Public Release Summary
on

Evaluation of the new active

ACETAMIPRID

in the product

SUPREME 225 SL INSECTICIDE

Australian Pesticides and Veterinary Medicines Authority

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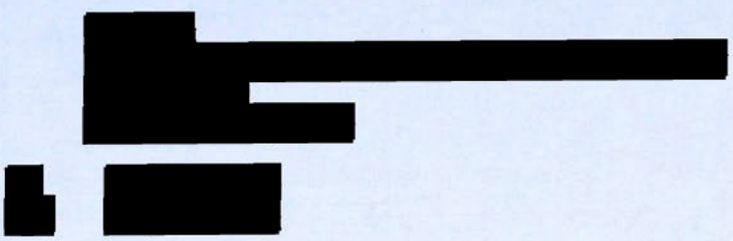

FOREWORD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) 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 APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Office of Chemical Safety), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (Worksafe Australia) and State departments of agriculture and environment.

The APVMA 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 APVMA 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 APVMA's publications *[Ag or Vet] Manual: The Requirements Manual for [Agricultural/Veterinary] Chemicals* and [*Ag/Vet*] *Requirements Series*.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the APVMA 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 APVMA. Alternatively, the reports can be viewed at the APVMA Library, 1st Floor, 22 Brisbane Avenue, Barton, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Program Manager—Pesticides Division, Australian Pesticides and Veterinary Medicines Authority, PO Box E240, Kingston ACT 2604.

CONTENTS

LIST OF ABBREVIATIONS AND ACRONYMS

AC	active constituent
ACR	Acute to chronic ratio
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose (for humans)
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
CRP	Chemistry and Residues Program
d	day
DAT	Days After Treatment
DM	Dry Matter
DT_{50}	Time taken for 50% of the concentration to dissipate
DT_{90}	Time taken for 90% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
FW	Fresh Weight
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
HDPE	High-density polyethylene
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
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
K_{oc}	Organic carbon partitioning coefficient
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
LC-MS/MS	liquid chromatography, mass spectroscopy
LOEC	Lowest Observable Effect Concentration
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet

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NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
PHI	Pre-harvest interval
po	oral
POEM	Predictive Operator Exposure Model (UK)
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TRR	
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

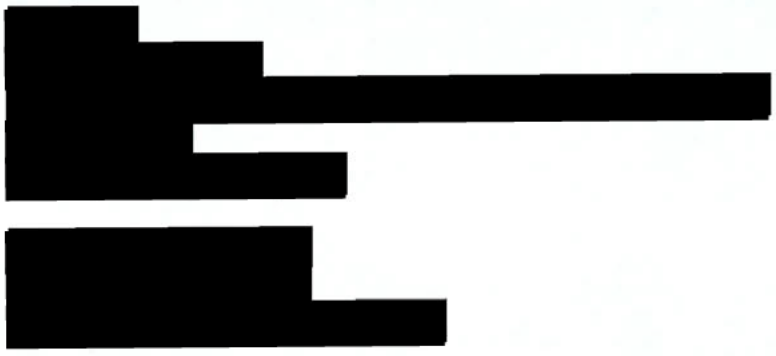
INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *SUPREME 225 SL INSECTICIDE,* which contains the new active constituent acetamiprid. The product is proposed to be used for the control of cotton aphid in cotton and green peach aphid in potatoes.

Responses to this Public Release Summary will be considered prior to registration of the product. They will be taken into account by the APVMA 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 acetamiprid, covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request (see order form on last page). They can also be viewed at the APVMA library located at the APVMA offices, First Floor, 22 Brisbane Avenue, Barton ACT 2604.

Written comments should be received by the APVMA by 13 June 2003. They should be addressed to:



Applicant
Certis Australia Pty Limited

Product Details
It is proposed to register Supreme 225 SL Insecticide, containing acetamiprid at 225g/L as a liquid concentrate formulation. Supreme 225 SL Insecticide will be imported fully formulated and packaged in 1 L, 5 L, 10 L, 20 L and 100 L containers.

Acetamiprid is a systemic insecticide belonging to the chloronicotinyl group, with translaminar activity and with contact and stomach action. It is an agonist of the nicotinic acetylcholine receptor, affecting the synapses in the insect central nervous system. With respect to insect resistance, acetamiprid is classed as a Group 4A Insecticide.

Application is as a foliar spray to the control infestations of cotton aphids (*Aphis gossypii*) in cotton and green peach aphid (*Myzus persicae*) in potatoes.

Overseas registrations, Acetamiprid formulations are currently registered in the following countries; Argentina, Belize, Bolivia, Brazil, Bulgaria, Chile, China, Colombia, Costa Rica, Cuba, Cyprus, Czech Republic, Dominican Republic, Ecuador, Guatemala, Honduras, Hungary, Indonesia, Israel, Jamaica, Japan, Macedonia, Mexico, Morocco, Myanmar, Nicaragua, Pakistan, Panama, Paraguay, Peru, Poland, Romania, Russia, Slovak Republic, South Africa, South Korea, Taiwan, Thailand, Tunisia, Turkey, Uzebek, Vietnam and Yugoslavia. It is used for the control of *Hemiptera*, especially aphids, *Thysanoptera* and *Lepidoptera* on a wide range of crops, including cotton, vegetables, fruit and tea.

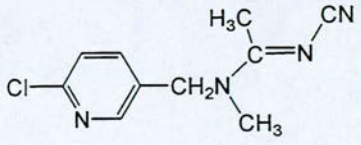
CHEMISTRY AND MANUFACTURE

Active Constituent

The chemical active constituent has the following properties:

Common name (ISO):	Acetamiprid
Chemical name (IUPAC):	(*E*)-N^1-[(6-chloro-3-pyridyl)-N^2-cyano-N^1-methylacetamide
CAS Registry Number:	135410-20-7
Empirical formula:	$C_{10}H_{11}ClN_4$
Molecular weight:	222.7
Physical form:	crystaline powder
Colour:	pale brown
Odour:	odourless
Melting point	98.9^0C
Density:	1.33
Octanol/water partition coefficient (K_{OW}):	$P_{ow} = 6.25$, $\log P_{ow} = 0.80$
Vapour pressure at 25°C:	$<1.0 \times 10^{-6}$ Pa

Structural formula:



Summary of the APVMA's Evaluation of Acetamiprid

The Chemistry and Residues Program (CRP) has evaluated the chemistry aspects of acetamiprid (manufacturing process, quality control procedures, batch anaylsis results and analytical methods) and found them to be acceptable.

Acetamiprid is a new active constituent and there is no compendial specification available for acetamiprid. On the basis of the data provided it is proposed that the following minimum compositional standard be established for acetamiprid:

Active constituent	Minimum content
Acetamiprid	Not less than 990 g/kg

Other characteristics of acetamiprid (toxicology, environmental fate *etc.*) are covered in subsequent sections of this Public Release Summary.

Formulated Product

Product name:	Supreme 225 SL Insecticide
Formulation type:	Liquid Concentrate
Active constituent concentration:	225 g/L acetamiprid

Physical and Chemical Properties of the Product

Physical state:	Liquid
Colour:	Pale yellow
Specific gravity:	1.09-1.13g/mL @ 20^0C
pH:	5-7
Flash point, flammability and auto flammability:	89^0C (Tag closed cup), 102^0C (Cleveland closed cup)
Storage stability:	Stable for at least 2 years when stored under ambient temperature.

Summary of the APVMA's Evaluation of Supreme 225SL Insecticide

The Chemistry and Residues Program (CRP) has evaluated the chemistry aspects of Supreme 225 SL Insecticide (manufacturing process, quality control procedures, batch analysis results, analytical methods and storage stability) and found them to be acceptable.

TOXICOLOGICAL ASSESSMENT

ACETAMIPRID

Evaluation of Toxicology

The Toxicological database for acetamiprid, 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 with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species-specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. 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

In rats, absorption through the gastro-intestinal (GI) tract was extensive and peak blood concentrations of acetamiprid occurred at around 1 hour after oral dosing of 1 mg/kg and at 4 hours after oral dosing of 50 mg/kg. Low levels were present in the blood after 48 hours. Generally, 70-80% of the administered radiolabel was excreted in the urine within 24 hours. Faecal excretion at 1 mg/kg accounted for 10-12% of the pyridine-radiolabel and 4% of the cyano-radiolabel excreted up to 24 hours. In bile-cannulated rats dosed with 1 mg/kg acetamiprid, recovery of administered radioactivity in the bile was 18-21%. Less than 1% of the administered radioactivity was present in the tissues 4 days after dosing. Highest tissue concentrations were generally found in the carcass, except within the first 5 hours after dosing, when the highest concentrations were found in the kidney. Acetamiprid is extensively metabolised, primarily by cleavage of the side-chain and demethylation at the side-chain. Dosing with 1 mg/kg/day of acetamiprid for 14 days appeared to retard absorption from the GI tract. Up to 6.4% of a 9.53 $\mu g/cm^2$ dose applied for 24 hours was absorbed through the skin.

