Biological Control
kg	Kilogram
Koc	Adsorption coefficients based on organic carbon content
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOEC	lowest observed effect concentration
mg	milligram
mL	Millilitre
MRL	maximum residue limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	no observable effect concentration/level
%OC	Percentage organic carbon
pka	Acid dissociation constant
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
s	Second
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
T-Value	a value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TGAC	technical grade active constituent
WHP	withholding period

SUMMARY

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is considering an application to register the product Proclaim Insecticide (Proclaim). This product contains the new active emamectin (as emamectin benzoate). This product claims to control diamondback moth (cabbage moth) on brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower).

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of emamectin. Before deciding whether to approve this product for use in Australia, the NRA invites public comment. Comments should be submitted by 3 February 2000, to the NRA at the address indicated on page 1.

The NRA and its advisers have assessed the data submitted by the applicant in support of the proposed use of emamectin and provides the following information for public comment.

Public Health Aspects

Toxicology

Emamectin, the active ingredient in Proclaim has moderate acute oral toxicity, low skin and inhalation toxicity and is a severe eye irritant, but does not cause skin irritation or sensitisation.

Proclaim has low acute oral and dermal toxicity and is a slight eye and skin irritant; it is expected that the inhalational toxicity of the product will be low and it will not cause skin sensitisation.

Short or long term administration of emamectin caused nervous system toxicity in a range of animal species. The main effects were tremors, reduced activity, reduced food consumption, weight loss and unsteadiness. Affected animals showed degeneration of the brain, spinal cord and nerves. Emamectin did not cause foetal malformations in rabbits. In rats, variations in bone development occurred, but only at doses which caused severe toxicity in the mothers. There was no evidence that emamectin caused genetic damage or cancer in animals.

Conclusion

Based on an assessment of the toxicology, it was considered that there should be no adverse effects on human health from the use of Proclaim, providing it is used according to the directions on the label.

Residues in food and trade aspects

Australian residue data for use of emamectin in brassica crops were presented. Overseas trial data were also provided for cabbages, cauliflower, broccoli and some leafy vegetables. Data for residues in brassica waste, a potential animal feed commodity were not provided and it was argued that brassica waste could be expected to constitute only a minor portion of the diet for livestock. A label restraint stating that treated crops should not be fed to livestock is included on the label. Animal commodity MRLs have been set at the Limit of Quantitation (LOQ) for analysis of emamectin in milk, meat and edible offal based upon use of another emamectin product on cotton.

Occupational health and safety aspects

NOHSC has conducted a risk assessment on Proclaim containing 44gl/kg emamectin (as emamectin benzoate) as water soluble granules, for use on brassica vegetables. Proclaim can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Emamectin is not listed in the NOHSC List of Designated Hazardous Substances. The applicant has determined emamectin and Proclaim to be hazardous according to NOHSC Approved Criteria for Classifying Hazardous Substances.

Proclaim possesses low acute oral toxicity in rats and low acute dermal toxicity in rabbits. The product is a slight skin and eye irritant in rabbits. The Therapeutic Goods Administration (TGA) has concluded that the inhalation toxicity of the product is expected to be low as the formulation does not contain respirable particles.

Proclaim is proposed for use in brassica crops to control diamondback moth (cabbage moth). It will be applied by ground application a maximum of four times per season with minimum retreatment intervals of seven days. The proposed rate of application is 250-300 g/ha in a minimum 400 L water/ha.

No worker exposure data were available for emamectin or Proclaim. The occupational health and safety risk assessment was based on estimates obtained from an exposure model.

First Aid Instructions and Safety Directions are provided on the product label to minimise exposure to the product. Mixer/loaders need to wear cotton overalls buttoned to the neck and wrist or equivalent clothing and elbow length PVC gloves when opening the container and preparing the spray. Additional information is available on the product Material Safety Data Sheet.

Environmental Aspects

Environment Australia concludes that photolysis on soil, plant surfaces and in water is likely to be the principal means of degradation of emamectin in the environment, with metabolism of residues absorbed into plants also important. Microbial degradation in soil and sediment may also assist dissipation, but at a slower rate, whereas abiotic hydrolysis is likely to be insignificant under environmental conditions. Emamectin is not volatile and is not expected to leach in soil as it is strongly adsorbed to soil particles. It is not expected to bioaccumulate. Overall, Environment Australia concludes that emamectin is moderately toxic to birds, but the toxicity varies depending on the species and means of exposure. It is moderately to highly toxic to fish, but highly to very highly toxic to aquatic invertebrates, particularly mysid shrimp. It is very highly toxic to bees and other insects through direct contact, contact with fresh residues and presumably by oral exposure, but degradation and/or adsorption of foliage residues evidently reduces the contact toxicity of foliage residues within ~1 day. Emamectin evidently has low toxicity to earthworms and microorganisms and terrestrial plants, and is not toxic at expected environmental levels to algae and aquatic plants.

While emamectin is used at a very low rate per hectare (maximum 15 g ai/ha), it is a highly toxic substance to some species. Analyses of the hazard from the proposed use of emamectin indicated only a low hazard to birds, earthworms, soil microorganisms, terrestrial and aquatic plants, algae and fish. A high hazard was indicated to bees: the danger to bees is indicated on the product label, together with a warning against spraying while bees are foraging. A hazard was also indicated to aquatic invertebrates. For this reason, the label carries appropriate statements warning of the need to avoid spray drift and aquatic contamination. While included primarily for resistance management reasons, the number of uses of the product is limited to four per annum, which also assists in ameliorating the potential environmental hazard.

Efficacy and crop safety aspects

Diamondback moth (cabbage moth) is showing resistance to a range of pesticides and the long term success of the Integrated Pest Management programs are dependent upon a range of possible control options, particularly of options that are soft on the key beneficial insects. If Proclaim does not adversely impact on beneficials then it may be an important addition to the management options. It will be useful for rotations of chemical groups.

The data presented supported the claim of control of diamondback moth on brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower). The design, analysis and conduct of the

efficacy trials were adequate. The trials presented showed clearly that all rates of Proclaim that were presented were efficacious against diamondback moth.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical emamectin (Proclaim Insecticide) as an insecticide for the control of diamondback moth (cabbage moth) in brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower).

Responses to public consultation will be considered prior to registration of the product. They will be taken into account by the NRA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

Copies of full technical evaluation reports on emamectin, covering toxicology, occupational health and safety aspects, environmental impacts and residues in food, are available from the NRA on request. They can also be viewed at the NRA library located at the NRA's offices, 22 Brisbane Ave, Barton, ACT.

Written comments should be received by the NRA by 3 February 2000. They should be addressed to:

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Applicant

Novartis Crop Protection Australasia Limited

Product Details

Emamectin will be marketed under the trade name Proclaim (containing 44gkg emamectin as emamectin benzoate) as water soluble granule formulation.

Proclaim will be formulated overseas and imported into Australia in sale packs.

Novartis Crop Protection Australasia Limited intend to market Proclaim in all States and Territories for the control of diamondback moth (cabbage moth) in brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower.)

