Public Release Summary
on

Evaluation of the new active

CLOTHIANIDIN

in the products

Sumitomo Shield Systemic Insecticide
Sumitomo Samurai Systemic Insecticide
Sumitomo Stealth Systemic 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), the Department of the Environment and Water Resources (Risk Assessment and Policy Section) and State Departments of Primary Industries.

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 *The Manual of Requirements and Guidelines (AgMORAG and VetMORAG).*

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 at 18 Wormald Street, Symonston, ACT 2609.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Pesticides Program Manager, Australian Pesticides and Veterinary Medicines Authority, PO Box 6182, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ALP	alkaline phosphatase (an enzyme found in all body tissues)
ALT	alanine transaminase (a liver enzyme)
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	Acute Reference Dose
AST	aspartate transaminase (a liver enzyme)
BN0230M	N'-[Amino(2-chlorothiazol-5-ylmethylamino)methylene]acetohydrazide (a metabolite of clothianidin)
BN0335E2	N'-[(2-Chlorothiazol-5-ylmethylamino)(methylamino)methylene]-2-oxopropanohydrazide (a metabolite of clothianidin)
BUN	blood urea nitrogen level
bw	bodyweight
CAS	Chemical Abstracts Service
CNS	Central Nervous System
d	day
DAT	days after treatment
DEW	The Department of the Environment and Water Resources
DT_{50}	time taken for 50% of the concentration to dissipate or degrade
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
F_0	original parental generation
F_1	offspring of the original parental generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hb	haemoglobin
Hct	haematocrit
HDPE	high density polyethylene
Hg	haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
HSIS	NOHSC Hazardous Substances Information System database
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
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{oc}	organic carbon partitioning coefficient
K_{ow}	octanol-water partitioning coefficient

L	litre
lb	pound, unit of weight (= 0.454 kg)
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
LOD	Limit of Detection – level at which residues can be detected
LOEL	Lowest-Observable-Effect-Limit
LOQ	Limit of Quantitation – level at which residues can be quantified
MAI	3-methylamino-1H-imidazol[1,5-c]imidazole (a degradation product of clothianidin)
MCH(C)	mean corpuscular haemoglobin (concentration)
MCV	mean corpuscular volume
MFL	maximum feeding level
mg	milligram
MG	methylguanidine (a metabolite of clothianidin)
mL	millilitre
MNG	methylnitroguanidine (a metabolite of clothianidin)
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
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
NOHSC	National Occupational Health and Safety Commission
OC	organic carbon
OCS	Office of Chemical Safety
OM	organic matter
Pa	pascal
PBT	criteria relating to persistence, bioaccumulation potential and toxicity
PCV	packed cell volume
PHED	Pesticide Handlers Exposure Database
po	oral
P_{ow}	octanol-water partitioning coefficient
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
PTMG	clothianidin metabolite
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
TGAC	technical grade active constituent
TI-435	development code for clothianidin
TRR	total radioactive residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TMG	thiazolylmethylguanidine (a metabolite of clothianidin)
TZMU	thiazolylmethylurea (a metabolite of clothianidin)
TZNG	thiazolylnitroguanidine (a metabolite of clothianidin)
TZU	thiazolylurea (a metabolite of clothianidin)
μg	microgram

USEPA	United States Environmental Protection Agency
vmd	volume median diameter
WG	water dispersible granule
WHP	withholding period

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INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *SUMITOMO SHIELD SYSTEMIC INSECTICIDE, SUMITOMO SAMURAI SYSTEMIC INSECTICIDE* and *SUMITOMO STEALTH SYSTEMIC INSECTICIDE* which contain the new active constituent clothianidin. The product *SUMITOMO SHIELD SYSTEMIC INSECTICIDE* is for the control of aphids and mirids in cotton and for the control of rust thrips and weevil borer in bananas. *SUMITOMO SAMURAI SYSTEMIC INSECTICIDE* is for the control of woolly aphid in apples; mealybugs and codling moth in apples and pears and green peach aphid and oriental fruit moth in peaches and nectarines. *SUMITOMO STEALTH SYSTEMIC INSECTICIDE* is for control of African black beetle larvae in turf. The purpose of this summary is to inform the public of the proposed registrations and invite comment on this proposal.

Responses to this Public Release Summary will be considered prior to registration of the products. They will be taken into account by the APVMA in deciding whether the products should be registered and in determining appropriate conditions of registration and product labelling.

Copies of full technical evaluation reports on clothianidin, 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 of this document). They can also be viewed at the APVMA library located at the APVMA offices, 18 Wormald St, Symonston, ACT 2609.

Written comments should be received by the APVMA by 05 December 2007. They should be addressed to:

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Applicant

Sumitomo Chemical (Australia) Pty Ltd

Details of Products

It is proposed to register *SUMITOMO SHIELD SYSTEMIC INSECTICIDE* (SHIELD), containing clothianidin at 200 g/L as suspension concentrate formulation; *SUMITOMO SAMURAI SYSTEMIC INSECTICIDE* (SAMURAI), containing clothianidin at 500 g/kg as a water dispersible granule formulation, and *SUMITOMO STEALTH SYSTEMIC INSECTICIDE* (STEALTH) containing clothianidin at 500 g/kg as a water dispersible granule formulation.

Clothianidin is a chloronicotinyl nitroguanidine in the neonicotinoid class (Group 4) of insecticides. These compounds are acetylcholine receptor agonists/antagonists. Their mode of action is through the binding to the acetylcholine receptor and thus interfering with nerve transmission. Insects are exposed by either contact or ingestion.

Clothianidin formulations are currently registered overseas in North America and Asia.

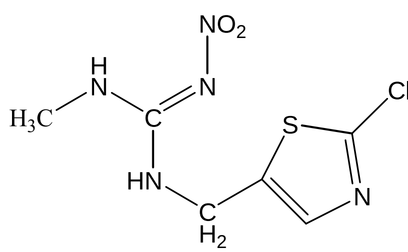
CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent clothianidin is manufactured in Japan by Sumitomo Chemical Takeda Agro Company Ltd, Hikari Plant, 4720 Takeda, Mitsui, Hikari Yamaguchi 743 8502 and is approved by the APVMA (Approval Number: 54438).

Chemical Characteristics of the Active Constituent

Common name:	Clothianidin
Development code:	TI-435
Chemical name (IUPAC):	(*E*)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
(CA):	(*E*)-*N*-[(2-chloro-5-thiazolyl)methyl]-*N’*-methyl-*N’’*-nitroguanidine
Chemical Abstracts Service (CAS) Registry Number:	210880-92-5 (formerly 205510-53-8)
Molecular formula:	$C_6H_8ClN_5O_2S$
Molecular weight:	249.7
Minimum purity:	min. 950 g/kg
Chemical structure:	



Physical and Chemical Properties of the Active Constituent (refers to active of purity 99.7% unless otherwise specified)

Physical state:	Solid, powder
Colour:	Clear and colourless
Odour:	Odourless (incl. 97.6% purity)
Optical rotation:	Not optically active
Melting point:	176.8 °C
Relative density:	1.61 g/mL, 1.59 g/mL (purity 97.6%)
Bulk density:	0.8 g/cm^3
pH:	6.24 (purity 97.6%, 23 °C)
Vapour pressure:	1.3×10^{-10} Pa (25 ºC) 3.8×10^{-11} Pa (20 °C, extrapolated)
Henry’s law constant:	2.9×10^{-11} Pa × m^3/mol (20 °C)
Water solubility:	0327 g/L (20 °C)
Octanol-water partition coeff.:	Log P_{ow} = 0.7 (25 °C)
Solubility in organic solvents (25°C):	Acetone 15.2 g/L Dichloromethane 1.32 g/L

	Ethyl acetate 2.03 g/L
	Heptane <0.00104 g/L
	Methanol 6.26 g/L
	Octanol 0.936 g/L
	Xylene 0.128 g/L
Flammability:	Not highly flammable
Explosive properties:	Not explosive (incl. 97.6% purity)
Oxidising properties:	Not an oxidising substance (colour change from purple to black noted with potassium permanganate) (incl. 97.6% purity)
Corrosion characteristics:	Not corrosive (incl. 97.6% purity)
Hydrolysis rate (dark, 25 °C):	Stable (pH 5, 7 and 9
(dark, 50 °C):	Stable (pH 4 and 7), DT_{50} = 14.4 (pH 9)
(dark, 62 °C):	DT_{50} = 14.4 d (pH 9)
(dark 74 °C):	DT_{50} = 0.7 d (pH 9)
Dissociation constant:	pK_a = 11.09 (20 °C)
Direct phototransformation:	DT_{50} = 35.4 - 37.4 min (25 °C)
Quantum yield of direct phototransformation:	$\phi = 0.014$
Storage stability:	Stable at 54 °C for 2 weeks and is expected to be stable for
at least 2 years	
Stability in the presence of metals:	Stable in the presence of elemental Zn, Fe and Al
	Stable in the presence of Zn, Fe and Al ions (acetate)
UV Spectrum (water):	Neutral: λ_{max} = 265.5 nm, $\varepsilon = 1.71 \times 10^4$ $L.mol^{-1}.cm^{-1}$
	Acidic: λ_{max} = 265.5 nm, $\varepsilon = 1.72 \times 10^4$ $L.mol^{-1}.cm^{-1}$
	Basic: λ_{max} = 246 nm, $\varepsilon = 1.34 \times 10^4$ $L.mol^{-1}.cm^{-1}$
^{1}H-NMR Spectrum:	(DMSO-d_6): δ 9.10 1H br, 8.00 1H br, 7.60 1H br, 4.50 2H d, 2.81 3H d
^{13}C NMR Spectrum:	(DMSO-d_6): δ 157.3, 150.5, 139.9, 138.5, 37.2, 28.3
Chemical family:	Neonicotinoid

Formulated Products

Distinguishing name:	***Sumitomo Samurai Systemic Insecticide***
Formulation type:	Water dispersible granule (WG)
Active constituent concentration:	Clothianidin (500 g/kg)
Mode of Action:	Agonist of the nicotinic acetylcholine receptor

Physical and Chemical Properties of the Product

Physical state:	Solid, granules
Colour:	Light tan
Odour:	Odourless
Bulk density:	0.51 g/mL
pH value:	7.02 (1% suspension in water)
Acidity/Alkalinity:	0.01% w/w as NaOH
Explosive properties:	None
Oxidising/Reducing properties:	None
Flammability:	Not flammable
Auto-flammability:	208 °C
Corrosion characteristics:	Not corrosive to HDPE bottles
Dangerous goods classification:	Not classified as a dangerous good
Storage stability:	Stability data provided by the applicant supports a storage life of at least 2 years when stored under normal conditions in high density polyethylene (HDPE) containers.
Low temperature stability:	Not applicable to solid preparations