Acute Studies

In acute studies in rats, acetamiprid had oral LD_{50}s of 417 mg/kg in males and 314 mg/kg in females, a dermal LD_{50} of >2000 mg/kg (no deaths), and an inhalation LC_{50} of >1150 mg/m^3 (no deaths). The oral LD_{50} in mice was <150 mg/kg. It was not a skin irritant but was a slight eye irritant in male rabbits, and was non-sensitising in guinea pigs. In a detoxification study in mice, several compounds were dosed intravenously to counteract the toxicity of single oral doses of 150 mg/kg acetamiprid. Glutathione at 10 and 30 mg/kg, glycyrrhizin at 2 and 6 mg/kg, and L-methionine at 20 and 50 mg/kg reduced the acetamiprid-related mortalities and clinical signs of toxicity.

Supreme 225 SL Insecticide, a soluble concentrate containing 225 g/L of acetamiprid, had acute oral LD_{50}s of 335 mg/kg and 404 mg/kg in male and female mice, and 580 mg/kg in male and female rats. In rats, it had an acute dermal LD_{50} of >2000 mg/kg (no deaths), and an

inhalation LC_{50} of >6540 mg/m^3 (no deaths). It was not a skin irritant but was a moderate eye irritant in female rabbits, and was non-sensitising in female guinea pigs.

Short-Term Studies

Rabbits received dermal applications of 0, 100, 500, or 1000 mg/kg/day acetamiprid for 6-6½ hours, 5 days per week, for at least 3 weeks ie., 15 or 16 dermal applications. Body weight gains and food consumption were reduced at 1000 mg/kg/day. There were no deaths or clinical signs of toxicity. There were no macroscopic abnormalities at necropsy, and no changes in haematology, serum chemistry, organ weights, or histopathology attributable to acetamiprid treatment.

Dogs received 0, 250, 500, or 1000 ppm of acetamiprid in their diet for 4 weeks. Another group received 13 days of treatment with 125 ppm, then the level of acetamiprid was increased to 3000 ppm and administered for 4 weeks. There were no deaths. Both 3000 ppm females had an emaciated appearance at termination. Throughout treatment, all 3000 ppm dogs lost weight, 1000 ppm dogs retained their initial weights and all other dogs gained weight. Slight reductions in food consumption occurred at 1000 ppm, with larger reductions at 3000 ppm. There were no treatment-related changes to haematology, serum biochemistry, macroscopic necropsy, or organ weights.

Long-Term Studies

Mice were fed 0, 400, 800, 1600, or 3200 ppm of acetamiprid in their diet for 13 weeks. Four out of 10 3200 ppm animals died or were killed *in-extremis* and tremors occurred in 3200 ppm females. There were significant reductions in body weight gain at 1600 ppm and significant body weight losses at 3200 ppm. Food consumption was significantly decreased in 1600 ppm females and at 3200 ppm. A slight decrease in haemoglobin was noted in 1600 ppm females (3200 ppm groups were not examined). Decreases were evident in serum glucose at ≥1600 ppm, and serum cholesterol in ≥1600 ppm males and ≥800 ppm in females. At 3200 ppm, increases were seen in AST, ALT, and BUN, and in Ch-E and urine pH in males only. Relative liver weights were increased at ≥800 ppm. A slight increase in thymic atrophy observed macroscopically at 3200 ppm, was confirmed histologically in 2/10 animals. Hypertrophy of the liver and fat depletion in the adrenal cortex were evident at 3200 ppm. A NOEL was established at 400 ppm (65 mg/kg/day), based on the increased relative liver weights and reductions in serum cholesterol at 800 ppm.

Rats were fed 0, 50, 100, 200, 800, or 1600 ppm of acetamiprid in their diet for 13 weeks. There were no deaths or treatment-related clinical signs. Reductions in body weight gain and food consumption occurred at ≥800 ppm. Serum cholesterol was increased at 1600 ppm. Liver weights in both sexes and thyroid weights in males were increased at ≥800 ppm. An increase in centrilobular hepatocellular hypertrophy was observed at ≥800 ppm. A NOEL was established at 200 ppm (12 mg/kg/day), based on the reductions in body weight gain and food consumption, increased relative liver weight and liver hypertrophy, and increased thyroid weight at 800 ppm.

Beagle dogs were fed 0, 320, 800, or 2000 ppm of acetamiprid in their diet for 94-95 days. There were no deaths or treatment-related clinical signs. Initial body weight losses were seen in 800 ppm males and at 2000 ppm, with weight gains thereafter in males but not females. Food consumption was decreased at 2000 ppm. There were slight increases in blood urea nitrogen and slight decreases in total protein in 2000 ppm females at weeks 7 and 13. Thyroid follicular cell hypertrophy was observed in females at 2000 ppm. A NOEL was established at 320 ppm (14 mg/kg/day), based on the reductions in body weight gain at 800 ppm.

Mice were fed 0, 130, 400, or 1200 ppm of acetamiprid in their diet for 18 months. There were no treatment-related effects on survival, palpable masses, haematology, or at macroscopic necropsy. Decreased defecation occurred at 1200 ppm, mainly during the first 20 weeks of the study. Significant reductions in body weight gain occurred in ≥400 ppm males and 1200 ppm females, and food consumption decreased at 1200 ppm. Liver weights increased at ≥400 ppm and adrenal weights decreased in ≥400 ppm females. The incidence of liver centrilobular hypertrophy increased at 1200 ppm. A NOEL was established at 130 ppm (equivalent to 25 mg/kg/day), based on the reduced body weight gains, increased liver weights, and decreased adrenal weights at 400 ppm.

Rats were fed 0, 160, 400, or 1000 ppm of acetamiprid in their diet for 2 years. There were no treatment-related effects on survival, clinical signs, palpable masses, water consumption, ophthalmoscopy, haematology, serum biochemistry, urinalysis, or at macroscopic necropsy. Body weight gains and food consumption were reduced in 1000 ppm males and ≥400 ppm females. Liver weights were increased at 1000 ppm. Histopathology revealed increased centrilobular hepatocellular hypertrophy in ≥400 ppm males and 1000 ppm females and increased hepatocellular vacuolation in ≥400 ppm males. Kidney micro-concretions (calculi) increased in 1000 ppm males. Mammary gland hyperplasia was increased in 1000 ppm females, however adenomas were not increased and mammary gland adenocarcinoma was increased but to an incidence close to the top of the historical control range. A NOEL was established at 160 ppm (equivalent to 9 mg/kg/day), based on the reduced body weight gains and food consumption, and the increased incidence of hepatocellular hypertrophy and vacuolation at 400 ppm.

Beagles were fed 0, 240, 600, or 1500 ppm of acetamiprid in their diet for 367-368 days. There were no deaths, and no effects on clinical signs, haematology, urinalysis, macroscopic and microscopic necropsy, and organ weights attributable to treatment. Initial body weight losses were seen at 1500 ppm, with weight gains thereafter in males but not females. Food consumption was initially decreased at 1500 ppm, with recovery thereafter. Significant increases in AST, creatinine, and creatine kinase, and slight increases in ALT and BUN occurred in 1500 ppm females at termination. The NOEL was 600 ppm (equivalent to 20 mg/kg/day), based on the body weight, food consumption, and serum biochemistry changes at 1500 ppm.

Reproduction and Developmental Studies

In a two generation study, rats (F_0 and F_1) received 0, 100, 280, or 800 ppm of acetamiprid in their diet from 10 weeks prior to mating, through to the end of lactation. Body weight gains were reduced in 800 ppm F_0 and F_1 parental animals throughout pre-mating and mating. The body weight differences between 800 ppm and control females were maintained throughout gestation, lactation, and post-weaning, and there were concomitant decreases in food consumption in 800 ppm F_0 and F_1 parental animals. There were no treatment-related effects on oestrous cycling, semen analyses, macroscopic or microscopic necropsy, and organ weights. Copulation and fertility indices, precoital interval, pregnancy rates, gestation index and duration, and numbers of implantation sites per dam in F_0 and F_1 rats, were similar in control and treated rats. Pup weight was lower and mortality higher at 800 ppm in both generations and were associated with delays in pup developmental landmarks. A NOEL was established at 280 ppm (at least 14 mg/kg/day), based on reduced body weight gains, food consumption, and pup survival at 800 ppm. There were no effects on reproductive performance or fertility up to 800 ppm (at least 41 mg/kg/day).

Pregnant female rats received oral gavage doses of 0, 5, 16, or 50 mg/kg/day acetamiprid between gestation days 6 and 15. There were no mortalities or clinical signs of toxicity. At 50 mg/kg/day, body weight gains and food consumption were decreased. Maternal kidney and

liver weights were increased at 50 mg/kg/day. A slight increase in the incidence of placental haemorrhage and subcutaneous foetal haemorrhage and an increase in the incidence of shortened 13th ribs occurred at 50 mg/kg/day. There were no adverse effects of acetamiprid treatment on the sex of foetuses, foetal and placental weights, the type and incidence of visceral malformations, and on ossification. Maternal and developmental NOELs were 16 mg/kg/day, based on reduced body weight gain and food consumption, increased organ weights, placental and foetal haemorrhage, and shortened 13th ribs at 50 mg/kg/day.

Pregnant female rabbits received oral gavage doses of 0, 7.5, 15, or 30 mg/kg/day acetamiprid between gestation days 6 and 18. There were no treatment-related deaths or clinical signs. Body weight losses and food consumption decreases (on days 7, 8, and 10 of gestation) during the treatment period were used to establish at maternal NOEL at 15 mg/kg/day. There was no evidence of embryo- or foetal toxicity related to acetamiprid treatment at 30 mg/kg/day.