CHEMISTRY AND MANWFACTURE

Active constituent

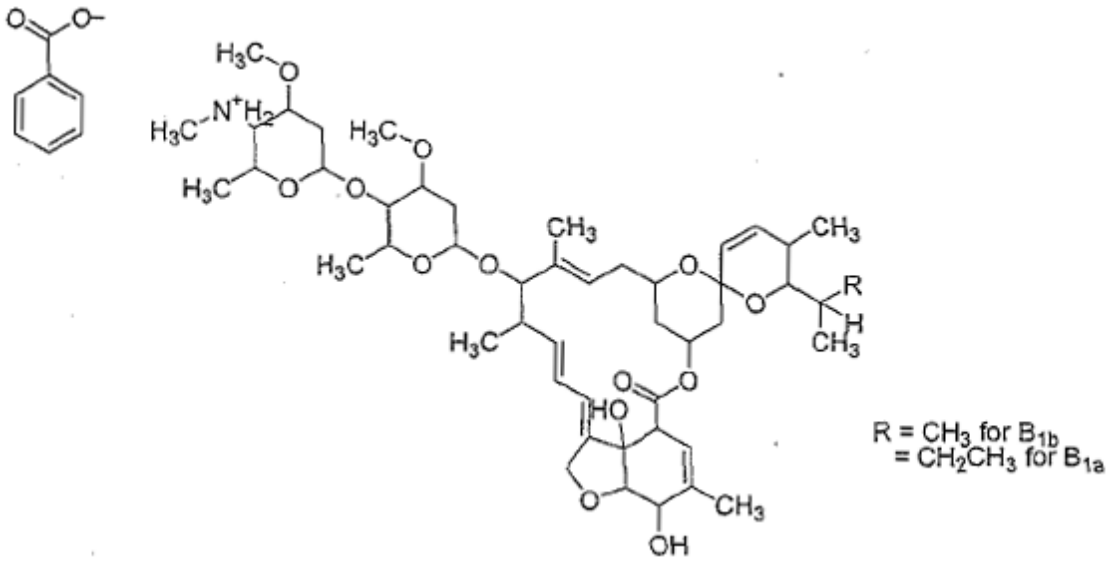
The chemical active constituent emamectin benzoate has the following properties:

Common name (ISO):	emamectin benzoate
Chemical name:	90% content (Bla): (10E,14E,16E,22Z)-(1R,4S,5S,6S,6R,8R,12S,13S20R,21R,24S)-((S)-sec-buty1)-6 dihydroxy-21,24 tetrarnethyl-5,11,13,22 oxo-2-trioxa-3,7,19 tetracyclo(l5.6.1.1$^{4.8}$.0 ^{20,24}) pentacosatetraene-10,14,16,22 spiro-6 (dihydro-5,6,2Hpyran)-2 yl-12 dideoxy-2,6 0-methyl-3 0-(tridesoxy-2,4,6 0-methyl-3 methylamino-4- L-lyxohexopyranosyl)-4-L-arabino-hexopyranoside benzoate salt 10% content (Blb): (10E,14E,16E,22Z)-(lR,4S,5S,6S,6R,8R,12S,13S,20R,21R,24S)-dihydroxy-21,24 isopropyl-6 tetramethyl-5,11,13,22 oxo-2 trioxa-3,7,19 tetracyclo(15.6.1.1$^{4.8}$.0^{20,24})pentacosatetraene- 10,14,16,22 spiro-6 (dihydro-5,6,2H-pyran)-2 yl-12 dideoxy-2,6 0-methyl-3 0-(tridesoxy-2,4,6 0-methyl-3 methylamino-4-L-lyxohexopyranosy1)-4-L-arabino-hexopyranoside benzoate salt
Product name:	Proclaim Insecticide
CAS Registry Number:	137512-74-4
Empirical formula:	B1 a: $C_{56}H_{81}NO_{15}$ B1 b: $C_{55}H_{79}NO_{15}$
Molecular weight:	B1 a: 1008.26 B1 b: 994.23
Physical form:	Solid-powder
Colour:	White to off-white
Melting point:	131-146^{o}C
Density (at 23^{o}C)	1.20g/cm3
Octanol/water partition coefficient	log P= 3.0 (pH 5.07) at 23^{o}C log P= 5.0 (pH 7.00) at 23^{o}C

(K_{ow}): log P= 5.9 (pH 9.04) at 23°C

Vapour pressure at 21.1°C 3 +or - 1x10-8 torr

Structural formula:



TOXICOLOGICAL ASSESSMENT

The toxicological database for emamectin, which consists primarily of toxicity tests conducted using animals, is quite extensive. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared to likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

Emamectin was readily absorbed when administered orally to rats (55-74%), but absorption through the skin of monkeys was minimal (<2%). In rats, dogs and monkeys, more than 90% of an orally administered dose was excreted in the faeces. Emamectin did not accumulate in the organs of rats after single or low doses; however, after multiple high doses there was some accumulation in the lung, spleen and secretory glands. A single demethylated metabolite was identified in faeces, liver, kidney, muscle and fat, indicating that emamectin undergoes limited metabolism in the body.

Acute Studies

Technical grade emamectin possessed moderate oral toxicity in mice and rats (LD_{50} 63 mg/kg in male rats), low dermal toxicity (>2000 mg/kg with no deaths in rats and rabbits) and moderate inhalational toxicity in rats (LC_{50} <2120 mg/m^3/4h, 3/5 deaths in males). The compound is a severe eye irritant but does not cause skin irritation in rabbits or skin sensitisation in guinea pigs.

Proclaim Insecticide showed low acute oral toxicity in rats (LD_{50} 1516 mg/kg) and low acute dermal toxicity in rabbits (LD_{50} >2000 mg/kg, no deaths), and was a slight skin and eye irritant in rabbits. The inhalational toxicity of the product is expected to be low, and it is not expected to cause skin sensitisation.

Short Term Studies

Mice fed emamectin in the diet for 13 weeks showed no effect at 10 mg/kg/day, but a substantial reduction in body weight gain occurred at 15 mg/kg/day.

Rats fed emamectin in the diet for 2 weeks showed body weight loss at 10 mg/kg/day and signs of neurotoxicity (tremors, decreased activity) at 20 mg/kg/day. Dietary administration for 14 weeks produced decreased body weight gain, decreased serum glucose and evidence of kidney damage (reduced blood urea nitrogen and reduced urine output), and microscopic evidence of muscle wasting and neurotoxicity (tremors, decreased co-ordination, degeneration in the brain, spinal cord and sciatic nerve) at 5 mg/kg/day and above, but there was no effect at 2.5 mg/kg/day.

Application of emamectin to the skin of rabbits at up to 1000 mg/kg/day for 21 days did not produce any outward signs of toxicity; however, there was microscopic evidence of degeneration in the sciatic nerve and spinal cord in some rabbits at 250 mg/kg/day and above.

Dogs given oral doses of up to 1.5 mg/kg/day emamectin for 2 or 14 weeks showed reduced food consumption, body weight loss, decreased activity, unsteady gait, pupil dilation, tremors and sedation, with microscopic evidence of degeneration in the brain, spinal cord and sciatic nerve, and muscle wasting at doses of 0.5 mg/kg/day and above.