Distinguishing name:	***Sumitomo Shield Systemic Insecticide***
Formulation type:	Suspension concentrate (SC)
Active constituent concentration:	Clothianidin (200 g/L)
Mode of Action:	Agonist of the nicotinic acetylcholine receptor

Physical and Chemical Properties of the Product

Physical state:	Liquid
Colour:	Milky white
Odour:	Mild aromatic odour
Density:	0.998 g/mL
pH value (20 °C):	7 (direct)
Explosive properties:	None
Oxidising/Reducing properties:	None
Flammability:	Not flammable
Corrosion characteristics:	Not corrosive to HDPE bottles
Dangerous goods classification:	Not classified as a dangerous good
Storage stability:	Stability data provided by the applicant supports a storage life of at least 2 years when stored under normal conditions in high density polyethylene (HDPE) containers.
Low temperature stability:	Not applicable to solid preparations

Distinguishing name:	***Sumitomo Stealth Systemic Insecticide***
Formulation type:	Water dispersible granule (WG)
Active constituent concentration:	Clothianidin (500 g/kg)
Mode of Action:	Agonist of the nicotinic acetylcholine receptor

Physical and Chemical Properties of the Product

Physical state:	Solid, granules
Colour:	Light tan
Odour:	Odourless
Bulk density:	0.51 g/mL
pH value:	7.02 (1% suspension in water)
Acidity/Alkalinity:	0.01% w/w as NaOH
Explosive properties:	None
Oxidising/Reducing properties:	None
Flammability:	Not flammable
Auto-flammability:	208 °C
Corrosion characteristics:	Not corrosive to HDPE bottles
Dangerous goods classification:	Not classified as a dangerous good
Storage stability:	Stability data provided by the applicant supports a storage life of at least 2 years when stored under normal conditions in high density polyethylene (HDPE) containers.
Low temperature stability:	Not applicable to solid preparations

Recommendation

Based on a review of the data provided by the applicant, the registrations of *Sumitomo Samurai Systemic Insecticide*, *Sumitomo Shield Systemic Insecticide* and *Sumitomo Stealth Systemic Insecticide* are supported in relation to their chemistry and manufacturing details.

TOXICOLOGICAL ASSESSMENT

The toxicity of the active constituent clothianidin

The active constituent clothianidin is new to the Australian marketplace.

The active constituent clothianidin is rapidly absorbed after oral administration in rodents, is widely distributed in the body and quickly excreted, predominantly in the urine. It was of low acute oral, dermal and inhalation toxicity in rats, but was of moderate acute oral toxicity in mice. It was not an eye or skin irritant or a skin sensitiser.

The main effects of feeding clothianidin in the diet to rats, mice and dogs were lower food consumption and bodyweight gain. There were some effects on blood cell numbers and blood chemistry and organ weights, but most of these changes occurred in short term studies at doses causing reduced food consumption and weight gains. Toxic effects were observed in several organs with little consistency among studies or between species. The liver, kidney, reproductive organs, gastrointestinal tract and immune system showed evidence of being targets for the toxic effects of clothianidin. Although there were effects on reproductive organs in some studies, there were no effects on mating or fertility. Clothianidin did not affect the development of rat or rabbit foetuses at doses that were not toxic to the mother. Special studies showed that clothianidin was not neurotoxic except on the day of administration of high doses, when it caused minor effects that were transient. It did not affect neurological development in rat foetuses or neonates.

Some batches of clothianidin caused damage to bacterial genetic material. This may have been due to the presence of an impurity, but known genotoxic impurities will be limited by requirements of compositional standards to concentrations at which no genetic damage is expected. In addition, in a range of other special studies, clothianidin did not damage genetic material. Furthermore, there was no evidence that clothianidin caused cancer in long term studies in mice and rats.

The toxicological database for clothianidin, 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 (Acceptable Daily Intake (ADI) and Acute Reference Dose (ARfD)) at which no adverse health effects in humans would be expected.

Metabolism and toxicokinetic studies

In mice given [nitroimino-^{14}C]clothianidin by oral gavage, urine was the main route of excretion (about 90% of dose). The residual concentrations of radioactivity in major tissues 7 days after administration were low and parent clothianidin was the main compound present. The metabolism of clothianidin in mice was similar to rats and involved demethylation, cleavage of the nitrogen-carbon bond between nitroguanidine and the thiazolylmethyl group, and removal of nitrate.

The toxicokinetic behaviour and metabolism of clothianidin was studied in rats using [nitroimino-^{14}C]- and [thiazolyl-2-^{14}C]clothianidin given by oral gavage. Low and repeated doses were rapidly and extensively absorbed from the gastrointestinal tract and peak plasma and tissue concentrations were achieved within 2 hours. Within 24 hours the radiolabel was almost completely eliminated, predominantly in the urine (about 90% of dose). High doses of clothianidin saturate the gastrointestinal absorptive mechanism leading to a prolonged absorption phase and a subsequent delay in excretion. The metabolites of [thiazolyl-2-^{14}C]clothianidin remain in tissues longer than metabolites of [nitroimino-^{14}C]clothianidin. The main substance (over 50% of dose) identified in blood, tissues, urine and faeces was clothianidin. The main routes of metabolism were oxidative N-demethylation and cleavage of the nitrogen-carbon bond between the thiazolylmethyl group and the nitroguanidine moiety. Other minor routes included N-oxidation and dehalogenation and the metabolism of the nitroimino moiety to give urea and guanidine derivatives. Some urinary metabolites were not found in the tissues. Other than saturated absorption and delayed elimination of high doses, the kinetics and metabolism of clothianidin were not markedly influenced by dose level, dose regimen and sex.

Acute Studies

Clothianidin was of low acute oral (LD_{50} >5000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalation (LC_{50} >6140 mg/m^3) toxicity in rats, but it was of moderate acute oral toxicity (LD_{50}= 389 mg/kg bw in females and 465 mg/kg bw in males) in mice. It was not a skin or eye irritant in rabbits and it did not induce skin sensitisation in guinea pigs.

Short-term Studies

In mice (6/sex/group) fed clothianidin in the diet at concentrations of 0, 500, 1000, 2000 and 4000 ppm, the mean achieved doses were 0, 90, 190, 383 and 683 mg/kg bw/day over the 4 weeks of treatment. Two females at 4000 ppm were found dead, and 4 males and 4 females at this dose were killed due to poor or moribund condition. Lethargy, tremors, hunched posture, piloerection, emaciation, half-closed eyes, unsteady gait, apparent hypothermia and pale extremities were observed at 4000 ppm and thin appearance and hunched posture occurred in animals treated at 2000 ppm. Body weight gains were lower at ≥1000 ppm and food consumption was lower in all treated groups. Lower RBC, Hb, PCV, MCV and MCH were observed in the surviving males at 4000 ppm. Neutrophil counts in all male groups and neutrophil and eosinophil counts of females at 2000 ppm were slightly elevated and total white blood cell counts were lower in males at 4000 ppm. Results of biochemistry tests were only available for one male at 4000 ppm since insufficient plasma was collected from the other surviving male. Plasma AST and ALT were higher in females at 2000 and the male at 4000 ppm with ALT also higher in males at 2000 ppm. The plasma concentrations of K^+ were slightly elevated in the male at 4000 ppm and in females at 1000 and 2000 ppm. Plasma Na^+ was higher in males at 2000, the male at 4000 ppm and females at 1000 and 2000 ppm and plasma Cl^- was higher in males at 2000, the male at 4000 ppm and in all treated groups of females. Glucose and triglycerides were lower in males at 2000, the male at 4000 ppm and in females at 2000 ppm. Urinary protein levels were lower in all treated male and female groups, and murine urine specific gravity was slightly increased in males at 4000 ppm. Liver and kidney weights were lower in both sexes at 2000 ppm and in males at 4000 ppm and thyroid weight was lower in males at 4000 ppm, with no histological changes observed in these organs. Testes weights were lower in males at 4000 ppm with testicular atrophy and prostate and seminal vesicles were small and had reduced amounts of colloid present. Epididymes were also small at 4000 ppm. Ovaries were small, lower in weight and had no corpora lutea and uterus walls were thinner in females at 2000 ppm. Spleen weights were lower with atrophy/reduced cellularity and thymus glands were small, lower in weight and had thymic involution in both sexes at 2000 ppm and in males at 4000 ppm. Most mice at 2000 and 4000 ppm had less adipose tissue.

In rats fed clothianidin in the diet at concentrations of 0, 1250, 2500, 5000 and 7500 ppm, the mean achieved doses were 0, 120, 249, 475, and 602 mg/kg bw/day. There were no deaths and clinical signs included eyes half closed at ≥ 5000 ppm and brown nasal staining and emaciation at 7500 ppm. Body weight gain and food consumption were lower at ≥ 2500 ppm. RBC, Hb and PCV were higher in both sexes at ≥ 2500 ppm, Hb was higher in females at 1250 ppm, and MCHC was higher in females at ≥ 2500 ppm. In males, reticulocytes, total white blood cell counts and neutrophils were lower at 5000 and 7500 ppm with all other white cell counts lower at 7500 ppm. In females, reticulocytes were higher at 7500 ppm and eosinophils were lower at ≥ 2500 ppm. Blood urea nitrogen concentration was higher in both sexes at 5000 and 7500 ppm, alkaline phosphatase activity was higher in females at 5000 and 7500 ppm, AST activity and bilirubin concentrations were higher in both sexes at 7500 ppm, and triglyceride concentrations were higher in both sexes at ≥2500 ppm. Urinary pH was increased and urinary specific gravity and protein content decreased in both sexes at 7500 ppm and in males at 5000 ppm. Spleens were smaller, weighed less and had reduced numbers of cells in the white pulp in animals at 7500 ppm and spleen weight was also lower at 5000 ppm. Thymus glands were smaller, weighed less and had reduced numbers of cells in the medulla or involution at 5000 and 7500 ppm. Prostate and seminal vesicles were smaller and had reduced amounts or no colloid present and testes were smaller, weighed less, and were atrophic at 7500 ppm. Ovaries were smaller and weighed less and uteri were smaller and had reduced mural thickness at 5000 and 7500 ppm. Distension of the colon was observed in both sexes, and small liver was observed in some males at 7500 ppm. All animals at 7500 ppm had less adipose tissue.

After application of clothianidin to the skin of rats at doses of 0, 100, 300, and 1000 mg/kg bw/day for 28 days, there were no effects of treatment, other than a transient reduction in weight gain in males at 1000 mg/kg bw/day.