Genotoxicity

Acetamiprid was non-genotoxic in the following studies; a bacterial mutation assay with *S. typhimurium* and *E. coli*, a mammalian cell mutation assay (CHO-HGPRT), a mouse micronucleus test, an *in-vivo* rat bone marrow metaphase analysis, and *in-vitro* and *in-vivo* rat hepatocyte UDS assays. Acetamiprid did increase chromosomal aberrations in an *in vitro* CHO chromosome aberration assay, in the presence of S9 (there were no increases in the absence of S9).

Special Studies

There was no impact on the results of annual health examinations on production workers involved in the non-continuous production of acetamiprid between April 1996 and May 1998. There were no reports of acute poisoning by exposure, or skin or eye irritation, with workers wearing protective equipment (including safety goggles, a filter respirator, and rubber gloves) during production.

Pharmacology studies

In-vitro, acetamiprid at 10^{-4} and 10^{-3} g/mL caused contraction followed by relaxation in isolated guinea pig ileum, and 10^{-3} g/mL acetamiprid inhibited contraction by agonists.

Mice were given single i.p. injections of acetamiprid. At 10 mg/kg, there was vocalisation, decreased activity, and enhancement of pentobarbital-induced anaesthesia. At 20 mg/kg, there were additional effects, such as decreased grip strength, staggering gait, reduced muscle tone and analgesic properties. At a dose of 30 mg/kg, there were convulsions and reduced reflex activity, while all mice died at 60 mg/kg. Anticonvulsant activity was not observed at doses up to 20 mg/kg i.p. Gastric motility was inhibited with an oral dose of 40 mg/kg but not at lower doses.

Rats given single i.p. doses up to 20 mg/kg showed no effects on body temperature, clotting time, haemolysis of erythrocytes, and plasma cholinesterase activity. Urine volume and electrolyte excretion was decreased at 20 mg/kg, but not at lower doses.

Rabbits given single i.v. injections of acetamiprid showed no behavioural changes at 10 mg/kg. At 30 mg/kg, there were slight decreases in activity, muscle tone, reflexes and coordination, and slight increases in convulsions, respiratory rate and mydriasis. Animals receiving 60 mg/kg showed in addition, pupil dilation, abnormal breathing, cyanosis and death within 60 minutes. In anaesthetised rabbits, a slight increase in respiratory rate and a decreases in blood pressure were recorded at $\geq$3 mg/kg i.v.

Neurotoxicity studies

Rats received single oral gavage doses of 10, 50, or 100 mg/kg acetamiprid in an acute dose range-finding assay. There were no deaths. Tremors were increased in ≥50 mg/kg females and 100 mg/kg males and hunched posture and dilated pupils were observed at 100 mg/kg. Body temperature was reduced at 100 mg/kg, but only slightly in males. Body weight gains were reduced in 100 mg/kg females on the day of dosing, with recovery thereafter. There were no effects at 10 mg/kg.

Rats received single oral gavage doses of 0, 10, 30, or 100 mg/kg acetamiprid. There were no deaths. In 100 mg/kg males, body weight gains were significantly reduced throughout the study and food consumption was significantly reduced during the first week. All other signs of toxicity occurred during the day of dosing and included reluctance to move, cold to touch, nasal staining, tremors, unsteady or impaired mobility, hunched posture, and dilated pupils at 100 mg/kg. There were reductions in body temperature at 100 mg/kg and locomotor activity was decreased in ≥30 mg/kg males and 100 mg/kg females, at 6 hours after dosing only. No treatment-related effects occurred on brain measurements or neurohistopathology.

Rats were fed 0, 100, 200, 800 or 1600 ppm acetamiprid in their diet for 13 weeks. There were no deaths or clinical signs of toxicity. At ≥800 ppm, there were reductions in body weight gains and food consumption throughout the study. No evidence of treatment-related neurotoxicity occurred in this study. There were no effects at 200 ppm (equivalent to 15 mg/kg/day).

Metabolites studies

In acute oral studies in rats, acetamiprid metabolites were less toxic than acetamiprid, with LD_{50}s ranging from 900-1000 mg/kg to >5000 mg/kg. Metabolite IM-1-4 had an acute dermal LD_{50} of >2000 mg/kg (no deaths) in rats. None of the metabolites were genotoxic.

Rats received 0, 160, 800, 4000, or 20000 ppm of metabolite IM-0 ((6-chloro-3-pyridyl)methanol, a plant and animal metabolite) in their diet for 13 weeks. There were no deaths and no clinical signs of toxicity related to IM-0 treatment. Body weight gains and food consumption were significantly reduced throughout the study at 20000 ppm. Serum alkaline phosphatase significantly increased in 20000 ppm females. There were no effects related to treatment on ophthalmology, urinalysis, macroscopic necropsy, and organ weights. Histopathology revealed an increase in the incidence of eosinophilic intranuclear intrusions in the proximal tubular epithelium of the kidney in ≥4000 ppm males and 20000 ppm females, which was used to establish a NOEL of 800 ppm (equivalent to 49 mg/kg/day).

Rats were fed 0, 200, 600, 1800 or 5400 ppm of metabolite IM-1-4 (N-methyl-(6-chloro-3-pyridyl)methylamine, a plant and animal metabolite) in their diet for 13 weeks. There were no deaths or clinical signs of toxicity related to treatment. Body weight gains and food consumption were decreased at 5400 ppm and were associated with reduced serum protein. Urine specific gravity increased in 5400 ppm females. There were no effects related to treatment on ophthalmology, haematology, serum biochemistry, macroscopic necropsy, and organ weights. An increase in pigment was noted in the splenic sinusoids at 5400 ppm. A NOEL was established at 1800 ppm (equivalent to 112 mg/kg/day), based on the reductions in body weight gain and food consumption, increased urine specific gravity, and splenic sinusoids at 5400 ppm.

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.

On the basis of its toxicity, the NDPSC has included acetamiprid in Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The Acceptable Daily Intake is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOEL obtained in the most sensitive species. This NOEL is then divided by a safety factor which reflects the quality of the toxicological database takes into account the variability in responses between species and individuals.

The ADI for acetamiprid was established at 0.1 mg/kg/day based on a NOEL of 9 mg/kg/day in a 2-year rat dietary study and using a 100-fold safety factor in recognition of the extensive toxicological database available for acetamiprid.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated event. The ARfD is derived from the lowest single or short term dose which caused no effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The highest acute dose of acetamiprid at which no evidence of toxicity was detected was 10 mg/kg (in an acute neurotoxicity study). The ARfD was established at 0.1 mg/kg on the basis of this NOEL and using a 100-fold safety factor.

RESIDUES ASSESSMENT

Metabolism

The metabolism of acetamiprid was investigated in plants (eggplant, apple, cabbage and carrots) and in animals (rats, mice, lactating goats and laying hens) using pyridine-2,6-^{14}C-labelled and ^{14}C-cyano-labelled acetamiprid.

The predominant radioactive residue in plants following treatment with [^{14}C-pyridine] acetamiprid was parent compound. In eggplants, greater than 85% of TRR in leaves and fruit treated with acetamiprid was parent compound. Acetamiprid was the major residue in apple leaves and fruit after foliar spraying or fruit treatment of single fruit. Parent compound comprised more than 49% TRR in leaves up to 90 days after treatment, with the metabolite N-demethyl acetamiprid being the predominant metabolite accounting for 15% TRR. Acetamiprid was also the major residue in cabbages and carrots treated with a foliar spray of ^{14}C-acetamiprid. Very little translocation to untreated plant parts occurred.

Acetamiprid is the predominant residue in eggplant, apple, cabbage and carrots. Minor metabolic pathways for acetamiprid in plants involve cleavage of the N-methyl bond, hydrolysis of the cyano group and conjugation with glucose. N-demethyl acetamiprid was a minor component of the radioactive residues in plant parts, comprising up to 7.2% of TRR in cabbages. The proposed metabolic pathway in plants is shown in figure 1.