Long Term Studies

Mice fed emamectin in the diet at up to 12.5 mg/kg/day for 78 weeks showed reduced body weight gain and developed tremors and minor neurological abnormalities (e.g. forelimb twitching), with microscopic evidence of sciatic nerve degeneration.

Rats fed emamectin in the diet for 53 or 105 weeks showed evidence of liver toxicity (vacuolated hepatocytes, increased serum triglyceride and bilirubin levels) at doses of 1 mg/kg/day and above. At 5 mg/kg/day, rats showed tremors, decreased fore limb grip strength, and nerve degeneration in the brain and spinal cord. The NOEL was 0.25 mg/kg/day.

Dogs administered oral doses of emamectin up to 1 mg/kg/day for 53 weeks showed tremors, stiffness of gait, pupil dilation, decreased food intake and weight loss, at doses of 0.75 mg/kg/day and above. Microscopic evidence of nerve degeneration was found in the central and peripheral nervous system of dogs receiving doses of 0.5 mg/kg/day and above. The NOEL was 0.25 mg/kg/day.

Reproduction and Developmental Studies

In a two-generation reproduction study, rats were given emamectin in the diet at doses up to 3.6 mg/kg/day. At doses of 3.6 mg/kg/day, adults of both generations had reduced body weight gain and food intake, with reduced fertility and a slight reduction in the percentage of live pups per litter. The pups from groups treated with 3.6 mg/kg/day showed body tremors, splayed hind limbs, and reduced body weight and food consumption. Most animals given 3.6 mg/kg/day showed nerve degeneration in the brain and spinal cord.

Pregnant rats given oral doses of up to 8 mg/kg/day emamectin throughout the period of foetal development had reduced body weight gain and food intake at doses of 8 mg/kg/day. At 8 mg/kg/day, a slight reduction in the foetal body weight and variations in bone development (supernumerary ribs) occurred.

Pregnant rabbits given oral doses of up to 8 mg/kg/day emamectin throughout the period of foetal development showed signs of diarrhoea, pupil dilation, decreased body weight and decreased food consumption from 6 mg/kg/day. A slight decrease in foetal body weight was noted in animals treated with 8 mg/kg/day, but there was no effect of treatment on foetuses at doses of 6 mg/kg/day emamectin.

Genotoxicity

Emamectin was negative in tests for mutagenicity in *S. typhimurium*, *E. coli* and Chinese hamster lung cells, in tests for chromosomal damage in Chinese hamster ovary cells and mouse bone marrow cells, and did not cause DNA strand breaks in rat hepatocytes.

Neurotoxicity studies

Emamectin did not produce any evidence of neurotoxicity when administered to CD-1 mice for 2 weeks at dietary doses up to 2 mg/kg/day; however, CF-1 mice administered emamectin in the diet for 16 days showed signs of neurotoxicity (tremors) at doses of 0.3 mg/kg/day and above. The CF-1 mouse strain is particularly sensitive to the neurotoxic effects of emamectin, due to a genetic deficiency of P-glycoprotein, and this result is not considered relevant to humans.

In rats, signs of acute neurotoxicity (lethargy, tremors, ataxia, ptosis) occurred at single oral doses ≥10 mg/kg emamectin; microscopic evidence of neurotoxicity (nerve degeneration in the central and peripheral nervous systems) was noted at single doses ≥25 mg/kg. Dietary administration of emamectin to rats for 14 weeks did not produce any signs of neurotoxicity at 1 mg/kg/day, but doses of 5 mg/kg/day caused reduced body weight gain, muscle wasting and neurotoxicity (mild tremors, incoordination, and degeneration in the brain, spinal cord and sciatic nerve).

There was no evidence of neurotoxicity at single dermal doses of 500, l000 or 2000 mg/kg in rabbits.

Dogs administered daily oral doses of emamectin for 5 weeks showed decreased food consumption, body weight loss, unsteady gait, dilation of the pupil, salivation and tremors leading to inactivity and sedation at doses ≥1.5 mg/kg/day, with histological evidence of degeneration in the brain, spinal cord and sciatic nerve at 1.5 mg/kg/day.

In a developmental neurotoxicity study, administration of up to 3.6 mg/kg/day emamectin to pregnant rats caused increased maternal weight gain but did not affect reproductive performance. Decreased pup body weight, delayed development and physical signs of neurotoxicity (tremors, splayed hindlimbs) were seen in the offspring at 2.5 mg/kg/day. There were no adverse effects on offspring at 0.6 mg/kg/day.

Studies on photodegradates

Acute toxicity studies on emamectin photodegradates revealed only one compound that produced neurotoxicity in the sensitive CF-1 mouse. However, in field trials, the compound was not detectable and it is expected that the levels in residues will be negligible. Emamectin photodegradation products have also been tested in bacterial mutagenicity assays and showed no mutagenic potential in this system.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

The NDPSC recommended that emamectin be listed in Schedule 7 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). Products containing 5 per cent or less, but more than 2 per cent, of emamectin are included in Schedule 6 of the SUSDP. Products containing 2 per cent or less of emamectin are included in Schedule 5 of the SUSDP.

There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The NOEL, based on a 53-week dog study and a 105-week rat study, is 0.25 mg/kg/day. In order to calculate the acceptable daily intake (ADI) for humans, a safety factor is applied to the NOEL. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animals data to humans, variation within the human population, the quality of experimental data, and the nature of potential hazards. Using a safety factor of 100, an ADI of 0.002 mg/kg/day was chosen for emamectin.

RESIDUES ASSESSMENT

Residues in Food Commodities

Australian residue data were provided for use of emamectin in brassica vegetable crops. Overseas trial data were also provided for cabbages, cauliflower, broccoli and some leafy vegetables. Residues in brassica waste, a potential animal feed commodity were not presented as it was argued that brassica waste could be expected to constitute only a minor portion of the diet for livestock. Animal commodity MRLs have been set at the Limit of Quantitation (LOQ) for analysis of emamectin in milk, meat and edible offal. These MRLs were recommended for use of another emamectin product in cotton and it is considered that residues in animal tissues and milk should not be exceeded when used on brassica crops and observance of the following label restraint:

Do Not Use Treated Produce For Stockfood

Brassica crops

Australian trials in brassica crops were based on a minimum of 6 repeat treatments at 15 g a.i./ha. Residues in brassica crops treated 6-8 times at 15 g a.i./ha ranged from <1.52 to <14.2 µg/kg at a sampling interval of 3 days. The proposed label use-pattern permits a maximum of 4 sprays at 15 g a.i./ha at a minimum retreatment interval of 7 days. Australian residue trials therefore addressed an overall rate ~1.5x - 2x the proposed maximum label rate. A withholding period of 3 days has been recommended. An MRL of 0.02 mg/kg is recommended for brassica crops (cabbage, cauliflower, broccoli and Brussels sprouts) in accordance with the proposed use-pattern in Australia. A Supervised Trials Median Residue (STMR) of 0.006 mg/kg is estimated for brassicas (cabbage, cauliflower, broccoli and Brussels sprouts).