In a palatability study, dogs were given clothianidin at dietary concentration of 0 ppm for 11 days, or 3000 ppm (days 1 - 3), increased to 4000 ppm (days 4 - 8) and increased to 5000 ppm (days 9 - 11). Mean achieved dose levels for the treated groups were 51.1, 50.8 and 51.8 mg/kg bw/day for days 1 - 3, 4 - 8 and 9 - 11, respectively. Body weight gain and food consumption decreased as dose increased.

The doses achieved in dogs fed clothianidin at dietary concentrations of 0, 1250, 2500, and 5000 ppm were 0, 36, 36 and 62 mg/kg bw/day in males and 0, 36, 52 and 57 mg/kg bw/day in females. Lower body weight gain and food consumption were observed at all doses, with the achieved dose in males at 2500 ppm being lower than expected due to a marked reduction in food consumption in this group. Although it was intended that treated diet be fed to animals for 4 weeks, surviving animals at 5000 ppm were killed moribund after three weeks of treatment. Two dogs at 2500 ppm were also killed. Clinical signs began as early as day 8 of treatment at 5000 ppm and included prostration, hunched posture, mucoid or discoloured faeces, salivation, dyspnoea or polypnoea, sanguinous nasal discharge, thin appearance, pale gums and dehydration at 2500 and 5000 ppm. RBC, Hb and PCV were lower in males at 5000 ppm and in females at 2500 and 5000 ppm. White blood cell count, neutrophil, lymphocyte and platelet counts were lower in males at 5000 ppm and females at 2500 and 5000 ppm. Lower ALT activity was observed in all treated groups, total protein, albumin, and inorganic phosphorus were apparent at 2500 and 5000 ppm. Total protein was lower in both sexes at 2500 and 5000 ppm and was accompanied by lower albumin in the male at 5000 ppm. At 5000 ppm, higher plasma alkaline phosphatase activity was observed in both sexes. In the male at 5000 ppm, total cholesterol and triglyceride concentrations were higher and phosphorus, chloride and glucose lower. Globulin was lower in females at 5000 ppm. Testes and ovary weights were lower, but there were no corresponding histological changes. Diffuse hypocellularity of bone marrow with increased amounts of fat, congestion of marrow sinusoid, haemorrhage in bone marrow and depletion of lymphoid cells in the thymus, spleen and mesenteric lymph nodes were observed at 2500 and 5000 ppm. A subtle increase in the incidence and severity of duodenal crypt gland dilatation accompanied by some necrotic epithelial cells within the gland occurred at 2500 and 5000 ppm. One male at 5000 ppm had a higher liver weight, which correlated with chronic inflammation, increased vacuolation and granulomatous foci. The testes/epididymides weights in this animal were about 50 and 30% lower respectively, but there were no gross morphological or histological correlates for this observation. One female at 5000 ppm had lower ovary weights with small ovaries noted at necropsy, but there were no histological effects noted in the ovaries of this animal.

Subchronic Studies

Mice fed clothianidin at dietary concentrations of 0, 100, 500, 1000 and 1500 ppm for 13 weeks had intakes of 0, 16, 82, 160 and 263 mg/kg bw/day in males and 0, 22, 107, 207, and 239 mg/kg bw/day in females. There were no deaths attributable to treatment. A higher incidence of vocalisation was noted at 1500 ppm in both sexes. Bodyweight gain was lower at 1000 and 1500 ppm, but food consumption was similar in control and treated groups. There were no ophthalmological or haematological changes as a result of treatment. There were lower BUN and glucose in both sexes and higher potassium, sodium and ALP in females at 1500 ppm. ALP and sodium were also higher in females at 1000 ppm and glucose was lower in males at 1000 ppm. Urinary pH was lower in males at 1500 ppm. Kidney weights were lower in all treated groups of males, but there were no supporting macroscopic or microscopic pathological changes in the kidney. Ovaries from females at 1500 ppm had lower numbers of corpora lutea, lower numbers of large follicles and more signs of follicular degeneration. The NOEL was 500 ppm, equivalent to 82 mg/kg bw/day in males and 107 mg/kg bw/day in females

There were no treatment related deaths in rats fed clothianidin in the diet at concentrations of 0, 100, 250, 1250 and 2500 ppm for 13 weeks. The doses received were 0, 7.7, 19.7, 96 and 189 mg/kg bw/day in males and 0, 9.4, 24, 119 and 232 mg/kg bw/day in females. Bodyweight gain was lower at 2500 ppm. PCV, Hb, and RBC were higher in males at 2500 ppm and Hb, MCH and MCHC were higher in females at 2500 ppm. ALP was higher in females at 2500 ppm. Triglyceride and phosphate were higher and glucose was lower in males at 2500 ppm with phosphate also higher in males at 1250 ppm. Urine volume was higher in both sexes at 1250 ppm and 2500 ppm. Urinary pH was higher for both sexes at 2500 ppm and specific gravity and protein were lower in females at 1250 and 2500 ppm. There was a slightly higher incidence of parenchymal inflammation and sinusoidal congestion in the livers of males at 2500 ppm. Adrenal weights were higher in females at 2500 ppm, but there were no macroscopic or microscopic changes observed in these organs. Uterus and ovary weights were higher at 1250 and 2500 ppm with fluid distension of the uterus observed at a higher incidence in all treated groups and ovaries with more corpora lutea at 2500 ppm. More females in all treated groups were in the proestrus phase of the reproductive cycle compared with most females in control group being in the diestrus phase. The NOEL was 250 ppm, equivalent to 19.7 mg/kg bw/day in males and 24 mg/kg bw/day in females.

Rats fed clothianidin at dietary concentrations of 0, 150, 500 and 3000 ppm for 13 weeks received doses of 0, 9, 28 and 202 mg/kg bw/day in males and 0, 11, 34 and 254 mg/kg bw/day in females. At 3000 ppm, food consumption was lower than controls for 1 week, resulting in lower body weight gains. RBC, Hb and Hct, total protein and phosphorus were higher in males at 3000 ppm. At 3000 ppm hepatic enzyme activities, including cytochrome P-450, aminopyrine N-demethylase, and p-nitroanisole O-demethylase were higher in both sexes, and ethoxyresorufin O-deethylase, and pentoxyresorufin O-dealkylase were higher in males only. There were no treatment-related changes in organ weights and no gross morphological changes. A higher incidence of pigment deposition in the spleen was observed in males at 3000 ppm. All changes had normalised by the end of the recovery period. The NOEL was 500 ppm, equivalent to 27.9 and 34.0 mg/kg bw/day in males and females, respectively.

In dogs fed clothianidin in the diet at concentrations of 0, 325, 650, 1500 and 2250 ppm, the doses received were 0, 9, 19, 41 and 58 mg/kg bw/day in males and 0, 10, 21, 42, and 62 mg/kg bw/day in females. There were no deaths. Lower food consumption and reduced weight gain were observed in males at 2250 ppm and some dogs at 1500 and 2250 ppm were thin towards the end of the study. Total white blood cell, lymphocyte and neutrophil counts were lower at 2250 ppm. Plasma ALT activity and albumin were lower in both sexes at 1500 and 2250 ppm and total protein was lower in females at 1500 ppm and both sexes at 2250 ppm. There were no treatment -related effects on ophthalmology, neurology, urine parameters, organ weight, gross morphology or histology. The NOEL was 650 ppm, equivalent to 19.3 and 21.2 mg/kg bw/day in males and females, respectively.

Chronic Studies

In a carcinogenicity study, mice were fed clothianidin in the diet at concentrations of 0, 100, 350, 700 and 1250 ppm. The dietary concentration of the 700 ppm group was increased progressively from 700 through 2000 to 2500 ppm for both sexes and then reduced to 2000 ppm and 1800 ppm for males and females, respectively. Mean achieved dose levels were 0, 13.5, 47.2, 171.4 and 251.9 mg/kg bw/day (males) and 0, 17, 65.1, 215.9 and 281.1 mg/kg bw/day (females) in the 0, 100, 350, 1250 and 2000/1800 ppm groups respectively. There was an increased incidence of vocalisation at 1250, 1800 and 2000 ppm. Body weight gain was lower in males at 2000 ppm and in females at 1250 and 1800 ppm and food consumption was lower in both sexes at 2000/1800 ppm. Neutrophil counts were higher and lymphocyte counts were lower in females at 1800 ppm. Heart weight was lower in males at ≥ 350 ppm and kidney weights were lower in all treated groups of males. Liver weights were lower in females at 1250 and 1800 ppm and ovary weight was higher in females at 1800 ppm. The incidence of hepatocellular hypertrophy was higher in all treated groups of males except 350 ppm and higher in females at 1250 and 1800 ppm. Tumour incidences were unaffected. A NOEL could not be established in this study since hepatocellular hypertrophy was observed at the lowest dose.

Rats were fed diets containing clothianidin at concentrations of 0, 150, 500, 1500 and 3000 ppm for 104 weeks. The mean achieved doses were 0, 8.1, 27.4, 82 and 157 mg/kg bw/day (males) and 0, 9.7, 32.5, 97.8 and 193 mg/kg bw/day (females). Survival was higher than controls in both sexes at 1500 and 3000 ppm. There were no treatment-related clinical signs, ophthalmological findings or neurobehavioural findings in a battery of functional tests. Body weight gains and food consumption were lower in both sexes at 3000 ppm and in females at 1500 ppm. Serum phosphorus was elevated in males at 3000 ppm and possibly related to higher incidences of granular material or calculus in the kidneys and associated with increased incidences of pelvic mineralisation and hyperplasia of the transitional epithelium. The incidence and severity of angiectasis in the kidney pelvis was higher in females at 3000 ppm and the incidence and severity of tubular ectasis was higher in both sexes at 3000 ppm. A higher incidence of dark foci was observed in the glandular stomach at 3000 ppm, with some correlation to increased incidences of erosion (females), haemorrhage (males) and oedema in the glandular stomach at 3000 ppm. Eosinophilic foci in the liver were observed with a higher incidence in both sexes at 3000 ppm and interstitial cell hyperplasia in the ovary was increased in incidence in all treated groups of females. Significant effects on tumour incidences were not observed. A NOEL could not be established in this study because of the increased incidence of ovarian interstitial cell hyperplasia in all treated groups of females.

Male dogs received doses of 0, 7.8, 16.6, 36.3 and 46.4 mg/kg bw/day and females received doses of 0, 8.5, 15, 40 and 52.9 mg/kg bw/day after being fed clothianidin in the diet at concentrations of 0, 325, 650, 1500 and 2000 ppm for 52 weeks. There were no deaths. Neurological and ophthalmological examinations and urinalysis did not reveal any treatment-related effects. Redness of the skin inside the ears was observed in females at 1500 ppm and both sexes at 2000 ppm. Females at 2000 ppm were thin, probably as a result of lower food consumption and lower body weight gains. White blood cell and neutrophil counts were lower in females at 2000 ppm and plasma ALT was lower in both sexes at ≥ 650 ppm. There were no treatment-related effects on organ weights or on the nature and incidence of macroscopic and microscopic lesions at necropsy. The NOEL was 325 ppm, equivalent to 7.8 and 8.5 mg/kg bw/day in males and females, respectively.