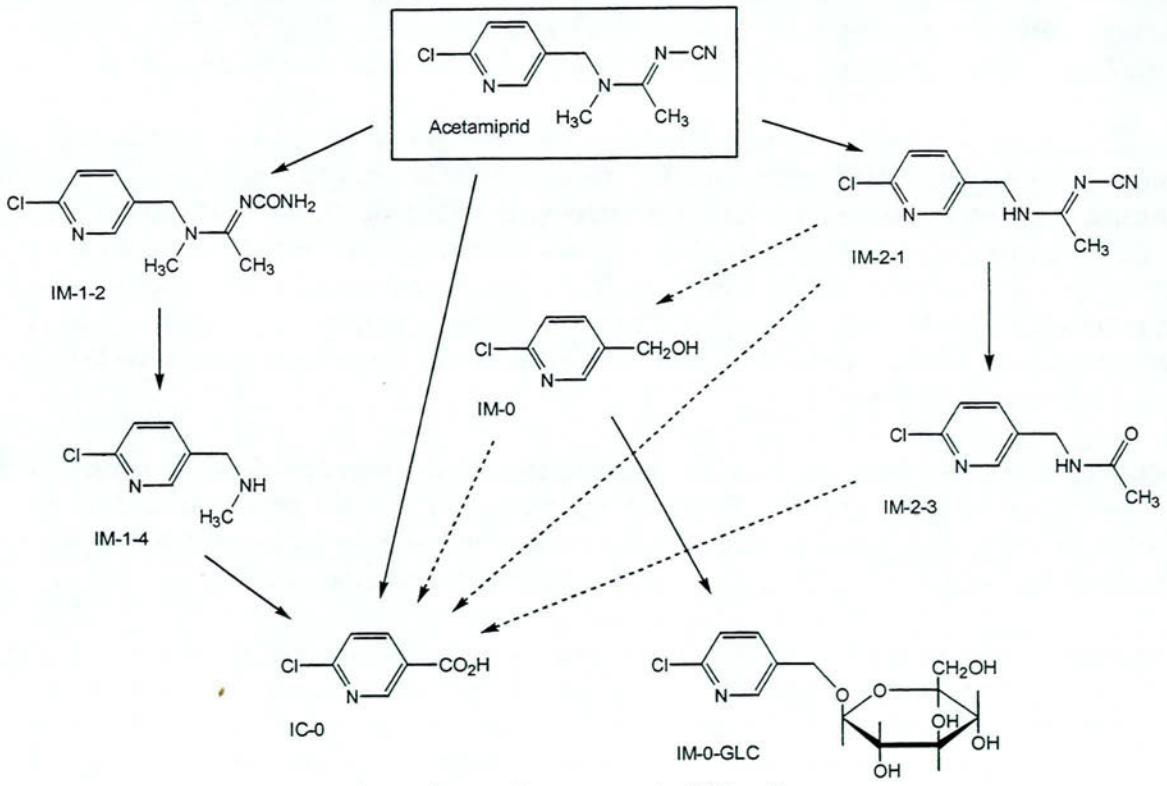


Figure 1. Proposed metabolic pathway for acetamiprid in plants

Two lactating dairy goats were orally administered [^{14}C-pyridine] acetamiprid by gelatin capsule for 7 consecutive days. More than 95% of the administered radioactivity was recovered in urine and faeces within 24 hours of the last dose. Less than 0.6% of the doses were recovered in milk and less than 2% was recovered in tissues and organs. Greater than 98% of the applied dose was recovered in the experiment. Highest tissue residue concentrations occurred in liver and kidney, and these were approximately 10 times the levels found in muscle and fat. The metabolite IM-2-1, N-demethyl acetamiprid, was the major

metabolite in liver, kidney and milk (>77% TRR) and excreta (>60% TRR), but only 10% TRR in muscle. The major radioactive residue in muscle was the N-demethylated metabolite of IM-1-2 (50% TRR).

Ten laying hens (white leghorn hybrids) were orally administered [^{14}C-pyridine] acetamiprid by single gelatin capsule for 14 consecutive days. More than 90% of the administered radioactivity was recovered in excreta within 24 hours of the last dose. Less than 1.5% of the doses were recovered in eggs and less than 1% was recovered in tissues and organs. More than 95% of radioactivity was recovered in the experiment. Highest tissue residues occurred in liver, which were more than 5 times the levels present in other tissues and eggs. Plateau levels of radioactivity in eggs were reached within 8 days of the first dose. The metabolite IM-2-1, N-demethyl acetamiprid, was the major metabolite in all tissues, eggs and excreta.

The metabolism of acetamiprid in rats and mice was consistent with that observed in target animals (goats and hens). The major metabolic route for acetamiprid in animals is cleavage of the N-methyl group. Minor metabolic pathways for acetamiprid in animals involve hydrolysis of the cyano group and conjugation with glucose.

Analytical Methods

Residue methods provided are capable of determining acetamiprid in plant commodities and acetamiprid and N-demethylated acetamiprid in animal commodities. Residues are extracted from plants using methanol then purified by solvent partitioning with hexane and dichloromethane and Florisil chromatography. A further cleanup step using a C18 solid phase extraction (SPE) cartridge may also be used. Determination is by GC with electron capture detection and comparison against a calibration curve derived from reference standards.

An additional method for "total acetamiprid residues" was provided. In this method, all residues with the (6-chloro-3-pyridyl)methyl moiety are derivatised to methyl 6-chloronicotinate by extraction, hydrolysis with sodium hydroxide solution, oxidation with potassium permanganate and esterification with diazomethane. The method involves a complicated series of chemical reactions, rather than a simple extraction, and may be considered laborious for routine analysis. Since the method involves derivatisation to a common derivative residues of only parent compound and N-demethyl acetamiprid (IM-2-1) cannot be determined separately.

Residues are extracted from macerated animal commodities using acetonitrile and purified by solvent partitioning using hexane and dichloromethane. Extracts are further cleaned up by Florisil chromatography and C18 cartridge before determination by HPLC with UV detection and comparison against a calibration curve derived from reference standards.

The methods are capable of achieving a limit of quantitation of 0.01 mg/kg for acetamiprid in plant material. However, the residue trials provided for potatoes and cotton were reported with a limit of quantitation of 0.05 mg/kg, which corresponds to the lowest fortification level used in recovery experiments in the trials. The method used for animal commodities has a limit of quantitation of 0.01 mg/kg for both acetamiprid and metabolite IM-2-1 in milk, eggs, muscle and fat and 0.05 mg/kg in liver and kidney.

Residue Definition

Acetamiprid is the predominant residue in treated plant commodities, and the N-demethylated acetamiprid metabolite (*E*)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyanoacetamidine is the predominant residue in commodities of animal origin. Analytical methods are capable of determination of acetamiprid in crop samples and acetamiprid and N-demethyl acetamiprid in

animal commodities. The "total" plant method is not capable of distinguishing residues of acetamiprid and IM-2-1 from other metabolites, therefore it is appropriate to set separate residue definitions for acetamiprid in plant and animal commodities as:

Acetamiprid: *Commodities of plant origin*: acetamiprid

Commodities of animal origin: sum of acetamiprid and N-demethyl acetamiprid ((*E*)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyanoacetamidine), expressed as acetamiprid

No change to the current residue definition for acetamiprid is required.

Residues in Potatoes

Eight Australian and one overseas residue trial on potatoes were provided in support of the use on potatoes. Acetamiprid residues in potatoes were below the limit of quantitation (0.05 mg/kg) following application at up to 1.5 times the maximum rate proposed for use in Australia (PHI 7 days). Even at exaggerated rates (3×) residues were <0.05 mg/kg at 7 days after treatment. A supervised trials median residue (STMR) of 0.05 mg/kg (1.5× rate, PHI 6-7 days) is estimated, with a highest residue of <0.05 mg/kg.

The residue trials provided support an MRL for potatoes at the limit of quantitation of 0.05 mg/kg (PHI 7 days). To preclude animals from grazing on treated crops the applicant has proposed a grazing restraint for potatoes. The following harvest and grazing withholding period statements are recommended:

Potatoes:
DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION

DO NOT GRAZE OR CUT FOR STOCK FOOD

Residues in Cotton

Eight Australian and four overseas residue trials on cotton were provided in support of the use on cotton. The first of two applications were at flowering and the second applications were between 28-87 days later. Residues in cottonseed following 2 applications at 22.5 g ai/ha (1× rate) were <0.05 mg/kg in all samples (PHI 6-10 days). Residues above 0.05 mg/kg were not detected in any cottonseed sample after application at up to twice the proposed maximum label rate. A STMR of <0.05 mg/kg (1× rate, PHI 6-10 days) for cottonseed is estimated, with a highest residue of <0.05 mg/kg. The residue data support an MRL for cottonseed set at the limit of quantitation of 0.05 mg/kg (PHI 10 days).

Residues data were provided for cotton lint and trash. Residues of acetamiprid in cotton lint were below the limit of quantitation (0.05 mg/kg) in all samples taken in six of the eight Australian trials (22.5 g ai/ha rate). In the two other trials, residues in lint were up to 0.146 mg/kg (PHI 10 days). Residues in trash from crops harvested 6-10 days after application ranged from 0.081-0.771 mg/kg, with a mean value of 0.275 mg/kg and a median residue of 0.195 mg/kg. No MRL is recommended for cotton trash as it is not considered to be good agricultural practice to feed cotton trash and gin trash to livestock.

The following harvest and grazing withholding period statements are recommended:

Cotton:

DO NOT HARVEST FOR 10 DAYS AFTER APPLICATION

DO NOT GRAZE OR CUT FOR STOCK FEED

Residues in Animal Commodities

Vegetable waste and cottonseed and meal could be fed to livestock. It is assumed that cottonseed (and meal) and vegetable waste could comprise up to 30% and 5%, respectively, of the livestock diet (see APVMA Information Document 1).

No quantifiable residues (>0.05 mg/kg) were detected in cottonseed or potatoes treated at up to twice the maximum proposed Australian application rate for cotton and three times the maximum rate for potatoes. The estimated maximum exposure of livestock (including poultry) to acetamiprid residues is approximately 0.02 ppm in the feed. Feeding of cotton trash is not considered good agricultural practice and therefore is not considered further.

Animal transfer studies were provided for lactating dairy cows and poultry, fed continuously for 28 days. Residues of acetamiprid and N-demethyl acetamiprid were determined in milk, eggs and tissues. At the expected feeding level of 0.02 ppm in the diet it is estimated that acetamiprid residues in eggs, milk and tissues will be well below the limit of quantitation for each animal commodity. MRLs for animal commodities are recommended at *0.01 mg/kg for eggs, poultry meat, meat (mammalian) and milk, and at *0.05 mg/kg for poultry offal and mammalian offal.