Overseas trial data for use of emamectin on brassica crops generally showed a rapid decline and nil detectable residues by 7 days after the sixth (final) application for rates of 16.8 g a.i./ha, equivalent to 1.04x the proposed maximum Australian label rate.

Animal commodities

Residues in animal commodities are not expected on the basis of feeding treated crops containing low residues of emamectin. Emamectin was rapidly eliminated in rat metabolism studies and it can be argued that the same elimination characteristics would be found in livestock and poultry. In the absence of animal transfer data in livestock, animal MRLs may be set 'at or about' the Limit of Quantitation (LOQ) in animal tissues and milk. Analytical methodology for emamectin in animal tissues allows animal MRLs to be set at the validated LOQs of 0.002 mg/kg for liver, kidney, muscle and fat, and 0.0005 mg/kg for milk.

Metabolism Studies

Plant Metabolism:

Plant metabolism studies in lettuce, cabbage and sweetcorn were provided. Each of these studies indicate that breakdown of the active occurs primarily through photodegradation at the outset and not metabolism, leading to very similar photodegradate/metabolite profiles in different crops. Residues were extracted from all three crops using the same procedure and it was found that approximately 80% of the total residue was extractable from the foliage of all three crops irrespective of the sampling interval. Translocation of residues to the inner leaves of the lettuce and cabbage, and the kernels and cob of corn was limited, little or none of the parent being observed in these plant parts.

Characterisation of the major degradates of the parent compound revealed that the same two degradates, the parent compound (which had been formylated at nitrogen, MFBlA) and the 8,9-Z

isomer of the parent (8,9-ZMA), were present in each crop. Neither of these degradates constituted more than 3% of the total radioactive residue (TRR). Other degradates which showed structural similarity to the parent, but were present at much lower levels were also characterised in each of the three crops. Virtually all of these degradates are either known to, or are expected to form from photolysis of the parent. Many discrete, but unidentified components were present in the residue, none of which exceeded 2% of the total residue in foliage. The largest contribution to the overall residue was a complex, polar fraction which constituted from 20% up to 85% of the total foliar residue in each crop depending on the sampling interval after treatment and rate. This polar fraction is complex and made up partly of sugars. It is proposed that this polar fraction results from further extensive metabolic degradation of the photodegradates already characterised.

After initial degradation due to photolysis, the remaining residue is rapidly metabolised in foliage and edible portions, to natural products (this was shown by extensive enzymatic treatment and extraction).

Rat Metabolism:

Rat studies were conducted to elucidate the pathways of absorption, distribution, metabolism and excretion of the active after both oral and intravenous administration. The applied dose was principally eliminated in faeces (>94% of the administered dose), the percentage eliminated in urine and found in tissues was considered to be negligible compared to the amount in faeces. No volatile radioactivity was detected in exhaled air. Deposition in tissues was limited, only low levels of radiation being found in all tissues examined (kidney, liver, fat, muscle, spinal cord, brain and secretory glands). Spleen, lung and the secretory glands were found to have the highest residues of all tissues examined. No difference was noted in the residue distribution pattern between orally and intravenously administered rats. There was no indication of bioaccumulative behaviour.

Characterisation of metabolites revealed the presence of only one compound different to the Parent, B 1a, a compound derived from demethylation at the nitrogen of the parent compound. This metabolite was found in faeces, liver, kidney, muscle and fat. Polar material, similar in nature to that observed in the plant metabolism studies, was noted in faeces, bile and urine. However, in contrast to the plant studies, it was only present as a very small proportion of the administered dose.

Animal Transfer Studies

No animal transfer studies were presented. Generation of animal transfer studies has been recommended to the applicant for inclusion in future applications for registration of this active in crops.

Dietary Intake Assessment

A dietary intake assessment was conducted using mean consumption figures provided by ANZFA (1995 National Nutrition Survey of Australia). The National Estimate of Dietary Intake (NEDI) of emamectin, for the general population aged 2 years and above was equivalent to 0.36% of the ADI. The STMR values for brassica vegetables and cotton seed and MRLs for meat, milk and edible offal were used in the estimate.

MRL Standard

The following amendments to the *MRL Standard* are recommended:

Table 1

Compound	Food	MRL (mg/kg)
DELETE:		
Emamectin VB 0040	Brassica (cole or cabbage) vegetables, head cabbages, flowerhead brassicas	T0.005
ADD:		
Emamectin VB 0040	Brassica (cole or cabbage) vegetables, head cabbages, flowerhead brassicas	0.02

Table 3

Compound	Residue
ADD:	
Emamectin VB 0040	Sum of emamectin B_{1a} emamectin B_{1b}

1. The following Withholding Period (WHP) in relation to the above MRLs are recommended:

Brassica Vegetables: DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION

2. In the absence of MRLs for animal feed commodities the following grazing/animal-feeding restraint is recommended:

DO NOT USE TREATED PRODUCE FOR STOCK FOOD.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Trade Implications

Commodities exported

Export statistics for brassica crops from the 1992/3 financial year were made available by the applicant. These figures are tabulated below:

Commodity	Total Australian Production (tonnes)	Total Export (tonnes)
Broccoli	32872	8440
Brussels sprouts	6013	264
Cabbage	69526	2653
Cauliflower	80203	12455

Countries Where Exported

Major export markets for Australian brassica crops are Singapore, Hong Kong, Malaysia, Japan, Taiwan and New Zealand. Of these countries, only Japan has MRLs in place for use of emamectin on head cabbage (included in 'Leafy Vegetables Group 1').

International MRLs

The following table lists the MRLs established for emamectin benzoate use in Japan.

Crop	MRL (mg/kg)
Leafy vegetables, Group 1 (includes head cabbage and Chinese cabbage)	0.1
Fruiting vegetables, Group 2 (all fruiting vegetables except bell peppers, peppers and okra)	0.5
Tea	0.1

The U.S. tolerance for emamectin in brassica crops, head and stem subgroup, head lettuce and celery has been established at 0.025 mg/kg.

Overseas Registrations and Use Patterns

Registrations of emamectin based products have been obtained in Japan and the U.S.A. Applications for registration of emamectin-based products have been submitted in South Korea and Taiwan.

The maximum use-pattern anticipated for registration in other countries is 6 applications of 250-300 g product/ha (13.5 - 16.2 g a.i./ha) applied at a retreatment interval of 7 days.

The Withholding Period associated with this maximum use-pattern is expected to be 3 to 7 days. This use-pattern is slightly higher than that proposed for Australia (up to 4 applications at 15.0 g a.i./ha applied at a minimum interval of 7 days with a 3 day Withholding Period).

CODEX Alimentarius Commission MRL

No CODEX MRLs have been established for emamectin.