Reproduction Studies

In a two-generation dose range-finding study there were no effects on any of the measured parameters in either generation of rats fed clothianidin in the diet at concentrations of 0, 50, 100 and 1000 ppm, equivalent to 3.4, 6.6, 34.2 and 68.6 mg/kg bw/day in females and 2.9, 5.8, 29.1 and 58.9 mg/kg bw/day in males respectively.

In the main two-generation reproduction study, rats were fed clothianidin at 0, 150, 500 and 2500 ppm in the diet. There were no clinical signs related to treatment in any generation. Body weight gains were lower in adults and pups of each generation at 2500 ppm, except in adults during lactation. Body weight gain was also slightly lower in F_1 pups at 500 ppm. Food consumption was higher at 2500 ppm. Preputial separation and vaginal opening were delayed in F_1 pups and sperm motility was decreased in both generations at 2500 ppm. There were no effects on mating or fertility, but there was an increased incidence of stillbirths at 2500 ppm. Lower organ weights in adults and pups of both generations (thymus, spleen) were consistent with lower body weight gains at 2500 ppm. There were no effects of treatment on gross and microscopic pathology in reproductive and other tissues in parental animals of either generation. The NOEL for parental and reproduction toxicity was 500 ppm equivalent to 32.7 and 37.9 mg/kg bw/day, in males and females, respectively. The NOEL for neonatal toxicity was 150 ppm, equivalent to 10.2 and 11.8 mg/kg bw/day in males and females respectively.

Developmental Studies

Oral gavage doses of 0, 125, 250, 500 and 1000 mg/kg bw/day clothianidin were given to pregnant rats on days 6 to 19 of gestation in a dose range finding study. All animals treated at 1000 mg/kg bw/day died or were killed prematurely. Few faeces and a red coloured perivaginal substance were observed at 250 mg/kg bw/day and at higher dose levels, decreased motor activity, tremors, chromorhinorrhoea, ptosis, cold to touch, emaciation, dehydration, piloerection and urine-stained fur were observed. Food consumption and body weight gains and gravid uterus weights were lower in all treated groups. Foetal resorptions were higher at 250 and 500 mg/kg bw/day, resulting in reduced live litter size. Foetal bodyweights were lower at 250 and 500 mg/kg bw/day and only female foetuses were observed at 500 mg/kg bw/day. One out of seventy foetuses in 5 litters at 250 mg/kg bw/day had short snout, flexed fore/hindlimbs, curled tail, exencephaly, gastroschisis, depressed eye bulges and a short trunk. The three live foetuses from two different litters at 500 mg/kg bw/day had anasarca, two of which also had short trunk and one also had short tail and umbilical hernia.

In the main developmental study, pregnant rats were given oral gavage doses of clothianidin at 0, 10, 40, and 125 mg/kg bw/day for days 6 to 19 of gestation. No deaths or premature deliveries occurred and there were no treatment-related clinical signs. Bodyweight gain and food consumption were transiently lower at 40 mg/kg bw/day and lower throughout the study period at 125 mg/kg bw/day. There were no gross lesions at necropsy of dams. Litter parameters were similar in control and treated groups and there were no treatment-related effects at any dose level on the nature and incidence of external, soft tissue and skeletal malformations and variations. The NOEL for maternal toxicity was 10 mg/kg bw/day and the NOEL for developmental toxicity was 125 mg/kg bw/day, the highest dose tested.

Pregnant rabbits were given oral gavage doses of clothianidin at 0, 62.5, 125, 250 and 500 mg/kg bw/day from days 6 to 28 of gestation in a dose-range finding experiment. All animals treated at 125, 250 and 500 mg/kg bw bw/day died or were killed prematurely due to moribund condition or abortion. Clinical signs included dark urine at 62.5 mg/kg bw/day and above, mucoid faeces and few or no faeces at 125 mg/kg bw/day and above, decreased activity, perinasal substance, emaciation and laboured breathing at 250 mg/kg bw/day and above, and impaired or absent righting reflex, lacrimation, red substance in vagina and head tilt at 500 mg/kg bw/day. Maternal weight loss and severely reduced food consumption were observed at 125 mg/kg bw/day and above. At necropsy, there were no treatment-related gross lesions in does. There were no litters from the groups treated at 125, 250 and 500 mg/kg bw/day because of death, premature delivery, abortion or moribund sacrifice. There were no treatment-related effects at 62.5 mg/kg bw/day on litter parameters and none of the foetuses had external alterations. Detailed internal and skeletal examinations were not conducted.

In the main developmental study in rabbits, oral gavage doses of clothianidin of 0, 10, 25, 75, and 100 mg/kg bw/day were given from day 6 to 28 of gestation. Treatment-related deaths or moribund sacrifices occurred at 75 and 100 mg/kg bw/day and abortions and premature deliveries occurred at 100 mg/kg bw bw/day. Deaths were preceded by weight loss, reduced food consumption, reduced faecal output, orange urine, decreased activity and loss-of-righting reflex. Clinical signs in survivors included reduced faecal output and orange urine at ≥25 mg/kg bw/day. Bodyweight gain and food consumption were lower at 75 and 100 mg/kg bw/day. Effects on litter parameters included increased resorption and reduced live foetal weight at 100 mg/kg bw/day. There was a higher incidence of absent intermediate lobe of the lung at 75 and 100 mg/kg bw/day and reduced ossification at 100 mg/kg bw/day. The NOEL for maternal toxicity was 10 mg/kg bw/day and the NOEL for developmental toxicity was 25 mg/kg bw/day.

Genotoxicity Studies

Clothianidin was mutagenic in a bacterial reverse mutation assay with metabolic activation but only in *Salmonella* strain TA1535 and it was not mutagenic without metabolic activation. The same batch of clothianidin was clastogenic in a chromosome aberration assay in Chinese hamster lung cells *in vitro* with and without metabolic activation. It also increased the frequency of mutation in mouse lymphoma cells *in vitro* with and without metabolic activation. However, most of the observed increase in mutant frequency was due to small colonies, which is an indication of clastogenicity. The same batch of clothianidin did not induce forward mutations in Chinese hamster lung cells *in vitro* and it was not mutagenic in another bacterial reverse mutation assay. Furthermore, it did not induce unscheduled DNA synthesis in rat hepatocytes after single oral doses of 2500 and 5000 mg/kg bw and it was not clastogenic in a mouse micronucleus assay after single oral doses of 25, 50 and 100 mg/kg bw. Two other batches of clothianidin were not mutagenic in bacterial reverse mutation assays and one of them was not genotoxic in a *Bacillus subtilis* DNA repair assay.

Special studies

Neurotoxicity studies

In an acute neurotoxicity study rats were given clothianidin by oral gavage at doses of 0, 100, 200 and 400 mg/kg bw. There were no deaths and clinical signs of toxicity included tremors, decreased activity and ataxia at 400 mg/kg bw. Decreased activity, lower motor and locomotor activity, constriction of the pupils, uncoordinated righting reflex and lower body temperatures were observed in males and females at 200 and 400 mg/kg bw and males at 100 mg/kg bw were sluggish with lower motor and locomotor activity. There were no histological changes and no changes in brain or body weight that were attributable to treatment.

In two studies, male rats given clothianidin by oral gavage at 0, 20, 40 and 60 mg/kg bw or 0, 63 and 76 mg/kg bw showed no treatment-related clinical signs, no effects in a functional observation battery and no treatment-related effects on motor and locomotor activity.

Rats fed clothianidin in the diet at concentrations of 0, 150, 1000 and 3000 ppm received doses of 0, 9.2, 60 and 177 mg/kg bw/day (males) and 0, 10.6, 71 and 200 mg/kg bw/day (females) for 28 days. Body weight gains and food consumption were lower at 3000 ppm. There were no effects in functional observation battery or motor/locomotor tests and no ophthalmological, gross necropsy or histological findings related to treatment.

In a developmental neurotoxicity study, pregnant rats were fed clothianidin in the diet at concentrations of 0, 150, 500 and 1750 ppm from conception until day 22 *post partum,* equal to doses of 0, 12.9, 42.9 and 142 mg/kg bw/day during gestation and 0, 27.3, 90 and 299 mg/kg bw/day during lactation. There were no deaths and no clinical signs related to treatment. Food consumption was lower at 1750 ppm and, although there were brief periods during which maternal bodyweight gains were lower at 1750 ppm, overall they were similar in treated and control groups. The duration of gestation, mean number of implantation sites/litter, the proportion of pregnant dams producing live litters, the numbers of live and stillborn pups and dams with total litter loss were comparable in all treatment and control groups. F_1 pup bodyweight gain was lower in females at 500 ppm and in both sexes at 1750 ppm but there were no effects on physical development or gross morphology. Following weaning there were five deaths at 1750 ppm and body weight gain remained depressed initially, however it was similar in control and treated groups at the end of the study. Sexual maturation, assessed by vaginal patency and preputial separation, was unaffected by treatment at all dose levels. Brain weights were similar in control and treated groups. Morphometric measurements showed that the dentate gyrus of the hippocampus was thicker at day 12, but thinner at terminal sacrifice in females at 1750 ppm. The cerebellum was higher and the external germinal layer of the cerebellum was thinner at the day 12 sacrifice in females at 1750 ppm. Learning and memory were not affected by treatment and there were no consistent effects on motor activity.

Studies on metabolites

Seven metabolites of clothianidin identified in animals and a degradation product were investigated for acute oral toxicity and mutagenic activity in bacterial reverse mutation assays. TZNG, TZMU, TMG, MG (methyl guanidine) and MNG are all metabolites found in laboratory rodents. BN0230M (ATG-Ac or N'-[Amino(2-chlorothiazol-5-ylmethylamino)methylene]acetohydrazide) is a metabolite found in laying hens and BN0335E2 (ATMG-Pyr or N'-[(2-Chlorothiazol-5-ylmethylamino)(methylamino)methylene]-2-oxopropanohydrazide) is a metabolite found in lactating goats. MAI (3-methylamino-1H-imidazol[1,5-c]imidazole) is a product of the aqueous photolytic degradation of clothianidin.

Methyl guanidine had the highest acute oral toxicity to the rat with an oral LD_{50} value of 498 mg/kg bw. Clinical signs evoked by high dose levels of metabolites TZMU, MG, TZNG, TMG and MAI were postural abnormalities, lethargy, palpebral closure, signs of parasympathetic stimulation, and ataxia and/or tremors. BN0230M evoked tachypnea. The acute oral toxicity was not influenced by sex. Metabolites TZMU, MG, TZNG, TMG and MAI were more toxic to the rat by acute oral administration than the parent molecule (LD_{50} >5000 mg/kg bw). The metabolites from laying hens and lactating goats were both of low acute oral toxicity in rats (LD_{50} >2000 mg/kg bw). None of the metabolites showed mutagenic activity, either with or without metabolic activation, in the *Salmonella* reverse mutation assay.