Processing Studies

No processing studies were provided. Acetamiprid has a log P_{OW} of 0.80 therefore residues are not expected to concentrate in oil. Given that residues in cottonseed above the limit of quantitation were not detected following application at up to twice the proposed maximum Australian rate, there is no reasonable expectation that quantifiable residues will occur in cottonseed oil or meal as a result of the proposed use.

Storage Stability

Samples collected in the Australian residues trials on potatoes were stored frozen for between 1 and 11 months, while in the Australian cotton trials, samples were stored for between 5 and 8 months prior to residue analysis. Storage stability data indicate that acetamiprid residues in potatoes and cotton are stable when frozen for up to 7 months (potatoes) and 5 months (cotton). More than half of the samples collected in the trials were stored for less than 7 months (potatoes) and 5 months (cotton) therefore it is concluded that the results reported in the trials are a true reflection of the residues present at sampling.

No storage stability data for animal commodities were provided, however all tissue samples were analysed within 1 month of sacrifice. It is concluded that the results from the animal transfer study are a true reflection of residues present at sampling.

Dietary Risk Assessment

The chronic dietary risk is estimated by the National Estimated Daily Intake calculation encompassing all registered/temporary uses of the chemical and dietary intake data from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance

with the Guidelines for predicting dietary intake of pesticide residues (revised) (World Health Organisation, 1997). The NEDI of acetamiprid is equivalent to 0.3% of the ADI. It is concluded that the chronic dietary exposure is small and the risk is acceptable.

The acute dietary risk is estimated by the National Estimated Short Term Intake calculation, and is made in accordance with the procedures used by the JMPR. The NESTI calculation for cottonseed, potatoes and animal commodities is less than 1% of the acute reference dose (0.1 mg/kg bw) for all of the commodities for which permanent MRLs are proposed in this application. It is concluded that the acute dietary exposure to acetamiprid is small and the risk is acceptable.

Bioaccumulation Potential

The log P_{ow} for acetamiprid is 0.80. According to the FAO Manual the compound should not be designated as fat soluble.

Conclusion

Adequate residues data were provided to support the registration of Supreme 225 SL Insecticide for use on cotton and potatoes.

Recommended Amendments to the MRL Standard:

Table 1

Compound	Food		MRL (mg/kg)
DELETE			
Acetamiprid	SO 0691	Cottonseed	T0.05
	MO 0105	Edible offal (mammalian)	T*0.05
	PE 0112	Eggs	T*0.01
	MM 0095	Meat [mammalian]	T*0.01
	ML 0106	Milks	T*0.01
	VR 0589	Potato	T*0.01
	PO 0111	Poultry, edible offal of	T*0.05
	PM 0110	Poultry meat	T*0.01
ADD			
Acetamiprid	SO 0691	Cottonseed	*0.05
	MO 0105	Edible offal (mammalian)	*0.05
	PE 0112	Eggs	*0.01
	MM 0095	Meat [mammalian]	*0.01
	ML 0106	Milks	*0.01
	VR 0589	Potato	*0.05
	PO 0111	Poultry, edible offal of	*0.05
	PM 0110	Poultry meat	*0.01

The above MRLs will be conveyed to Food Standards Australia New Zealand fore inclusion in Standard A14 of the Food Standards Code.

The following withholding periods are recommended in relation to the above MRLs.

Withholding Periods:

Potatoes:
DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION
DO NOT GRAZE OR CUT FOR STOCK FOOD

Cotton:
DO NOT HARVEST FOR 10 DAYS AFTER APPLICATION
DO NOT GRAZE OR CUT FOR STOCK FEED

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Relevant Export Commodities

Cottonseed and meal are significant export commodities. In 2000-1 Australia exported 657 kt of cottonseed, 0.64 kt cottonseed oil and 59 kt of cottonseed and sunflowerseed oil (Australian Commodity Statistics 2001, ABARE). Potatoes are a minor export commodity. In 1999/2000 Australia exported approximately 21 kt of potatoes valued at $8.9m.

Cattle, pigs, sheep and poultry are all significant export commodities. All of these species may consume straw, forage and/or grain from cotton crops treated with Supreme 225 SL Insecticide. Cattle could also be exposed to feed contaminated with acetamiprid residues from spray drift.

Overseas Registration Status and MRLs

The applicant has stated that acetamiprid is registered in several countries on various crops including cotton and potatoes, however no MRLs are established for the major export commodities in Australia's major trading partners. Residues present above quantifiable levels may therefore present a risk to Australia's trade.

Potential for Undue Prejudice to Australia's Export Trade

Residues above quantifiable levels (>0.05 mg/kg) are not expected to occur in cottonseed, meal or oil or potatoes as a result of the use of Supreme Insecticide as directed on the product label.

Animals consuming vegetable waste or cottonseed and meal treated with Supreme are not expected to contain residues of acetamiprid above quantifiable levels in eggs, milk or tissues.

Since Supreme may be applied by aerial spray the likely residues in pasture affected by spray drift and the tissues of animals grazing on that pasture was considered. A scenario in which 10% of the chemical applied to 1 ha of cotton crop drifts uniformly onto 1 ha of neighbouring pasture was considered. It was estimated that animals (cattle) grazing on pasture affected by 10% spray drift would develop residues in milk, offal and muscle of approximately 0.04, 0.07 and 0.03 mg/kg, respectively, based on results from the animal transfer study provided. The limits of quantitation are *0.01 mg/kg for milk and muscle and *0.05 mg/kg for offal.

It is acknowledged that the above scenario calculation may overestimate the risk of developing quantifiable residues in animal commodities as a result of spray drift. The amount of chemical drifting onto neighbouring pasture may be overly conservative, as the above calculations do not account for residue decline in pasture following application. No residue decline data for livestock or pasture were provided.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Assessment of Occupational Health & Safety

Acetamiprid has high acute oral toxicity in rats and mice and low inhalation and dermal toxicity in rats. It is a slight eye irritant in rabbits but not a skin irritant in rabbits or a skin sensitiser in guinea pigs. Effects on liver, kidney, adrenal, thyroid and mammary gland were seen in repeated dose studies in rats, dogs and mice. No evidence of effects on reproduction, development, neurotoxicity or behaviour was seen in rats. Weight of evidence from genotoxicity and chronic studies indicated that acetamiprid is not carcinogenic in animals.

Acetamiprid is not listed in the NOHSC *List of Designated Hazardous Substances*.
The applicant has determined both acetamiprid and Supreme 225 SL Insecticide to be hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances.*

The following risk phrase applies for acetamiprid:

R22 Harmful if swallowed.

(This classification applies to acetamiprid at a concentration of $\geq$ 25%).

Supreme 225 SL Insecticide has a high acute oral toxicity in rats and mice and low acute inhalation and dermal toxicity in rats. It is a severe eye irritant but not a skin irritant in rabbits, although the MSDS for a similar product indicated mild skin irritation potential. The product was not a skin sensitiser in guinea pigs.

Formulation, Packaging, Transport, Storage and Retailing

Supreme 225 SL insecticide is a pale yellow transparent liquid (soluble concentrate).

The product will be formulated overseas and imported fully packaged in 1 L, 5 L, 10 L, 20 L high-density polyethylene (HDPE) bottles. A 100 L HDPE cubic drum is also available.

Transport workers, store personnel and retailers will handle the packaged product and will only become contaminated if the packaging is breached.

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

Use and Exposure

Supreme 225 SL Insecticide is indicated for the control of green peach aphid (*Myzus persicae*) in potatoes and cotton aphid (*Aphis gossypii*) in cotton.

It will be applied a maximum of four times per season by ground and aerial applications. The maximum application rates for potatoes will be 200 mL/ha EUP in a minimum of 50 L water/ha (0.08% active ingredient) for ground boom spray (nozzle mounted) and in a minimum of 20 L water/ha (0.2% active ingredient) for aerial spraying. The maximum application rates for cotton will be 100 mL/ha EUP in a minimum of 50 L water/ha (0.04% active ingredient) for ground boom spray (nozzle mounted) and in a minimum of 20 L water/ha (0.1% active ingredient) for aerial spraying.

The main routes of exposure to acetamiprid are dermal and ocular. Although some inhalation exposure may occur as a result of airborne spray droplets or mist, the potential for inhalation exposure is limited by the low vapour pressure of acetamiprid and method of application. Categories of workers that can be exposed to the product are mixer/loaders, ground applicators, clean-up personnel, re-entry workers and flaggers/markers.

There are no available worker exposure data for Supreme 225 SL Insecticide. NOHSC used the UK Predictive Operator Exposure Model (POEM) to estimate exposures during mixing/loading and application.

Risks (skin and eye irritation) from acute exposure to Supreme 225 SL Insecticide (EUP) are significant during opening of containers and mixing/loading activities. At a maximum concentration of 1.0% (v/v) EUP in spray, acute risks to applicators are considered to be insignificant.

No risks from repeated exposure were identified for applicators during boom spraying for either cotton or potato crops. Risks to applicators (pilots) from aerial application cannot be modelled by POEM, but are considered low, due to the protection afforded by the closed cockpit. Similarly, exposures to flaggers/markers cannot be modelled by POEM, but are likely to be greater than for ground applicators and hence risks may be significant.