Australian MRLs

The MRLs recommended for inclusion in the Australian MXL Standard are as follows:

Brassica (cole or cabbage) vegetables, head cabbages, flowerhead brassicas	0.02 mg/kg

Potential Risk to Trade

Risks to trade on the basis of emamectin residues in brassica crops are not anticipated. Residues in these crops have been shown to be consistently at a level which support an Australian MRL in brassicas of 0.02 mg/kg. The Australian MRL is lower than the two relevant MRLs established for head cabbages in Japan and brassica crops in the U.S. The maximum use pattern proposed for registration overseas involves more repeat applications at a slightly higher rate than the use-pattern proposed for Australia. The establishment of lower MRLs in countries which import brassicas from Australia would therefore not be expected. In general, emamectin residues in brassica crops were below the Limit of Quantitation at 14 days after the final application of product, however finite residues in cabbages and broccoli were observed in 2 trials out of 15 after this time.

Animal transfer data were not presented with the application. Animal MRLs have been set at the Limit of Quantitation for the analytical method in animal tissues and milk for another emamectin product. A restraint stating that treated crops should not be fed to livestock is included on the label. Emamectin residues should not present a risk to meat exports as use of the product in brassica crops is unlikely to result in detectable residues.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Emamectin is not listed in the NOHSC List of Designated Hazardous Substances. The applicant has determined emamectin to be hazardous according to NOHSC Approved Criteria for Classifying Hazardous Substances based on acute oral toxicity and eye irritation effect. The following risk phrases have been assigned by the applicant:

R 28 Very toxic if swallowed
R 20 Harmful by inhalation
R 41 Risk of serious eye damage to eyes.

Substances containing emamectin are hazardous when it is present in concentrations above

3%.

Emamectin in the form of white to off-white, odourless powder. It has moderate acute oral and inhalation toxicity in rats and low acute dermal toxicity in rats and rabbits. It is a severe eye irritant in rabbits but does not cause dermal irritation in rabbits or skin sensitisation in guinea pigs. Emamectin is not genotoxic.

Proclaim has also been determined by the applicant to be hazardous according to NOHSC Approved Criteria for Classifying Hazardous Substances. Proclaim is a water soluble granule formulation. It possesses low acute oral toxicity in rats and low acute dermal toxicity in rabbits. The product is a slight skin and eye irritant in rabbits. The Therapeutic Goods Administration (TGA) has concluded that the inhalational toxicity of the product is expected to be low as the formulation does not contain any respirable particles. The product will be packed in 550 g, 1.0 kg and 1.1 kg wide mouth, high density, polyethylene containers and plastic bags within cardboard boxes.

Formulation transport, storage and retailing

Proclaim will be formulated overseas and imported into Australia in sale packs. Transport workers, store persons, and retailers will handle the packaged product and could only become contaminated if the packaging were breached.

Advice on safe handling of the product during routine use is provided in the Material Safety Data Sheet (MSDS).

End use

Proclaim is proposed for use on brassica vegetables for the control of diamondback moth (cabbage moth). It will be applied by ground application a maximum of four times per season with minimum retreatment interval of seven days. The proposed rate of application is 250-300 gi/ha in a minimum 400 L water/ha.

The main routes of exposure to the product are inhalational and dermal. The product is a granular formulation, however workers are still likely to be exposed to some product dust formed from broken granules. Workers may also be exposed to spray mist. Functions that can lead to exposure to the product include opening containers, mixing/loading, application, cleaning up spills, cleaning/maintaining equipment and re-entry into sprayed areas.

No worker exposure data were available for emamectin or Proclaim. The UK POEM was used by NOHSC to provide supplementary information on exposure during mixing/loading and application of Proclaim. The results indicated that workers involved in mixing/loading can be adequately protected with cotton overalls and gloves. The risk assessment indicated that cotton overalls buttoned to the neck and wrist or equivalent clothing and elbow-length PVC gloves are required when opening the container and preparing spray.

Entry into treated areas or handling treated crops

Workers re-entering treated crops may come into contact with product residues. Residue studies showed that the levels of dislodgeable residues on celery leaves following 2 applications of emamectin rapidly dissipated to non-quantifiable values 7 days after application. Based on the available information, the re-entry period of 8 hours proposed by the applicant is considered acceptable.

Recommendations for safe use

Workers involved in transport, storage, and retailing should be protected by safe work practices and training. End users should follow the First Aid instructions and Safety Directions on the product labels. Safety Directions include the use of cotton overalls buttoned to the neck and wrist and elbow-length PVC gloves when opening the container and preparing the spray.

The personal protective equipment recommended should meet the relevant Standards Australia standards specified below:

AS 2161-1978 Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)

AS 3765-1990 Clothing for protection against hazardous chemicals

Re-entry statement

'Do not allow entry into treated areas for 8 hours or until the spray has dried. When prior entry is necessary, wear chemical resistant gloves'.

Material Safety Data Sheets

Manufacturers and importers should produce a MSDS for hazardous products containing emamectin. These should contain information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that their employees have ready access to it.

Conclusions

Proclaim can be used safely if handled in accordance with the instructions on the product label. Additional information is available on the MSDS.

Environmental Assessment

Introduction

Novartis Crop Protection Australasia Pty Ltd has applied for clearance of a new end-use product, Proclaim Insecticide, containing the new technical grade active constituent (TGAC) emamectin as the benzoate salt, sufficient to give 44 g ai/kg. It is to be used to control diamondback moth on brassica vegetables. Emamectin is a semi-synthetic member of the avermectin class of macrocyclic lactone compounds. The environmental fate and toxicity studies related specifically to the benzoate salt, but for simplicity the substance is referred to as emamectin in this summary.

Environmental Fate

Hydrolysis

A study of the hydrolysis of emamectin at 25^{o}C conducted to meet USEPA Guidelines indicated that it is stable to hydrolysis at pH 5.2, 6.2, 7.2 and 8. At pH 9 the half-life of emamectin was 19.5 weeks and two unidentified hydrolysis products were observed. Hence emamectin is unlikely to hydrolysis at significant rates in the environment, though slight hydrolysis may occur at pH 9.

Photolysis

In an aqueous photolysis study conducted to meet USEPA Guidelines, photolysis of emamectin occurred relatively slowly (half lives of 32-65 days in buffered solution at pH 7 and 25^{o}C) when substances capable of stimulating phototransformation were absent. In the presence of ethanol (a radical hydrogen donor) or acetone (a photosensitiser) degradation was much more rapid (half-lives of 6.2-8.5 days and 13.3-22.5 h, respectively). This study used continuous irradiation from a lamp simulating natural sunlight wavelengths.

Another aqueous photolysis study conducted to meet USEPA Guidelines used natural sunlight in autumn at latitude 40°N. This study indicated photolysis half-lives of 22.4 days in pH 7 buffer, 6.9 days in natural pond water, and 1.4 days in pH 7 buffer with acetone added as a photosensitiser. Thus photolysis occurred relatively rapidly in natural waters or water containing a known photosensitiser, but was again relatively slow in purer water.