Studies on impurities

TI-435-CCMT-ADDUCT had low acute oral toxicity in the rat (LD_{50} >2000 mg/kg bw,). It was not a skin sensitiser, eye or skin irritant and did not have mutagenic activity in the *Salmonella* reverse mutation assay.

TI-435-benzyltriazinone did not have mutagenic activity in the *Salmonella* reverse mutation assay.

TI-435 hexahydropyrimidine was of low acute oral toxicity in the rat (LD_{50}>2000 mg/kg bw) and was not mutagenic in the *Salmonella* reverse mutation assay.

TI 435-Triazan was of low acute oral toxicity in the rat (LD_{50} >2000 mg/kg bw), it was not an eye or skin irritant in rabbits, but it was a sensitiser in guinea pigs when tested in a maximisation test. It was not mutagenic in a *Salmonella* reverse mutation assay.

Pharmacological studies
Oral gavage administration of clothianidin to rats caused central nervous system effects such as transiently reduced spontaneous activity at 50 mg/kg bw, decreased grooming and reactivity, reduced motor activity, body tone and rectal temperature, tremor, prone posture staggering, mydriasis and deep respiration at ≥100 mg/kg bw. In addition to the effects observed at 100 mg/kg bw, decreased touch response and grip strength occurred at 200 mg/kg bw and impaired reflexes, reduced limb tone, Straub tail, cyanosis and death were observed at 400 mg/kg bw. Hexobarbital -induced sleeping time was longer at 225 mg/kg bw and body temperature was lower at 300, 1000 and 3000 mg/kg bw. Clothianidin at ≥25 mg/kg bw potentiated the ability of electric shocks to induce convulsions, but had no effect on the dose of pentylenetetrazol needed to induce convulsions. Doses of 1000 and 300 mg/kg bw reduced blood pressure, but there was no dose related effect on heart rate. Intestinal transport was slowed by doses of 75 and 225 mg/kg bw and muscle strength was reduced at 225 mg/kg bw. Doses up to 3000 mg/kg bw had no effect on blood coagulation and, in an *in vitro* study, clothianidin at 10^{-4}mol/L inhibited the contractile response to barium, but there was no effect on the agonist-induced contractile response to acetylcholine or histamine.

Toxicity of the proposed products

The product *Sumitomo Shield Systemic Insecticide* is a suspension concentrate containing clothianidin at 200 g/L. It is intended to control cotton aphid and green mirids in cotton, and weevil borer and rust thrips in bananas. The product Sumitomo Stealth Systemic Insecticide is a water dispersible granular product containing clothianidin at 500 g/kg. It is intended to control African black beetle larvae in lawns and turf. The product *Sumitomo Samurai Systemic Insecticide* is a water dispersible granular product containing clothianidin at 500 g/kg. It is intended to control insect pests in fruit.

Sumitomo Shield Systemic Insecticide was of low acute oral (LD_{50} > 2000 mg/kg bw), dermal (LD_{50} >4000 mg/kg bw) and inhalation (LC_{50} >2628 mg/m^3) toxicity in rats. The acute oral toxicity was also low in female mice (LD_{50} >2000 mg/kg bw). It was not expected to be an eye or skin irritant in rabbits or a skin sensitiser in guinea pigs. No inhalational data were supplied, however, given the low inhalational toxicity of the active constituent and the nature and concentration of the excipients, the product is expected to have low inhalational toxicity.

The products *Sumitomo Stealth Systemic Insecticide* and *Sumitomo Samurai Systemic Insecticide* have moderate acute oral but low dermal and inhalation toxicity. They are likely to be slight eye irritants but are unlikely to be skin irritants or sensitisers.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the products and their active ingredient clothianidin 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 clothianidin in schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). On the basis of acute toxicity studies submitted for Sumitomo Shield Systemic Insecticide, the NDPSC has also included clothianidin in preparations containing 20 per cent or less of clothianidin in schedule 5.

There are provisions for appropriate safety directions, warning statements and first-aid instructions on the product labels.

NOEL/ADI

The Acceptable Daily Intake (ADI) is that quantity of an agricultural compound that 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 that reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for clothianidin was established at 0.05 mg/kg bw/day based on a Lowest-Observable-Effect-Level (LOEL) of 9.7 mg/kg bw/day from the long-term study in rats and a safety factor of 200. This safety factor was used since a NOEL could not be established in this study and, at this dose, the incidence of the effect in the ovaries was only slightly higher than the historical control range.

Acute Reference Dose (ARfD)

The Acute Reference Dose (ARfD) 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 causes 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 clothianidin at which no evidence of toxicity was detected was 25 mg/kg bw in the Irwin screen (effects on CNS) tests in mice and in the rabbit developmental study. The ARfD was established at 0.2 mg/kg bw on the basis of this NOEL and using a 100-fold safety factor.

Recommendation

Based on a review of the data provided by the applicant, the registrations of *Sumitomo Samurai Systemic Insecticide*, *Sumitomo Shield Systemic Insecticide* and *Sumitomo Stealth Systemic Insecticide* are supported in relation to their human health aspects.

METABOLISM AND TOXICOKINETICS ASSESSMENT

Metabolism and toxicokinetic studies

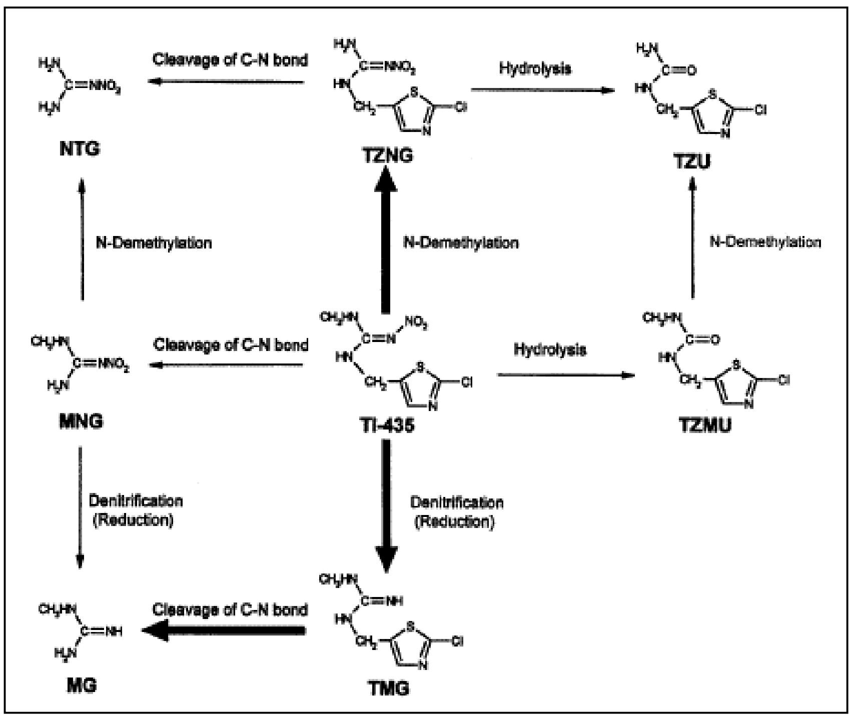
In mice given [nitroimino-^{14}C]clothianidin by oral gavage, urine was the main route of excretion (about 90% of dose). The residual concentrations of radioactivity in major tissues 7 days after administration were low and parent clothianidin was the main compound present. The metabolism of clothianidin in mice was similar to rats and involved demethylation, cleavage of the nitrogen-carbon bond between nitroguanidine and the thiazolylmethyl group, and removal of nitrate.

The toxicokinetic behaviour and metabolism of clothianidin was studied in rats using [nitroimino-^{14}C]- and [thiazolyl-2-^{14}C]clothianidin given by oral gavage. Low and repeated doses were rapidly and extensively absorbed from the gastrointestinal tract and peak plasma and tissue concentrations were achieved within 2 hours. Within 24 hours the radiolabel was almost completely eliminated, predominantly in the urine (about 90% of dose). High doses of clothianidin saturate the gastrointestinal absorptive mechanism leading to a prolonged absorption phase and a subsequent delay in excretion. The metabolites of [thiazolyl-2-^{14}C]clothianidin remain in tissues longer than metabolites of [nitroimino-^{14}C]clothianidin. The main substance (over 50% of dose) identified in blood, tissues, urine and faeces was clothianidin. The main routes of metabolism were oxidative N-demethylation and cleavage of the nitrogen-carbon bond between the thiazolylmethyl group and the nitroguanidine moiety. Other minor routes included N-oxidation and dehalogenation and the metabolism of the nitroimino moiety to give urea and guanidine derivatives. Some urinary metabolites were not found in the tissues. Other than saturated absorption and delayed elimination of high doses, the kinetics and metabolism of clothianidin were not markedly influenced by dose level, dose regimen and sex.

RESIDUES ASSESSMENT

Metabolism - plants

The metabolism of clothianidin was examined in sweet corn, sugar beet, tomato, and apples. In plants clothianidin is the predominant residue observed across all crops tested, following a range of routes of application including foliar application, seed treatment and soil application. Two major metabolites methylguanidine (MG) and methylnitroguanidine (MNG), constituted the largest proportion of the minor metabolites observed. A number of minor metabolites each constituting around 10% of the TRR were also observed and these are tabulated below. Both compounds are products of mammalian metabolism and in comparison to clothianidin are not considered of neurotoxicological significance. The remaining metabolites observed in plants, thiazolylmethylguanidine (TMG), thiazolylnitroguanidine (TZNG) and thiazolylmethylurea (TZMU) are considered to be of neurotoxicological significance. Of TZNG and TZMU only TZMU exceeds the 10% threshold. The USEPA[1] have indicated that the absence of the nitro group in this compound significantly diminishes its neurotoxicity and it is considered of less toxicological significance than clothianidin.