The risk assessment indicates that workers should wear cotton overalls (buttoned to neck and wrist), face shield or goggles and rubber gloves to protect against acute and/or repeated exposures to Supreme 225 SL Insecticide.

Entry into Treated Areas

Workers may be exposed to product when entering fields that have been treated with product. No post-application worker exposure data were available.

The draft label suggests a restriction on re-entry until the spray has dried. As the highest final concentration of acetamiprid in the spray would be 0.2% (1% EUP), the risk to workers entering treated areas is not considered to be significant. NOHSC considers the restricted re-entry statement on the draft label to be appropriate.

Recommendations for Safe Use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of rubber gloves, cotton overalls (buttoned to neck and wrist), face shield or goggles and rubber gloves, when preparing the spray and cotton overalls (buttoned to neck and wrist) when using the prepared spray.

The personal protective equipment recommended should meet the relevant Standards Australia standards.

Re-entry statement

To ensure there is no risk from exposure to wet spray, the following re-entry statement should be included on the product label:

Do NOT allow re-entry into treated areas until the spray deposits have dried. When prior entry is necessary, wear cotton overalls, buttoned to neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing should be laundered each day.

Precautionary statement

To ensure there is no risk to flaggers/markers during aerial spraying, the following Precautionary statement should be included on the product label:

Do NOT use human flaggers/markers unless they are protected by engineering controls such as vehicles with enclosed cabs.

Information provision

A MSDS for Supreme 225 SL Insecticide was not provided as part of the submission for registration (an MSDS for a similar product was provided).

A MSDS for Supreme 225 SL Insecticide should be provided by suppliers and made available to Australian workers. It should reflect the NOHSC hazard classification and contain other relevant information, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets.

Conclusion

Supreme 225 SL Insecticide can be safely used by workers when handled in accordance with instructions and other control measures described above.

ENVIRONMENTAL ASSESSMENT

Environmental Exposure

Supreme 225 SL Insecticide, containing the technical grade active constituent acetamiprid at 225 g a.i.(active ingredient)/L, is a Group 4A insecticide (acetylcholine receptor agonist/antagonist) proposed for the control of green peach aphid in potatoes and cotton aphid in cotton. The product is to be applied as a foliar spray at a maximum application rate of 200 mL of EUP per ha in potatoes, equivalent to 45 g a.i./ha. The label recommends that a non-ionic wetter be applied in conjunction with Supreme 225 SL Insecticide. A lower rate, 50-100 mL/ha is proposed for cotton, with a maximum application rate of 22.5 g a.i./ha plus 0.2% Pulse Penetrant. For both crops, if repeat sprays are necessary, applications should be alternated with an insecticide in a different group for resistance management, subject to the Avcare resistance management strategy. The company advises that a maximum of three applications per year should be applied based on the current cotton resistance strategy.

Environmental Chemistry and Fate

Abiotic transformation

Acetamiprid was stable at pH 4, 5 and 7 but hydrolysed very slowly at pH 9 and 25°C with a half-life of 420 d. The secondary amine IM-1-4 and chloronicotinic acid metabolites IC-0 were also stable to hydrolysis. Acetamiprid photolysed in water with a half-life of 34 d with the major degradation product IB-1-1 which peaked at 35% after 30 d. The metabolite IM-1-4 only photolysed to 96% after 28 d of continuous irradiation while IC-0 photolysed in water with a half-life of 6 h with formation of unidentified products. When applied to a microbially active loamy sand, acetamiprid degraded with a half-life of 17 d when irradiated and 10 d in the dark control, indicating that photolysis is not expected to be a major route of dissipation. Computer modelling calculated a half-life of 4.5 d for acetamiprid in the atmosphere by reaction with hydroxyl radicals.

Biotic transformation

Acetamiprid biodegraded rapidly in a loamy sand with a half-life and DT90 of 1.4 and 4.7 d, respectively, while the main secondary amine metabolite IM-1-4 further degraded with a DT50 of 25.6 d. Degradation was complete as 55% of the originally applied radioactivity was identified as $^{14}CO_2$ at 112 DAT. In another experiment in the same soil, acetamiprid rapidly biodegraded to the N-acetyl urea metabolite IM-1-2 with a half-life of <1 d and was nondetectable by 7 DAT. IM-1-2 (peak of 55% 1 DAT) subsequently decomposed to IM-1-4 (peak of 16% 7 DAT) and the chloronicotinic acid IC-0 (peak of 11% 2 DAT). Once formed, IC-0 was rapidly degraded to $^{14}CO_2$. In a third experiment in three soils, acetamiprid biodegraded rapidly with a DT50 of 0.8-5.5 d at 20°C and 7.9 d at 10°C. The DT50 and DT90 values for IM-1-4 in the clay loam were 4.2 and 14 d, respectively, but the DT50 in the sandy loam was significantly higher at 252 d. These values for IC-0 in the clay loam were 4.8 and 16 d, respectively. In a separate experiment in three soils, IC-0 biodegraded with DT50 and DT90 values of 2.9-6.5 and 6.6-13.3 d, respectively.

Anaerobic biodegradation in the surface water was quick with DT50 and DT90 values of 1.7 and 19.2 d, respectively, but slow in flooded soil (DT50 of 194 d) giving a whole system DT50 of 71 d (no DT90 could be calculated). The secondary amine IM-1-4 was the main component from 119 DAT (maximum of 51%) and degradation followed essentially the same pathway as for aerobic biodegradation except that the amide IM-1-3 was also formed from IM-1-2.

When applied to two natural systems of anaerobic sediment and aerobic water, acetamiprid steadily transferred from the water phase to the sediment with about 50% left in the water by

7 DAT. The whole system DT50 and DT90 values were 21-29 and 94-122 d, respectively, with the main metabolite in water being IM-1-4 (peak of 10-12%) and IC-0 (peak of 26%), and IM-1-4 in sediment (peak of 16-31%).

Mobility
Acetamiprid was highly mobile in five soils of varying texture and organic carbon content (0.4-4.4%) in a standard adsorption/desorption study, while IM-1-4 showed medium to high mobility in the same soils. IC-0 also showed medium to high mobility in five different soils and a sediment. When acetamiprid was aerobically aged for 2 d in a loamy sand and the resulting residues leached through a 30 cm soil column with the equivalent of 200 mm of rain, 89-92% of the applied radioactivity was retained by the soil with the majority (85-91%) in the top 20 cm. Only ≤1.3% of the radioactivity was found in the leachates with most of it (0.8%) as IM-1-4.

Acetamiprid did not significantly volatilise from a bare loamy sand or french bean plants when treated at 263 g a.i./ha and exposed to air speeds up to 1 m/s.

Field dissipation
A soluble powder formulation of acetamiprid sprayed onto bare ground at four locations in Europe at 208-395 g a.i./ha dissipated with DT50 and DT90 values of 0.7-5.7 d and 12-63 d, respectively. For the secondary amine metabolite IM-1-4 the DT50 and DT90 values were 17-39 d and 56-131 d, respectively. Acetamiprid and IM-1-4 remained in the top 10 cm of all soils at all sampling times.

Environmental Toxicology

Birds
Acetamiprid was moderately toxic to young adult mallard ducks with a single oral dose LD50 of 98 (81, 119) mg a.i./kg bw, but practically nontoxic to mallard ducklings and northern bobwhite quail chicks in 5-d dietary tests with an LC50 of >5,000 mg a.i./kg food. In one generation dietary toxicity tests, mallards were more sensitive with NOEC and LOEC values of 125 and 228 mg a.i./kg food, respectively, than quail with 484 and 1,026 mg a.i./kg food, respectively, for various reproductive parameters.

Fish
Although the 96-h LC50 of acetamiprid to juvenile rainbow trout was >100 mg a.i./L, the EC50 based on measured concentrations and sublethal effects of equilibrium loss, darkened body and abdominal swelling was 77.4 (65.2, 97.2) mg a.i./L which is considered harmful to aquatic life. Bluegill sunfish were less sensitive with a 96-h LC50 of >119.3 mg a.i./L. Carp were apparently less sensitive still with a 96-h LC50 most likely between 320 and 560 mg a.i./L when an acetamiprid formulation was used. The secondary amine metabolite IM-1-4 was more toxic to juvenile trout with a 96-h EC50 of 15.6 (12.5, 19.4) mg/L (harmful to aquatic life). Fathead minnow embryos and larvae had a NOEC and LOEC of 19.2 and 34.8 mg a.i./L, respectively, with a geometric mean MATC of 27.2 mg a.i./L when chronically exposed to acetamiprid for 35 d; this was only very slightly toxic.

Aquatic invertebrates
Water fleas were more sensitive to technical acetamiprid (48-h EC50 = 49.2 (39.3, 61.5) mg a.i./L) than when formulated as Supreme 225 SL Insecticide (48-h EC50 = 111 (100, 124) mg a.i./L). The secondary amine metabolite IM-1-4 was more toxic with a 48-h EC50 of 43.9 (34.8, 55.9) mg/L than the N-acetyl urea metabolite IM-1-2 (48-h EC50 > 99.8 mg/L), the chloronicotinic acid metabolite IC-0 (48-h EC50 > 95.1 mg/L) or the phototransformation product IB-1-1 (48-h EC50 > 100.8 mg/L). In a chronic 21-d exposure, the NOEC and LOEC of acetamiprid to daphnids were 5 and 9 mg a.i./L, respectively, with a MATC of 6.7 mg

a.i./L; this is only very slightly toxic. The acute to chronic ratio (ACR, calculated as EC50/MATC) is relatively low at 7.3. Chironomids were about 1000 X more sensitive to acetamiprid with 28-d NOEC and LOEC values of 4.6 and 9.4 µg a.i./L, respectively, with a MATC of 6.6 µg a.i./L.