A soil photolysis study conducted to meet USEPA Guidelines showed that cyclic illumination with a lamp simulating natural sunlight wavelengths reduced the degradation half-life of emamectin on a thin layer of soil to 5.2 days, compared with 8.0 days in the dark. There was a range of metabolites produced in these studies. Some of the metabolites identified may be photoproducts not found in metabolism studies conducted in the dark, but the hypothesised metabolic pathway appears to be similar after degradation of these products. Photolysis in water under Australian conditions could be a significant route of degradation, but may be reduced to some extent where the water is turbid. Photolysis on soil and on other surfaces may also be a significant means of initial degradation.

Soil and Water Metabolism Studies

A 12 month aerobic soil metabolism study to USEPA Guidelines using a single soil indicated that the overall half-life of emamectin incubated in the dark was 193 days. However, degradation appeared to be biphasic, with a half-life of 74 days over the first 62 days, followed by much slower degradation (half-life 349 days).

A similar study investigated degradation when anaerobic conditions were introduced for 60 days after 30 days initial incubation under aerobic conditions. The degradation rate slowed markedly once anaerobic conditions were introduced. The overall half-life for 0-90 days was 174 days, but most of the degradation of emamectin occurred over days 0-30 and the half-life during the anaerobic period was 427 days.

Analysis of metabolites identified several substances with minor changes from the original molecule. Further degradation of these metabolites evidently occurs to form more polar substances, as the largest overall component in soil extracts was a complex mixture of polar substances. Exploration of unextracted residues suggested that these too were relatively polar substances. Some evolution of CO_2 occurred over the study period, indicating that the emamectin molecule ultimately mineralises (cumulative evolution 16.5% of applied in the 12 month aerobic study and 3% of applied in the 90 day aerobic/anaerobic study).

No aerobic aquatic metabolism studies are available as yet for emamectin, but from studies available with the similar substance abamectin, Environment Australia expects that emamectin would partition largely to sediment and gradually degrade.

Mobility studies

Chemical and physical data indicate that emamectin is very slightly volatile and unlikely to evaporate significantly from soil or water.

Batch equilibrium studies to USEPA Guidelines of the adsorption and desorption of emamectin on four soils indicate that emamectin is immobile in soil. K_{oc} values ranging from 25,363 to 728,918 for adsorption and 23,570 to 559,986 for desorption. However, adsorption of emamectin to soil did not appear to be correlated with soil characteristics such as organic carbon content (OC% range 0.03-2.62%), clay content (0-40%) or cation exchange capacity (0.4-31.7 mequiv/100 g). Hence it is more appropriate to consider the untransformed K_d values (219-2037 for adsorption and 127-4088 for desorption).

Immobility in soil was confirmed by a soil TLC (Thin Layer Chromatography) with six soils, with the Rf value (movement relative to the solvent, water) for emamectin being 0 in each case. A column leaching study with aged soil again indicated that emamectin was immobile, but indicated that some leaching of residues occurred, presumably as relatively polar metabolites moved down the column and into leachate.

Even with very slow degradation under anaerobic conditions, emamectin would not be expected to leach into groundwater, and little desorption of emamectin would be expected from residues adsorbed to soil particles. This was confirmed by estimations of the Gustafson Ubiquity Score (GUS ≈ 0, even with the long half-life indicated under anaerobic conditions).

Field dissipation

In field dissipation studies at each of three sites in the USA, emamectin was applied on a total of 6 occasions at weekly intervals to bare soil (total dose ~101 g ai/ha, compared to ≤60 g ai/ha according to the proposed Australian labels). At each application, initial degradation was very rapid (half-lives 4.1-10.2 h over all sites at applications 1, 3 and 6). A small amount of carryover from earlier applications was evident by the sixth application. Following the sixth application, the degradation rate decreased progressively, such that 87.5% degradation estimated at each site did not occur until 14.0-46.2 days or 11.2-49.9 days, according to the degradation model used.

The data suggest that emamectin may accumulate to some extent with repeated weekly application, but residues subsequently dissipate. Peak mean measured concentrations at each site were 5.4-10.8 ng/g in the surface 15 cm, occurring immediately following the sixth application (the localised concentration at the soil surface is likely to have been much higher). Concentrations of emamectin in the soil were generally undetectable (<0.2 ng/g) by ~180 days after the last application. There was no quantifiable detection below the surface 15 cm of soil, consistent with laboratory mobility studies.

Photolysis of residues on the soil surface is likely to have been important in the degradation of emamectin in these studies, as the applications were to bare soil and no cultivation occurred until after the final application.

Dissipation of emamectin applied to plants

Studies of the metabolism of emamectin applied to plants indicate that the substance is likely to degrade prior to harvest, with rapid degradation of much of the applied substance within 3 days of application. Because of the nature of metabolites found, photolytic activity is clearly implicated in that degradation. Analyses indicate that absorbed emamectin is degraded further in the plant and metabolised into sugars and polymeric substances. Provided rain does not immediately follow application, emamectin applied to plant surfaces is likely to degrade on or within plant tissue and should not reach soil.

Pond drift and runoff simulation studies with abamectin

No aquatic field dissipation study is available with emamectin, but a sequence of pond drift and runoff simulation studies is available for the similar substance abamectin.

In a drift simulation investigation, residues in water decreased to <10% of the hypothetical maximum concentration in ~1-2 days, presumably due to partitioning to the sediment and degradation by photolysis and microbial action. Sediment concentrations also decreased over time, with indicated half-lives of the order of 2-4 weeks. Environment Australia suggests that if a similar study were conducted with emamectin, greater partitioning of emamectin to the sediment may be expected, reducing peak water concentrations.

In a simulation of runoff occurring immediately after application of abamectin, some desorption of abamectin occurred in the days following the simulated runoff event, with water concentrations peaking at 2-15 days after application. Environment Australia suggests that if a similar study were conducted with emamectin, less desorption of emamectin from the soil particles in simulated runoff may be expected.

In a simulation of runoff occurring 90 h after application, significant dissipation of the applied abamectin occurred prior to the runoff event, preventing significant contamination of the pond. Environment Australia suggests that a similar outcome may be expected with emamectin.

Accumulation potential in soils

Environment Australia concludes that emamectin residues on plants are likely to dissipate to a large degree before harvest, without reaching the soil. Residues reaching soil during spraying are also likely to degrade rapidly initially (particularly while exposed to sunlight) and then more slowly, reaching low levels by the time post harvest cultivation occurs and declining gradually thereafter. The relatively low rate of application of emamectin together with its degradation behaviour mean that little or no carryover from year to year is expected of the parent substance or potentially harmful macrocyclic residues. Furthermore, Environment Australia concludes that if there were relatively intractable residues remaining in soil, they would be likely to have limited biological availability because of the strong adsorption of the substance to soil.

Bioaccumulation in aquatic organisms

A bluegill sunfish bioaccumulation study to USEPA Pesticide Guidelines indicated that the calculated bioconcentration factor (BCF) of total radioactive residues from ^{14}C-labelled emamectin with this species was 30, 116 and 80, respectively, in edible tissue, non-edible tissue and whole fish, respectively. The depuration half-life of these residues was approximately 4 days. Analyses of the residues at the end of the 28 day uptake period indicated that approximately 50% were emamectin were parent substance and 12% closely related metabolites. Thus the calculated BCF values may be somewhat reduced. These results together with the expected rapid partitioning of emamectin to sediment under practical conditions mean that it should not bioaccumulate.