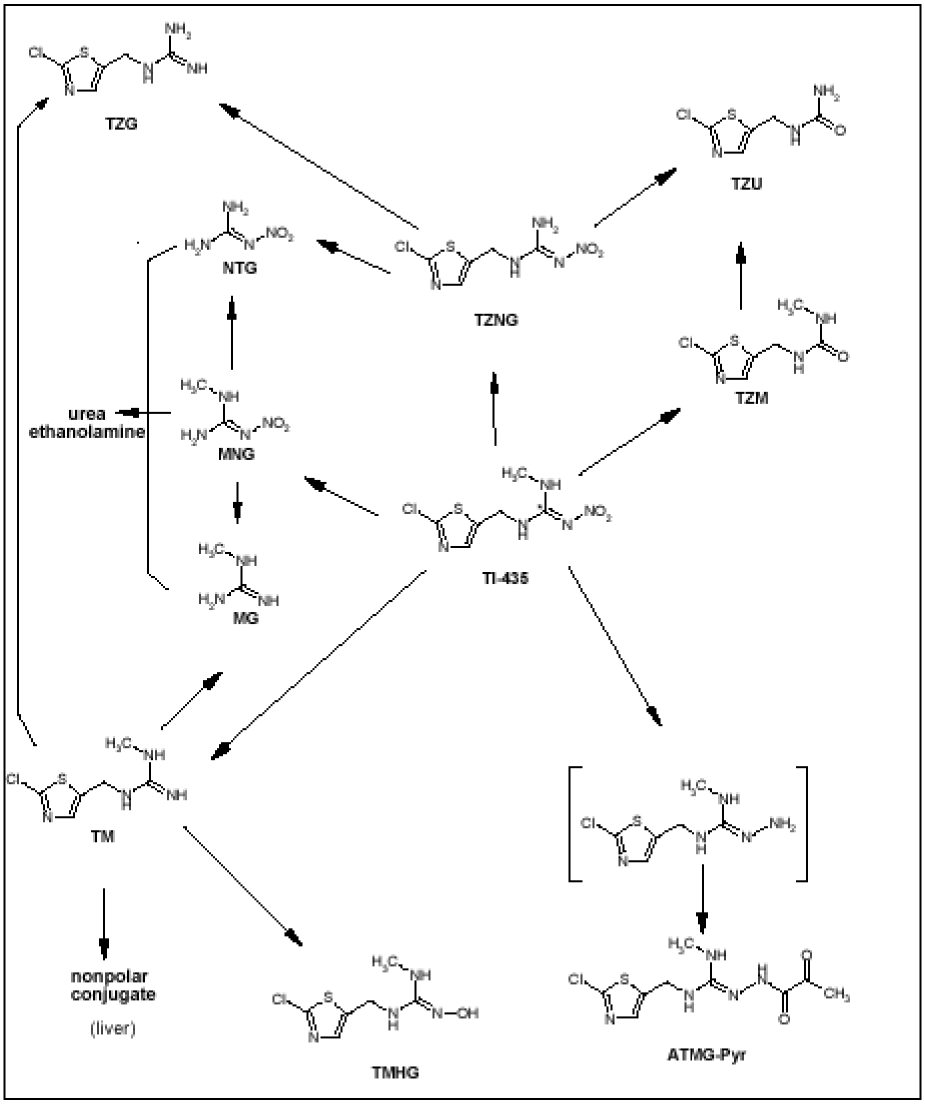
The proposed transformation pathway observed in plant commodities is shown below:

Metabolism - animals

In goats, the data demonstrate that parent clothianidin is the predominant component of radioactive residues in milk, muscle and fat. Parent compound was not observed in either liver or kidney. Thiazolylurea (TZU), TZMU and *N*'-[(2-Chlorothiazol-5-ylmethylamino)methylene]-2-oxopropanohydrazide (ATMG-Pyr) are the main metabolites present in kidney. These metabolites were also significant minor metabolites present in muscle. With the exception of ATMG-Pyr, these metabolites were also recorded in fat. TMG is the predominant radioactive component in liver, no other metabolites above 10% were observed in this tissue. TZNG was observed at levels of 14.50% TRR in milk but not observed in other tissues.

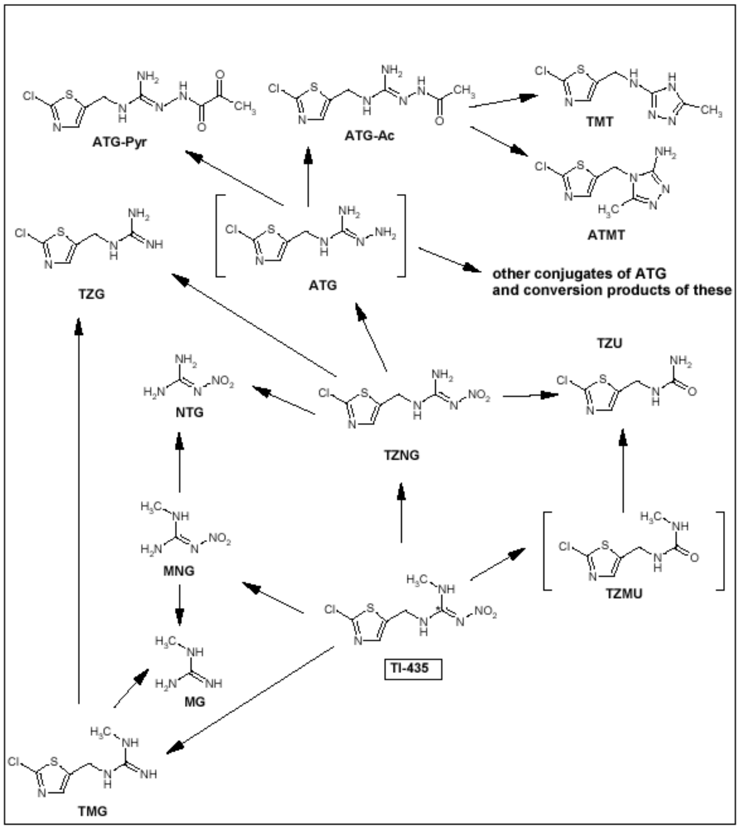
[1] MARC review of TI-435 residues of concern in plants, livestock, rotational crops and drinking water TXR No. 0051852

The proposed transformation pathway observed in goats is shown below:



In contrast to the goat studies parent compound was not the predominant residue in poultry tissues. TZNG is the major component of the recovered radioactivity in poultry liver, fat and eggs. Other metabolites, which are present at appreciable levels, are chlorothiazolymethylguanidine (TZG) and an acetohydrazide derivative of amino-chlorothiazol methylguanidine (ATG-Ac).

The proposed transformation pathway observed in poultry is shown below:



Analytical methods

Determination of clothianidin residues in plant tissues and animal tissues other than fat and milk

Samples were extracted using acetonitrile/water and filtered over diatomaceous earth if necessary. Filtrates were concentrated and cleaned up by solid phase extraction prior to elution, evaporation and dissolution in acetonitrile. Samples were analysed by reverse phase LC/MS/MS, with validation against an internal standard of deuterated clothianidin.

Determination of clothianidin residues in fat and milk samples

Milk samples were directly purified by solid phase extraction and eluted with an appropriate solvent, then made up to volume in acetonitrile. Fat samples were extracted with acetonitrile/water/hexane, centrifuged and partitioned against hexane, then the polar phase was concentrated and purified by solid phase extraction before elution and making up to volume with acetonitrile. Samples were analysed by reverse phase LC/MS/MS, with validation against an internal standard of deuterated clothianidin.

Analytical method validation

The linearity of detector response was tested in fortified solvent and in representative matrices, over 9 concentration levels between 0.0005-0.2 mg/L. Linearity calculations gave correlation coefficients between 0.998-1.000.

Table 1: Validation data for clothianidin and its metabolites in plant and animal matrices

Sample matrix	Analyte	Technique	LOQ, mg/kg
Sugar beet (root and tops), Rape (green material, straw and seed), Sunflower (plant and grain), Wheat (green material, grain and straw) Corn (plant, cob, grain and straw)	Clothianidin (only)	HPLC/MS/MS	0.02
Meat Liver Kidney Fat	Clothianidin TZG TZU PTMG	HPLC/MS/MS	0.02
Milks	Clothianidin TZG TZU PTMG	HPLC/MS/MS	0.01

Independent laboratory analyses of the method were undertaken for plant and animal materials. Acceptable recoveries (within APVMA guidelines 75 –120%) were obtained for clothianidin in plant samples at the LOQ 0.01 mg/kg, and for clothianidin, TZG, TZU and ATMG-Pyr in animal liver samples at the LOQ of 0.02 mg/kg.

Residue definition

Residues of clothianidin are likely to be detected in treated pome fruit and stone fruit, but not in cottonseed or banana. Available data shows that quantifiable residues of clothianidin are unlikely to be found in the tissues, milk or eggs of stock fed commodities derived from treated crops. Analytical methods are available for the determination of clothianidin in plant and animal commodities with LOQs of 0.01-0.02 mg/kg. Therefore, the following residue definition is recommended for clothianidin for the purposes of dietary exposure assessment and for compliance and monitoring:

Compound	Residue
Clothianidin	Clothianidin

Storage stability

The stability of pesticide residues in stored analytical samples of sugar beet (root), rape (seed), milk, meat, kidney, liver and fat samples (after extraction) was examined. Residues in the analytical (final) extracts were stable for at least 4 weeks of refrigerator storage.

A freezer storage stability study was conducted with sugar beet (root), corn (grain, forage, straw), and canola (seed) fortified with clothianidin (0.2 mg/kg). Samples were stored frozen at nominal intervals of 1, 3, 6, 12, 18 and 24 months.

After 24 months (nominal) of frozen storage, negligible decomposition, expressed in terms of the corrected recovery in the stored sample, was observed in corn (grain, forage, straw), sugar beet (root), and canola (seed). Clothianidin can be described as stable in the matrices chosen following storage at –20^{o}C for 24 months.

No data were submitted examining the stability of potentially neurotoxic metabolites in the matrices of concern. The data demonstrate that clothianidin is stable in animal tissues, seed, oil seed and plant matter for 24 months under frozen storage conditions.

Residue trials

Sumitomo Samurai Systemic Insecticide

The proposed uses of *Sumitomo Samurai Systemic Insecticide* in Australia are dilute foliar application to apples and pears at 20 g ai/100 L for control of woolly aphid, longtail mealybug, tuber mealybug, codling moth and oriental fruit moth, soil drench application to apples and pears at 1.25-2.5 g ai/tree for control of woolly aphid, and dilute foliar spray application to peaches and nectarines at 20 g ai/100 L or 5 g ai/100 L respectively for control of oriental fruit moth and green peach aphid.

Pome fruit

The applicant submitted a total of ten Australian trials in apples and pears to support the foliar use pattern. Only one trial in apples demonstrated residues (0.65 mg/kg) above the proposed MRL of 0.5 mg/kg following application at the rate 2x rate. Residues in the remaining trials were below 0.5 mg/kg at 21 days after treatment. Processing data demonstrated there was no concentration of residues into processed commodities. A further three trials were submitted in support of the soil drench treatment. Following a soil drench application to apples there were no detectable residues in fruit harvested in the following two seasons (56–371 DAT).