Aquatic plants

The freshwater green alga *Scenedesmus subspicatus* was not sensitive to acetamiprid as the E_bC50 and the E_rC50 were both >98.3 mg a.i./L. In a limit test, the freshwater diatom *Navicula pelliculosa*, marine diatom *Skeletonema costatum* and macrophyte duckweed showed no adverse effect of chronic exposures to 1.0-1.1 mg a.i./L, which was the NOEC.

Terrestrial invertebrates

Acetamiprid was relatively toxic to earthworms with a 14-d LC50 of 9.1 (8.1, 10.3) mg a.i./kg soil dw. In contrast, the metabolites IM-1-4 and IC-0 were both considerably nontoxic with 14-d NOEC and LOEC values of 1,000 and >1,000 mg/kg soil dw, respectively. There was moderate contact toxicity for honeybees with a 72-h LD50 of 2.2 µg a.i./bee (no confidence limits) but this value must be treated with caution; the NOEC and LOEC were <6.25 and 6.25 µg a.i./bee, respectively. Orally ingested acetamiprid was also moderately toxic with a 72-h LD50 of 10.1 (5.7, 25.9) µg a.i./bee. When formulated as a 20% soluble powder, acetamiprid solutions were moderately toxic with a 48-h oral LD50 of 8.8 (6.4, 10.0) µg a.i./bee and a 48-h contact LD50 of 9.3 (3.7, 17.5) µg a.i./bee. Bees directly sprayed had a 72-h LD50 of 153 (27, 939) mg a.i./L (dose could not be calculated in relevant application rates of µg a.i./bee or g a.i./ha) but this must be treated with extreme caution given the very wide confidence interval. Temporary abnormal behaviour was observed when bees returning to the hive were sprayed at 20 mg a.i./L but when marked bees were caged 200 m away and treated, only 36% returned to the hive. This dose had no adverse effect on bees foraging on sprayed lotus flowers. A summary stated that the 24-h contact LD50 to bees was >10 µg a.i./bee. No adverse effects on mortality, foraging activity, hive weight gain or colony population were observed when hives were located adjacent to a flowering canola field sprayed at 50 g a.i./ha with a 20% soluble powder formulation.

The 72-h LD50 to bumble bees was about 80 mg a.i./L (no confidence limits or doses in field relevant units possible) when directly sprayed, while the oral LC50 was 20.3 (14.8, 27.7) mg a.i./L. When tomato plants were sprayed at 20 mg a.i./L, there was no adverse effect on bumble bee mortality, development of larvae and foraging behaviour. Another study reported a NOEC of 200 mg a.i./L when bumble bees were directly sprayed, and no effects on two adult workers sprayed at 100 mg a.i./L; 200 mg a.i./L sprayed on tomato flowers also had no effect on foraging. Treatment of tomato plants with 14.8 g a.i./ha (3 X lower than the proposed rate of Supreme 225 SL Insecticide of 45 g a.i./ha) caused no adverse effects when bees were directly sprayed while foraging or exposed to 1 d old dried residues; bees dipped into the 0.2 g a.i./L spray solution for 5 s showed no mortality.

In a series of experiments exposing various beneficial arthropods to freshly treated (but dried) or aged residues on apple leaves treated at 13 and 100 g a.i./ha, ladybird beetle larvae were the most sensitive as leaves needed to be aged for 7 d in the low treatment before mortality decreased to that of controls, whereas even after 28 d aging in the high treatment, 26% mortality still occurred. Surviving beetles did not have reduced fecundity when allowed to reach reproductive maturity. Parasitic wasps were about as sensitive as residues needed to be aged for 7 and 21 d, respectively, before mortality decreased to that of controls, but both treatments also required 14 d aging before the fecundity of surviving wasps was similar to controls. The low treatment caused no adverse effects on mortality even when freshly dried to predatory mites or green lacewings, but they required 14 and 7 d old residues, respectively, before the high treatment caused no adverse effects. No reproduction effects were seen for either species except that mites needed 7 d old residues of the high treatment for this to occur.

In a cotton field trial, treatments of 11.2-33.8 g a.i./ha with or without Pulse Penetrant significantly reduced the abundance of transverse ladybirds at 14 DAT, but it is unknown if this effect was indirectly due to a reduction in prey cotton aphids. The parasitic wasp *Trichogramma praetiosum*, telonomid wasps and spiders were temporarily affected by some or all treatments but populations had recovered by 14 DAT (perhaps by migration from neighbouring untreated areas). Another cotton field trial at 45 g a.i./ha (twice the proposed rate in cotton but equal to that on potatoes) with Pulse Penetrant caused population declines of beneficial arthropods 4-7 d after the second treatment (which was 9 d after the first treatment).

Soil nitrification and respiration

Acetamiprid at 200 g a.i./ha (equivalent to 0.27 mg a.i./kg soil dw in the top 5 cm and 4.4 and 8.9 X higher than the proposed rate of Supreme 225 SL Insecticide in potatoes and cotton of 45 and 22.5 g a.i./ha, respectively), caused no adverse effect on soil microorganism respiration or nitrogen transformations after 28 d.

Terrestrial plants

Although not statistically significant, acetamiprid alone increased the number of rusty brown spots on cotton plants after 5 d when treated at 11-34 g a.i./ha. Phytotoxicity was significantly higher than control when Pulse Penetrant was applied at 0.2% with acetamiprid as low as 11 g a.i./ha, indicating the proposed rate in cotton of 22.5 g a.i./ha plus 0.2% Pulse Penetrant and the rate in potatoes of 45 g a.i./ha will be phytotoxic.

The company did not submit any further plant toxicity data when queried, but claimed that the proposed formulation of acetamiprid is registered on crops in many different countries at application rates higher than proposed in Australia, and therefore did not regard phytotoxicity as a concern.

Environmental Hazard

Estimated Environmental Concentrations

The maximum single application rate of Supreme 225 SL Insecticide in potatoes is 45 g a.i./ha while that in cotton is 22.5 g a.i./ha. Given a direct application to bare soil at the maximum rate, incorporation into the top 20 cm (≥85% of acetamiprid residues remained in the top 20 cm of soils in leaching experiments) and a soil bulk density of 1,300 kg/m^3, the estimated environmental concentration (EEC) of acetamiprid in soil would be 17.3 µg a.i./kg soil. Despite the maximum number of three applications per year, the aerobic soil metabolism DT50 is relatively fast (≤5.5 d) and no accumulation is expected provided at least about four weeks are allowed between applications.

In a worst-case scenario of a direct overspray of a 15 cm deep body of water with the maximum single application rate of 45 g a.i./ha, the EEC would be 30 µg a.i./L. The dissipation DT50 and DT90 values in natural water-sediment systems are relatively slow at 21-29 and 94-122 d, respectively, therefore in the worst case some accumulation may be expected depending on whether there is the maximum number of three applications per year, and the interval between applications.

Hazard to Terrestrial Organisms

The proposed use pattern of Supreme 225 SL Insecticide on potatoes and cotton will result in exposure of nontarget organisms. Due to the low maximum application rate of 45 g a.i./ha and the relatively low toxicity of acetamiprid and its major metabolites to these organisms, the acute and chronic hazards to birds, earthworms, honeybees, soil microoorganism respiration and nitrogen mineralisation processes, from a single application are expected to be low.

Transverse ladybirds, parasitic/telonomid wasps, spiders and predatory mites are expected to be adversely affected in the short term by proposed treatments. Provided recruitment of beneficial arthropods from neighbouring untreated areas is possible, these effects are expected to be temporary as residues of acetamiprid are not overly persistent. Nevertheless, acetamiprid may not be suitable for IPM programs.

Hazard to Aquatic Organisms

The direct overspray of a 15 cm deep water body with Supreme 225 SL Insecticide at the maximum application rate of 45 g a.i./ha represents an unacceptable acute hazard to aquatic invertebrates. However, the likelihood of direct repeated oversprays of natural waterways is minimal particularly if best management practices are followed. The more likely exposure through spray drift (worst case of 10% drift) reduces the hazard from the parent compound to an acceptable level for invertebrates in both acute and chronic exposures.

Parent acetamiprid, with its high solubility in water, showed high mobility and penetrated down to 20 cm in soil columns in various experiments. The major metabolites IM-1-4 and IC-0 were of medium to high mobility and IM-1-4 was detected in leachates. However in the worst case situation, the EEC from runoff was lower than the EC50/NOEC values for all aquatic organisms for which data were submitted, indicating no hazard. This is also true for the metabolites (for which ecotoxicological data were submitted) even if all the applied acetamiprid were converted to a single metabolite.

Desirable Vegetation

Individual terrestrial plants are likely to be exposed to spray drift and may be adversely affected by acetamiprid application. However, these effects should be limited and of severity low enough to not adversely affect populations of nontarget plants.

Conclusions and Recommendations

Certis Australia Pty Limited has applied for registration of a new end use product (EUP), Supreme 225 SL Insecticide which contains the new active constituent (AC) acetamiprid at 225 g a.i.(active ingredient)/L. The product will be marketed for the control of aphids in potatoes and cotton at a maximum application rate of 45 g a.i./ha three times per year.