Environmental effects

Avian

Toxicity tests on bobwhite quail and mallard ducks conducted to USEPA Guidelines showed that emamectin is moderately toxic to these species with acute oral exposure (LD50 = 264 and 76 mg/kg nominal concentrations, respectively) and slightly to moderately toxic with subacute dietary exposure (LC50 = 1318 and 570 ppm, respectively). In all cases there were temporary signs of toxicity and effects on feed consumption and bodyweight gain at much lower doses. Avian reproductive studies to USEPA Guidelines indicate No Observed Effect Levels (NOELs) of 125 ppm for bobwhite quail and 40 ppm for mallard ducks.

Aquatic

Acute toxicity tests conducted to USEPA Guidelines found that emamectin is highly toxic to rainbow trout, bluegill sunfish and fathead minnow (96 h LC50 = 174 µg/L and in the range 140-240 and 156-207 µg/L, respectively), and moderately toxic to sheepshead minnow (96 h LC50 = 1430 µg/L). An early life stage study with fathead minnow found a 32 d NOEC, LOEC and MATC of 12, 28 and 18 µg/L, respectively.

Acute toxicity tests conducted to USEPA Guidelines found that emamectin is very highly toxic to *Daphnia magna* and particularly mysid shrimp (48 h EC50 to daphnid = 1.0 µg/L and 96 h LC50 to mysid = 0.040 µg/L), and highly toxic to Eastern oyster (96 h shell growth inhibition = 530 µg/L, 96 h LC50 = 665 µg/L). A study of the toxicity of emamectin polar degradates found they had relatively low acute toxicity to daphnids compared to the parent substance (48 h EC50 > 728 µg/L).

Limit tests with emamectin indicated that emamectin is unlikely to harm green algae or duckweed at concentrations reached in the environment under the maximum proposed application rate (120 h EC50 >3.9µg/L and >94 µg/L, respectively).

Non-target invertebrates

In studies conducted to USEPA Guidelines, emamectin was found to have high toxicity to bees by acute contact exposure (48 h LD50 = 3.6 ng/bee) and with exposure to fresh residues on foliage (100%, 46% and 3% mortality with 3,8 or 24 h aging of foliage treated at approximately the proposed maximum rate). A study of foliage residue toxicity to a parasitic wasp on cabbages indicated little or no mortality after leaves had been aged for 2 hours following spraying. Very slight toxicity to earthworms was indicated in a study to OECD Guidelines (14 d NOEC = 1000 mg/kg soil).

No studies have been provided regarding the toxicity to soil micro-organisms, but an activated sludge respiration inhibition test with emamectin to OECD Guidelines found it was not toxic to bacteria. A study with the related substance abamectin found that nitrification appeared unaffected by concentrations of 0.04 and 0.4 mg/kg in soil.

Phytotoxicity

No adverse effects have been reported to target and non-target crops in field studies conducted in Australia and the USA.

Environmental hazard

Terrestrial hazard

The avian hazard from application of emamectin as proposed appears low, based on estimates of residues resulting in the field relative to the typical diet of bobwhite quail and mallard ducks and the available dietary toxicity data.

Direct exposure to spray is clearly likely to be hazardous to bees and other non-target insects and mites. Bees and other insects exposed to residues remaining on leaf surfaces (contact exposure only) may be harmed by fresh spray residues, but both the foliar contact bee and predatory wasp studies indicate that dried residues are likely to be safe after a sufficient period of aging. Suitable warnings regarding bee toxicity are provided on the product labels.

Even in the extreme worst case of four consecutive sprays at weekly intervals without any degradation occurring, Environment Australia estimates that peak soil concentrations would remain below 0.5 mg ai/kg soil, even if concentrated in the surface 1 cm of soil (noting the immobility of the substance). Hence use of the product as described is unlikely to present a hazard to earthworms. Information from an activated sludge respiration inhibition test with emamectin and from a nitrification study with abamectin suggest that it is unlikely that a hazard would arise to soil microorganisms from the proposed uses.

Aquatic hazard

Direct overspray

Environment Australia initially assessed the aquatic hazard from application of Proclaim by considering the expected environmental concentration of emamectin in a static, shallow (15 cm deep) pond following direct overspray at the maximum proposed single application rate of 15 g ai/ha. The estimated EEC was then compared with acute toxicity data for fish and aquatic invertebrates to determine the hazard quotient (Q = EEC/EC50 or LC50). This indicated that a clear hazard existed to daphnids and mysid shrimp, but no hazard was indicated to fish. The EEC was also compared with the Maximum Acceptable Toxicant Concentration (MATC) for available chronic exposure studies, confirming the hazard to daphnids, but indicating that even with repeated spraying, no hazard was indicated to fish. Emamectin is expected to adsorb rapidly and strongly to sediment. Hence Environment Australia considered the hazard from direct overspray further by allowing for 75% adsorption to sediment occurring within 24 h. This value has been estimated from laboratory studies and also available field data for the related substance abamectin. The Q ratios for daphnids and mysids were sufficiently high that a hazard was still clearly indicated to both species. Hence Environment Australia concludes that direct overspray of aquatic areas should be avoided. Proclaim is expected to be applied by ground based equipment, where direct overspray of waterbodies or streams is unlikely. While aerial application is unlikely, Environment Australia has recommended that it not be allowed, pending further information. The label also carries a standard warning against contamination of waterbodies with the product or used container.

Spray drift

A similar procedure was then followed for daphnids and mysids exposed to 10% spray drift in a similar pond. As this still indicated a hazard to both species even after 75% dissipation, the AgDRIFT^{TM} Tier I model was used to estimate spray drift at 10,30 and 100 m from a brassica crop where Proclaim was applied by boomspray. After allowing for 75% dissipation, neither an acute nor a chronic hazard was indicated to daphnids, even at a distance of 10 m, though a hazard or mitigable hazard was still indicated to mysids. However, Environment Australia believes that greater adsorption and/or greater water depth are likely to reduce the hazard at 10 m to a level which can be mitigated by suitable label advice regarding drift.

A similar approach using a less conservative drift model indicates a mitigable hazard at 10 m with 75% dissipation and 15 cm deep water, and no hazard at 30 m. Hence Environment Australia concludes that the hazard from spray drift from boomspray application to brassicas is acceptable. A suitable spray drift warning is provided on the product label.

Run-off

Emamectin may also enter waterways bound to particulate material carried in runoff waters, but Environment Australia expects that this hazard is low due to the likelihood that a significant proportion of applied spray will be intercepted by foliage and will not reach soil, that residues on soil will degrade to low levels within a few days of application, and that any residues remaining will be tightly held.

Hazard to benthic organisms

Environment Australia expects that because of the strength of adsorption, residues of the substance may have limited bioavailability, reducing the potential hazard to benthic organisms. However, because of the potential hazard to benthic organisms, direct or indirect contamination of waterbodies should be avoided and the number of sprays per year should be limited, with non-consecutive spraying as far as possible to allow some time for residues in sediment to degrade. Label advice for resistance management assists in this regard, and suitable spray drift and aquatic contamination warnings have also been provided.