Stone fruit

The applicant has conducted eight separate trials on peaches and nectarines using foliar application at rates of 20, 30, 40, 60 and 80 g ai/100L. Sufficient data were provided to allow for MRLs of 2 mg/kg for FS 0245 Nectarines and FS 0247 Peaches to be established in conjunction with a 21 day WHP.

Sumitomo Shield Systemic Insecticide

The proposed uses of *Sumitomo Shield Systemic Insecticide* in Australia are application to cotton at rates of 25-50 g ai/ha for control of aphids and mirids, and stem injection and stem spray in bananas at 0.6 g ai/tree or 0.9 g ai/tree respectively for control of rust thrips.

Bananas

Twelve trials on banana either a stem spray and stump injection techniques at rates ranging from 0.5-3x the proposed rate were submitted. Residues at the LOQ (0.02 mg/kg) following a stem injection at 1x the proposed rate were detected in a single trial. Residues in all other trials were <LOQ.

Cotton

Five trials on cotton at 1 and 2x the proposed maximum rate were submitted. No detectable residues were observed in seed 5 DAT.

The following MRLs are recommended:

Compound	Food		MRL (mg/kg)
Clothianidin	FP 0226	Apple	0.5
	FI 0327	Banana	*0.02
	SO 0691	Cotton seed	*0.02
	FS 0245	Nectarines	2
	FS 0247	Peaches	2
	FP 0230	Pear	0.5

*Indicates that the MRL is established at or about the limit of analytical quantitation.

The following withholding periods are required in conjunction with the above MRLs:

Crop	Withholding period
Apples, pears	DO NOT harvest for 21 days after application. DO NOT graze treated area or cut treated area for stock feed.
Bananas	Not required when used as directed.
Cotton	DO NOT harvest for 5 days after application. DO NOT GRAZE TREATED COTTON CROPS OR CUT FOR STOCK FEED.
Peaches and nectarines	DO NOT harvest for 21 days after application.

Animal feeds
Apple pomace is commonly used as a stockfeed, as are cotton by-products such as cottonseed meal and hulls.

Processing data was supplied for apples. Apples were sprayed with clothianidin at 47 g ai/100 L (2.35X the normal application rate). At 7 days after application, residues in whole apples were 0.38 mg/kg. After washing and enzymatic juice extraction, residues in wet pomace and juice were 0.092 mg/kg and 0.052 mg/kg respectively, giving processing factors of 0.24 and 0.14 for wet pomace and juice. As residues in pomace are not likely to exceed those in whole apples, an MRL for apple pomace is not required.

The label includes an instruction not to graze treated cotton crops or cut them for stockfeed. Cottonseed may be fed to livestock, however the MRL is proposed at the limit of quantitation for clothianidin.

Crop rotation

Rotational crop residue studies were provided for turnips (root crop), wheat (cereal), and mustard greens (leafy vegetable) planted at intervals of 1, 4, 8 and 12 months after the harvest of corn grown from seed treated at an exaggerated rate of 2 mg ai/seed. Clothianidin residues in turnip roots and tops, and wheat forage, hay, straw and grain were below the limit of quantitation at all plant-back intervals. In mustard greens, residues were below the LOQ for all trials, except one trial at 4 months and one at 8 months, where low residues of 0.01 mg/kg and 0.02 mg/kg respectively were observed. Given that the seed treatment rate is highly exaggerated, and the proposed use in cotton is a foliar application where the foliage will capture the majority of the spray, residues of clothianidin are unlikely to occur in rotational crops. Therefore plant back periods for rotational crops are not required.

Animal commodity MRLs

A feeding study was conducted in lactating cattle. Animals were dosed daily with clothianidin for 28 days at levels of 0, 4.6, 15.7, and 49.5 mg/animal/day, corresponding to 0, 0.28, 0.84 and 2.8 mg/kg in feed. No residues were detected in the milk, meat, fat, liver or kidney of the animals fed 4.6 or 15.7 mg/animal/day. Low levels (at the limit of quantitation) were detected in the tissues and milk of one animal in the 49.5 mg/animal/day group. The lowest feeding level was approximately twice the anticipated dietary burden of stock feed on commodities derived from treated crops. Therefore, MRLs at the limit of quantitation are proposed for mammalian meat, offal and milk.

No poultry animal transfer studies were submitted. Given that the expected dietary burden in poultry is low (0.0015 mg/kg bw/day), metabolism data can be considered in place of a feeding study. Laying hens were administered nitroimino-^{14}C-clothianidin orally for three days at a daily dose of 10 mg/kg bw, equivalent to

76.5 ppm in feed. The administered dose was 2500 times that expected as a result of feeding treated apple pomace and cottonseed to poultry. Scaling the highest residues observed in muscle, liver, kidney, fat and eggs to the expected dietary burden indicates that residues of clothianidin are unlikely to be detected in poultry commodities. Therefore, MRLs at the limit of quantitation are supported for poultry meat, offal, and eggs.

Based upon the feeding and metabolism studies, and the dietary burden calculations for stock, the following animal commodity MRLs are recommended:

Edible offal (mammalian)	*0.02 mg/kg
Eggs	*0.02 mg/kg
Meat (mammalian)	*0.02 mg/kg
Milks	*0.01 mg/kg
Poultry meat	*0.02 mg/kg
Poultry, edible offal of	*0.02 mg/kg

Estimated dietary intake

The chronic dietary intake risk for clothianidin has been assessed. The ADI for clothianidin is 0.05 mg/kg bw/day, based upon a LOEL of 9.7 mg/kg bw/day and a 200-fold safety factor. The NEDI of clothianidin is equivalent to 1.2% of the ADI. The acute reference dose (ARfD) for clothianidin is 0.2 mg/kg bw, based on a NOEL of 25 mg/kg bw and a 100-fold safety factor. The highest NESTI for clothianidin was calculated at 17.1% (for nectarines in 2-6 year olds). It is concluded that the acute and chronic dietary exposure to clothianidin is low and the risk from residues in food is acceptable when *Sumitomo Samurai Systemic Insecticide* and *Sumitomo Shield Systemic Insecticide* are used according to label directions.

Bioaccumulation potential

The octanol-water partition coefficient (log K_{OW}) of clothianidin is 0.7, indicating it is unlikely to preferentially partition into fat, or bio-accumulate. No preferential partitioning was observed in the metabolism or animal transfer studies.

Spray drift.

With respect to livestock feeding on pasture contaminated by spray drift, required no spray zones were calculated to achieve the maximum feeding level (MFL) of 2.80 mg a.i./kg in the dry feed. It is considered that aerial and ground buffers are applicable to cotton only due to the application techniques uses in the other crops. The potential for spray drift of from aerial application was determined using AgDRIFT® in combination with, parameters representative of realistic application situations and in accordance with label directions. From a residues perspective, it was determined that 'no spray zones' were not required for ground or aerial application.

Recommendations

The following amendments to the *MRL Standard* are recommended in relation to the proposed uses of *Sumitomo Samurai Systemic Insecticide* and *Sumitomo Shield Systemic Insecticide*:

Table 1

Compound	Food		MRL (mg/kg)
ADD:			
Clothianidin	FP 0226	Apple	0.5
	FI 0327	Banana	*0.02
	SO 0691	Cotton seed	*0.02

	MO 0105	Edible offal (mammalian)	*0.02
	PE 0112	Eggs	*0.02
	MM 0095	Meat (mammalian)	*0.02
	ML 0106	Milks	*0.01
	FS 0245	Nectarines	2
`	FS 0247	Peaches	2
	FP 0230	Pear	0.5
	PO 0111	Poultry, edible offal of	*0.02
	PM 0110	Poultry meat	*0.02
DELETE:			
Clothianidin	FP 0226	Apple	T0.5
	FI 0327	Banana	T*0.02
	SO 0691	Cotton seed	T*0.02
	MO 0105	Edible offal (mammalian)	T*0.02
	MM 0095	Meat (mammalian) [in the fat]	T*0.02
	ML 0106	Milks	T*0.01
	FS 0245	Nectarines	T2
	FS 0247	Peaches	T2
	FP 0230	Pear	T0.5

*MRL set at the limit of quantitation.

Table 3

Compound	Residue
DELETE:	
	{T} For commodities of plant origin: Clothianidin
	{T} For commodities of animal origin: Sum of clothianidin, 2-chlorothiazol-5-ylmethylguanidine, 2-chlorothiazol-5-ylmethylurea, and the pyruvate derivative of N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine, expressed as clothianidin
ADD: Clothianidin	Clothianidin

The following withholding periods are required in conjunction with the above MRLs:

Crop	**Withholding period**
Apples, pears	DO NOT harvest for 21 days after application. DO NOT graze treated are or cut treated area for stock feed.
Bananas	Not required when used as directed.
Cotton	DO NOT harvest for 5 days after application. DO NOT GRAZE TREATED COTTON CROPS OR CUT FOR STOCK FEED.
Peaches and nectarines	DO NOT harvest for 21 days after application.

Commodities exported, destination and value of exports

Pome and stone fruit are recognised as major export commodities, thus the presence of detectable residues in these commodities has the potential to prejudice trade.

The following information on the export of pome and stone fruit was obtained from 'The Australian Horticultural Statistics Handbook 2004'.

Apples

In 2002-2003 the total exports of Australian apples were 32 478 tonnes worth an estimated $41.374 million. The major export markets are shown below.

Table 1 2002-2003 the total exports of Australian apples

Importing country	*2001/02*		*2002/03*	
	tonnes	*$'000*	*tonnes*	*$'000*
United Kingdom	2 263	6 715	3 749	8 494
Malaysia	4 994	5 486	6 566	6,984
India	4 585	5 323	7 323	7 635
Singapore	3 528	4 411	2 240	2 725
Sri Lanka	2 898	2 965	4 182	4 015
Bangladesh	1 381	1 447	1 500	1 361
Hong Kong	379	456	830	880
Taiwan	1 543	2 270	2 929	4 589
Indonesia	850	1 374	687	944
Japan	125	358	109	336
Other	2 391	3 673	2 365	3 411
Total	24 937	34 478	32 480	41 374

Pears

In 2002-2003 the total exports were 17652 tonnes worth an estimated $22.406 million. The major export markets are shown below.

Table 2 2002-2003 exports of Australian pears

Importing country	*2001/02*		*2002/03*	
	tonnes	*$'000*	*tonnes*	*$'000*
Singapore	3 360	4 473	4 437	5 273
Malaysia	3 529	3 912	3 537	4 239
Indonesia	2 479	3 111	2 843	3 815
Hong Kong	1 001	1 268	670	874
New Zealand	1 336	1 524	1 910	2 143
Canada	1 811	2 225	2 099	2 635
Netherlands	170	198	192	181
Fiji	160	193	225	221
India	323	400	225	320
Switzerland	82	116	64	120
Other	1 761	2 423	1 467	2 135
Total	16 282	19 813	17 652	22 406

Peaches
In 2002-2003 the total exports were 1587 tonnes worth an estimated $5.543 million. The major export markets are shown below.