Due to the low maximum application rate and the relatively low toxicity of acetamiprid and its major metabolites to many organisms, the acute and chronic hazards to birds, earthworms, honeybees, soil microoorganism respiration and nitrogen mineralisation processes and all aquatic organisms are expected to be low. Some beneficial arthropods (i.e. transverse ladybirds, parasitic/telonomid wasps, spiders and predatory mites) are expected to be adversely affected by proposed treatments but provided recruitment from neighbouring untreated areas is possible, these effects are expected to be temporary as acetamiprid is not persistent. Nevertheless, acetamiprid may not be suitable for IPM programs. Individual terrestrial plants are likely to be exposed to spray drift and may be adversely affected by acetamiprid application. However, these effects should be limited and of severity low enough to not adversely affect populations of nontarget plants.

EFFICACY AND SAFETY ASSESSMENT

Justification and Proposed Use Pattern

Supreme 225 SL Insecticide (225g/L acetamiprid) is a member of the chloronicotinyl insecticide group, and therefore belongs to the insecticide group 4A for resistance management purposes. Acetamiprid works by interfering with the nicotinic acetylcholine receptors, causing disruption of the nervous system and subsequent death of the target pest. Chloronicotinyl insecticides have activity on a wide range of pests, including *Hemiptera, Coleoptera*, and *Thysanoptera*. Acetamiprid exhibits translaminar systemicity, making it effective as a foliar application for control of foliar insect pests, including those that feed on the under surface of the leaves.

The applicant proposes that Supreme be used as a foliar spray on commercially grown cotton and potatoes. The label-claims are that the insects controlled are cotton aphid (*Aphis gossypii*) in cotton and green peach aphid (*Myzus persicae*) in potatoes. Control of cotton aphid is claimed in QLD, NSW, WA and NT and green peach aphid in all States'.

The proposed rate of use is 50-100mL/ha + 0.2% Pulse® Penetrant for cotton aphid, and 200mL/ha for green peach aphid.

Supreme 225 SL Insecticide will be available in 1L, 5L, 10L, 20L and 100L high-density polyethylene containers.

Evaluation of Efficacy and Crop Safety

The efficacy of Supreme was shown in good-quality data from many of the trials. Data from 10 small plot trials in cotton are presented. In general, the design, conduct and analysis of each trial were of an excellent standard. At the recommended rates, Supreme provided control of cotton aphids that was equivalent or superior to that provided by other commercial standards.

In several trials, efficacy against a range of other sucking pests and beneficial insects was assessed. The data suggest that Supreme will control other sucking pests. It was shown to be relatively soft on *Trichogramma* and *Telenomus*, important egg parasitoids of heliothis. It was also shown to be softer on 'predators' than bifenthrin and similar to endosulfan. These attributes of Supreme make it a very useful tool for use in pest management in cotton.

In potatoes, the trials showed scientific rigour with adequate replication, generally similar and high pest densities across the randomly allocated treatment plots and sound statistical analysis to support the conclusions made.

The requested rate for registration has been demonstrated to provide equivalent or, in some cases, better pest control than currently registered products.

In addition, Supreme was shown in potatoes to be relatively non-disruptive to mummification of *Myzus persicae* by parasitoids.

The data as presented were adequate to demonstrate efficacy of the product when used according to the proposed label instructions, registration of this product is therefore recommended.

POISON

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

SUPREME 225 SL

INSECTICIDE

Active Constituent: 225 g/L ACETAMIPRID

Solvents: **515 g/L DIMETHYL SULFOXIDE**
334 g/L *N*-METHYL PYRROLIDONE

GROUP 4A INSECTICIDE

* L	For the control of cotton aphid in cotton and green peach aphid in potatoes, as specified in the DIRECTIONS FOR USE Table.

(label code)

* 1, 5, 10, 20, 100 L

DIRECTIONS FOR USE

CROP	PEST	STATE	RATE	WHP	CRITICAL COMMENTS
Cotton	Cotton aphid (*Aphis gossypii*)	Qld, NSW, WA and NT only	50 – 100 mL/ha + 0.2% Pulse® penetrant	10 days (H)	Use the high rate under sustained heavy aphid pressure. If repeat applications are required, alternate with products from a different insecticide group (refer to **Cotton Aphid Resistance Management** under General Instructions).
Potatoes	Green peach aphid (*Myzus persicae*)	All States	200 mL/ha	7 days (H)	Apply as a foliar spray when infestations reach a treatment (or economic) threshold. If repeat applications are required, alternate with products from a different insecticide group (refer to **Green Peach Aphid Resistance Management** under General Instructions). It is recommended that Supreme be applied with a **non-ionic wetter**. Check manufacturer's directions for the appropriate use rate in horticultural crops.

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

WITHHOLDING PERIOD (WHP) (H = Harvest, G = Grazing)

Harvest

Cotton - DO NOT HARVEST FOR 10 DAYS AFTER APPLICATION

Potatoes - DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION

Grazing

Cotton - DO NOT GRAZE OR CUT FOR STOCK FOOD

Potatoes - DO NOT GRAZE OR CUT FOR STOCK FOOD

GENERAL INSTRUCTIONS

Insecticide Resistance Warning

GROUP 4A INSECTICIDE

For insecticide resistance management, Supreme 225 SL Insecticide is a Group **4A** Insecticide. Some naturally occurring insect biotypes resistant to Supreme and other Group **4A** Insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if Supreme and other Group **4A** Insecticides are used repeatedly. The effectiveness of Supreme on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Certis Australia Pty Ltd accepts no liability for any losses that may result from the failure of Supreme to control resistant insects. Supreme 225 SL Insecticide may be subject to specific resistance management strategies. For further information contact your local supplier, Certis Australia representative or local agricultural department agronomist.

Cotton Aphid Resistance Management
If repeat applications are required, alternate Supreme with a registered insecticide from a different chemical group. Do not apply consecutive applications of group 4A insecticides.

Green Peach Aphid Resistance Management
This use is subject to an Avcare resistance management strategy.
If repeat applications are required, alternate Supreme with a registered insecticide from a different chemical group. Do not apply consecutive applications of group 4A insecticides in any season, or between seasons.

Mixing
Shake container prior to opening. Two thirds fill the spray tank with clean water, and with the agitator operating, add the required quantity of Supreme. Top up the spray tank to the required volume with clean water with the agitator running. Add the required quantity of non-ionic wetter or Pulse penetrant after mixing is complete and spray tank is filled to the required level. Maintain agitation while spraying.

Application
Cotton
Ground application: Ensure thorough coverage of foliage. This will require a water volume of at least 50 L/ha.
Aerial application: Ensure thorough coverage of foliage. This will require a water volume of at least 20 – 30 L/ha.

Potatoes
Apply by ground or aerial application methods in sufficient water to ensure thorough coverage of infested foliage.

RE-ENTRY

Do NOT allow re-entry into treated areas until the spray deposits have dried. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing should be laundered each day.

PRECAUTION

Do NOT use human flaggers/markers unless they are protected by engineering controls such as vehicles with enclosed cabs.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
DO NOT apply under weather conditions, or from spraying equipment, that may cause drift onto nearby susceptible plants/crops, cropping lands or pastures.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
DO NOT contaminate streams, rivers or waterways with the chemical or used containers.

STORAGE AND DISPOSAL (1, 5, 10, 20 L)
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 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.

STORAGE AND DISPOSAL (100 L refillable container)
Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.
Empty container by pumping through the dry-break connection system. Do not attempt to unscrew the valve or breach the locked filling point. Do not contaminate the container with water or other foreign material.
Ensure that the coupler, pump, meter and hoses are disconnected, triple rinsed with clean water and drained after each use. When empty, or contents no longer required, return the container to the point of purchase. This container remains the property of Certis Australia Pty Ltd.

SAFETY DIRECTIONS
Poisonous if swallowed. Will irritate the eyes. Avoid contact with eyes. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), butyl rubber gloves and face shield or goggles. When using the prepared spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing). If product in eyes, wash it out immediately with water. Wash hands after use. After each days use wash gloves and face shield or goggles and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre (telephone 13 11 26).

MATERIAL SAFETY DATA SHEET
Additional information is listed in the Material Safety Data Sheet available from Certis Australia Pty Ltd.

EXCLUSION OF LIABILITY
This product as supplied is of a high grade and suitable for the purpose for which it is expressly intended and must be used in accordance with the directions. The user must monitor the performance of any product as climatic, geographical or biological variables and/or developed resistance may affect the results obtained. No responsibility is accepted in respect of this product, save for those non-excludable conditions implied by the Trade Practices Act or any State or Federal legislation.

IN A TRANSPORT EMERGENCY DIAL 000 POLICE OR FIRE BRIGADE	FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY PHONE 1800 033 111

BAR
CODE

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Certis Australia Pty Limited
ABN 28 100 543 986
Level 1, Tower B, Zenith Centre
821 Pacific Highway
Chatswood NSW 2067
Phone: (02) 8448 8155
Fax: (02) 8448 8156

(label code)

Batch Number:
Date of Manufacture:

* drummuster logo required for 5, 10 and 20 L packs

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.

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Footnote:
Updated versions of these documents are available on the APVMA website http://www.APVMA.gov.au.