Conclusions

Environmental fate studies indicate that photolysis is likely to be the major means of degradation of emamectin in the environment, assisted by microbial degradation and metabolism in plants. Emamectin is highly immobile in soil. Environmental toxicity data indicate that among aquatic organisms it is particularly toxic to some aquatic invertebrates. As expected from its use as an insecticide/miticide, among non-target terrestrial organisms it is most toxic to insects such as bees exposed by direct contact or contact with fresh residues. Suitable label advice has been included to mitigate the hazard to aquatic organisms and to bees.

Efficacy and Safety Assessment

Justification for use

Diamondback moth (cabbage moth) is showing resistance to a range of pesticides and the long term success of the PM programs are dependent upon a range of possible control options, particularly of options that are soft on the key beneficial insects. If Proclaim does not adversely impact on beneficials then it may be an important addition to the management options. It will be useful for rotations of chemical groups.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Proclaim is proposed to be used to control diamondback moth on brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower). This use is proposed for all States and Territories, as specified in the directions for use on the product label (see pp 25) The maximum use pattern will be up to 4 treatments per season with a minimum retreatment interval of 7 days.

It is proposed the product will be available in 550g, 1.0, and 1.1kg pack size. The application rate for the product is 250-300gi/ha.

A 3 day withholding period for brassica vegetables has been recommended. The statement "Do not use treated produce for stock food" has been included on the product label.

Evaluation of efficacy

The data presented supported the claim of control of diamondback moth on brassica vegetables (broccoli, Brussels sprouts, cabbages and cauliflower). The design, analysis and conduct of the efficacy trials were adequate. The trials presented showed clearly that all rates of Proclaim that were presented were efficacious against diamondback moth.

Resistance management

The draft label includes a resistance note (see pp 26) and in addition the critical comments include the statement that Proclaim should be used in accordance with insecticide resistance guidelines developed by AVCARE.

LABELLING REQUIREMENTS

POISON

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

PROCLAIM® INSECTICIDE

Active Constituent: 44 g/kg EMAMECTIN (present as EMAMECTIN BENZOATE)

Controls Two Spotted Mite in Cotton

GROUP 6A INSECTICIDE

For the control of Diamondback moth (Cabbage moth) in Brassica vegetables.

550 g, 2.0, and 1.1 kg NET

Novartis Crop Protection Australasia Pty Limited
140-150 Bungaree Road, Pendle Hill NSW 2145

UN-Free
NRA Approval N0.:50919/

In a transport emergency dial 000, Police or Fire Brigade.

For specialist advice in an emergency only, call 1800 033 111 (24 hours)

NOVARTIS

Directions for Use:

Crop	Pest	State	Rate/ha	Critical comments
Brassica vegetables (Broccoli, Brussels Sprout, Cabbages, Cauliflower)	Diamondback moth (Cabbage moth) (*Plutella xylostella*)	NSW & QLD only	250 - 300 g/ha	Spray at first signs of insect infestation or as indicated by local spray thresholds. Use the lower rate on low to moderate infestations. Add Citowett* or Agal* at the appropriate label rate DO NOT make more than 4 applications to any brassica crop in any one season. Refer to resistance warning. PROCLAIM should be used according to Avcare insecticide resistance strategy.

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

WITHHOLDING PERIODS:

Brassica vegetables: **DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION.**
DO NOT USE TREATED PRODUCE FOR STOCK FOOD.

GENERAL INSTRUCTIONS

Mixing

Add the required amount of PROCLAIM to a partly filled spray tank, and then add the remainder of the water.

Application

Brassica vegetables: PROCLAIM is not systemic making good coverage essential – ensure thorough coverage of the foliage and heads. DO NOT apply by aerial application. Apply PROCLAIM in a minimum of 400 L water/ha.

Compatibility

PROCLAIM is compatible with Mavrik® Aquaflo Insecticide, Delfin® WG Insecticide, Chess® 250 WP Insecticide, Supracide® 400 EC, Citowett*, Agral*, Pirimor* WG Aphicide, Topas® 100EC Systemic Fungicide, Confidor* 200SC Insecticide and mancozeb.

Insecticide resistance warning **GROUP 6A INSECTICIDE**

For insecticide resistance management PROCLAIM is a Group 6A insecticide. Some naturally occurring insect biotypes resistant to PROCLAIM and other Group 6A insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if PROCLAIM and other Group 6A insecticides are used repeatedly.

The effectiveness of PROCLAIM on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Novartis Crop Protection accepts no liability for any losses that may result from failure of PROCLAIM to control resistant insects. PROCLAIM may be subject to specific resistance management strategies. For further information contact your supplier, Novartis Crop Protection representative or local agricultural department agronomist.

To minimise the chance of resistance developing, DO NOT make more than 4 applications of PROCLAIM to any brassica crop in any one season. Where more than one crop is grown DO NOT make more than 4 applications of PROCLAIM in any one year.

PRECAUTION

Re-entry period: Do not allow entry into treated areas for 8 hours or until the spray has dried. When prior entry is necessary, wear elbow-length chemical resistant gloves.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS, ENVIRONMENT

Dangerous to fish and other aquatic organisms. DO NOT contaminate streams, rivers or waterways with the chemical or used containers. DO NOT apply under weather conditions, or from spraying equipment, that may cause spray to drift from the target area.

PROTECTION OF LIVESTOCK

Dangerous to bees. DO NOT spray any plants in flower while bees are foraging.

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. DO NOT store for prolonged periods in direct sunlight. Triple or preferably pressure rinse containers before disposal. Add rinsings to the spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS

Harmful if swallowed. Will irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length PVC gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone 131 126.

MARTERIAL SAFETY DATA SHEET

If additional hazard information is required refer to the Material Safety Data Sheet. For a copy phone 1800 025 931 or visit our website at www.cp.au.novartis.com

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY

Novartis has no control over storage, handling and manner of use of this product. Where this material is not stored, handled or used correctly and in accordance with directions, no express or implied representations or warranties concerning this product (other than non-excludable statutory

warranties) will apply. Novartis accepts no liability for any loss or damage arising from incorrect storage, handling or use.

® Registered Trademark of Novartis AG, Switzerland.

* Registered Trademark

Batch Number	
Date of Manufacture	

N1

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product.
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer.
Chronic	Of long duration.
Codex MRL	Internationally published standard maximum residue limit.
Desorption	Removal of an absorbed material from a surface.
Efficacy	Production of the desired effect.
Formulation	A combination of both active and inactive constituents to form the end use product.
Genotoxicity	The ability to damage genetic material
Hydrophobic	Water repelling
Leaching	Removal of a compound by use of a solvent.
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient.
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light.
Photolysis	Breakdown of chemicals due to the action of light.
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

Suggested Further Reading

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard Maximum Residue Limits in Food and Animal Feedstuffs*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Labelling Code - Code of Practice for Labelling Agricultural Chemical Products*, NRA, Canberra.