Table 3 2002-2003 exports of Australian peaches

Importing country	2001/02		2002/03	
	tonnes	*$'000*	*tonnes*	*$'000*
Singapore	327	906	262	890
United Arab Emirates	257	780	235	771
Taiwan	505	1 747	593	2 065
Malaysia	177	286	65	219
United Kingdom	73	227	55	120
Hong Kong	107	355	122	423
Saudi Arabia	56	216	47	200
France	32	195	35	222
Thailand	13	61	4	15
Bahrain	22	67	17	51
Other	69	278	152	567
Total	1 638	5 118	1 587	5 543

Nectarines
In 2002-2003 the total exports were 7972 tonnes worth an estimated $22.693million. The major export markets are shown below.

Table 4 2002-2003 exports of Australian nectarines

Importing country	2001/02		2002/03	
	tonnes	*$'000*	*tonnes*	*$'000*
Taiwan	4 167	14 923	3 518	11 469
Hong Kong	4 065	9 969	3 662	8 762
Singapore	145	483	197	555
France	34	208	28	176
United Arab Emirates	139	400	123	378
Malaysia	123	307	151	362
Saudi Arabia	23	108	17	74
United Kingdom	76	250	78	292
Germany	1	11	0	0
Other	103	296	185	594
Total	8 876	26 955	7 972	22 693

Detectable residues of clothianidin may occur in pome fruit and stone fruit, and therefore, may prejudice trade in these commodities. To mitigate the potential risk to trade, a trade statement has been included on the product label:

'Treated fruit for export to particular destinations outside Australia may require a longer interval before harvest to comply with residues standards of importing countries. Please contact your industry body, exporter or Sumitomo Chemicals Australia before using Sumitomo Samurai Systemic Insecticide.'

Pomace, derived from apples treated with clothianidin, may be used as a livestock feed. The feeding of this commodity to livestock is not expected to result in detectable residues in animal commodities, and thus prejudice trade in animal commodities.

Detectable residues of clothianidin are unlikely to be found in treated cottonseed or bananas following use in accordance with label directions.

The feeding of cottonseed to livestock is unlikely to result in detectable residues in animal commodities. It is considered that the proposed use of clothianidin in cotton and banana is unlikely to unduly prejudice trade.

Overseas registration status

Codex MRLs have not been determined for clothianidin. The following relevant MRLs are established in other countries:

Table 2: Relevant overseas registration use pattern and tolerances.

Country	Formulation	Crops	Method of treatment	Dosage	PHI (days)	No. of Application	MRL (ppm)
Korea	8%WSG	Apple	Spray	X2000	7	3	1.0
		Pear	Spray	X2000	14	3	0.5
	8%WP	Apple	Spray	X2000	7	3	1.0
		Pear	Spray	X2000	10	3	0.5
		Peach	Spray	X2000	14	3	0.5
	8%SC	Apple	Spray	X2000	7	3	1.0
		Pear	Spray	X2000	10	3	0.5
Japan	16WSG	Peach	Spray	X2000-4000	7	3	0.5
		Pear	Spray	X2000 or X4000	14	3	0.5
		Apple	Spray	X2000-4000	7	3	0.5
USA	50WDG	Apple, pear	Spray	224 lb ai/acre	7	1	1.0*
Canada	50WDG	Apple, pear	Spray	-	-	-	-

Tolerance of each crop in Japan has not been determined by the Food Sanitation Law.

*Proposed tolerance

Potential risk to trade

Export of treated produce containing finite (measurable) residues of clothianidin may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

Commodities relevant to the current application are exported and detectable residues may occur above the standards of key export markets. Accordingly, a determination of undue prejudice to trade or commerce should be made following the completion of the trade consultation process.

The relevant industry groups should be given the opportunity to comment on the perceived level of risk and whether any industry-initiated strategies are required to manage the risk.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

The data provided in the acute studies submitted by Sumitomo Chemical Australia Pty Ltd were relied on by the OCS in considering whether the proposed use of the products would pose an undue health risk to the public. As no worker exposure studies were provided, the Office of Chemical Safety performed risk assessments using surrogate exposure data. The risk assessments indicated that the likely occupational exposure for mixer/loaders and applicators was sufficiently low to avoid the need for mitigation. Similarly, post-application exposure was considered to be low so no re-entry interval statements were required. First aid instructions for the active constituent have been established.

Sumitomo Shield Systemic Insecticide is intended to control cotton aphid and green mirids in cotton, and weevil borer and rust thrips in bananas. For use in cotton, it is to be applied twice per season (September to February) by aircraft or tractor mounted spraying equipment. For aerial application, the product is mixed with water and surfactants at 250 mL/30 L (0.83% product and 0.17% active in spray) and applied at 30 L/ha spray volume. The estimated maximum area treated per day is 300 ha (that is, 75 L product, 15 kg active per day). For ground application, the product is mixed with water and surfactants at 250 mL /100 L (0.25% product and 0.05% active in spray), and applied at 100 L per ha. The estimated maximum area treated per day will be 50 ha (i.e., 12.5 L product, 2.5kg active per day, default for boomspray). For use in bananas, the product is applied once per season (February to May) by stem injection or stem spray.

Sumitomo Stealth Systemic Insecticide is to be used on turf and lawns for the control of African black beetle larvae. The product is mixed in water at 400-600 g per minimum of 400 L. The dilution is applied at a minimum of 400 L per ha. The product is applied once or twice per year, usually between September and February. Application is via hand-held or backpack spray packs or low volume boom sprays. The applicant estimates that typically a maximum of 1 ha is treated per day.

Sumitomo Samurai Systemic Insecticide is used for the control of woolly aphid, long-tail and tuber mealy bug, codling moth in apples and pears; oriental fruit moth in pears; and oriental fruit moth and green peach aphid in peaches and nectarines. The product is applied using air blast applicator up to three times per year between September and February. It is diluted in water at 40 g product to 100 L water and surfactant. The applicant advises that up to 4000 L of diluted product may be used per day. The product may also be used as a soil drench, diluted in water at 2-5 g per 1 L and applied at 1 L per tree at the base.

In the absence of worker exposure data or appropriate models to estimate worker exposure during use of the products, the OCS used the Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Guide to estimate worker exposure during mixing, loading and application of the products. Based on the risk assessments, no personal protective equipment is required when using the products and there is no requirement for re-entry statements. *Sumitomo Shield Systemic Insecticide*, *Sumitomo Samurai Systemic Insecticide* and *Sumitomo Stealth Systemic Insecticide* can be safely used by workers when handled in accordance with the instructions on the product labels.

Clothianidin is not listed on the NOHSC Hazardous Substances Information System (HSIS) Database (NOHSC, 2005). Based on the repeat dose effects, the OCS classified clothianidin as a hazardous substance, in accordance with NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004), and assigned the following risk phrase:

R48/22 Danger of serious damage to health by prolonged exposure (oral route)

The OCS classified products containing 10% or more clothianidin as hazardous with this risk phrase.

Based on the acute oral toxicity of the product and the concentration of hazardous ingredients present, the OCS classified *Sumitomo Shield Systemic Insecticide* as a hazardous substance and assigned the following risk phrase:

R48/22	Danger of serious damage to health by prolonged exposure (oral route)

Based on the acute oral toxicity of the products and the amount of a hazardous substance present, the OCS classified *Sumitomo Stealth Systemic Insecticide* and *Sumitomo Samurai Systemic Insecticide* as hazardous substances and assigned the following risk phrases:

R22	Harmful if swallowed
R48/22	Danger of serious damage to health by prolonged exposure.

Recommendation

Based on a review of occupational health and safety details provided by the applicant, the registrations of *Sumitomo Samurai Systemic Insecticide*, *Sumitomo Shield Systemic Insecticide* and *Sumitomo Stealth Systemic Insecticide* are supported.

ENVIRONMENTAL ASSESSMENT

Environmental Degradation and Metabolism

Degradation

Hydrolysis

Clothianidin was found to be stable to hydrolysis at pH 5, 7, and 9 at 25°C. Significant degradation occurred only at elevated temperature and pH 9. A half-life of 1401 days was extrapolated for the hydrolysis at 20ºC and pH 9.

Aqueous Photolysis

The photolytic degradation of [nitroimino-^{14}C]- and [thiazolyl-2-^{14}C]-labeled clothianidin was investigated in a sterile aqueous buffer solution at pH 7, and in natural US river water. Clothianidin degraded rapidly in the sterile solution when exposed to simulated sunlight for 18 days. DT_{50}-values of 3.4 hours (nitroimino-label) and 3.1 hours (thiazolyl-label) were calculated (mean DT_{50} of the 2 substances was 3.3 hours). Clothianidin also degraded fairly rapidly in river water when exposed to natural sunlight for 29 days during the summer (July/August, Germany). The calculated DT_{50}-values were 25.0 hours for the nitroimino-label study and 27.8 hours for the thiazolyl-label study (first-order degradation). The mean DT_{50} for the two studies was calculated to be 26.6 hours.

Six major degradates were identified in sterile water: MG, TZMU, HMIO, MU, formamide (FA), and MIT. The concentrations of TZMU, HMIO, FA and MIT reached a peak during the study and began to decrease by the end of the study. The concentration of MG and MU had not peaked by the end of the 18-day study. Up to 34% of the applied radioactivity was photo-mineralised to CO_2 in sterile water. The major photolytic degradation products formed in river water were: MG, HMIO, MU, urea, TMG, MAI and CTCA. The degradation products decreased in concentration after having reached their peak concentrations, with the exception of MG (46.5% at the end of the study) and MU (12%). Up to 29% of the applied radioactivity photo-mineralized to CO_2 in river water.

Quantum yield measurements for direct photodegradation in aqueous solution indicated half life times of 3.38 days in winter and 1.1 day in summer under Australian latitudinal conditions.

Photolysis on soil

Photodegradation of clothianidin on surface soil (Howe sandy loam) maintained at 20ºC was investigated using [guanidine-^{14}C]-labeled test substance for a maximum of 17 days, under artificial sunlight. An experimental DT_{50} of 8.2 days ($R^2 = 0.973$; first-order linear regression) was calculated. The experimentally determined DT_{50} was equated to natural sunlight at intensive solar conditions (Phoenix, Arizona/USA, 33º latitude, midsummer sunlight conditions). For this condition, a DT_{50} of 34 summer solar days was calculated.

No major metabolites, but a large number of minor metabolites, were formed during the study, and therefore no degradation pathway could be determined. Up to 37% of applied radioactivity was bound residue.

Aerobic soil metabolism

The route and rate of aerobic degradation of clothianidin in soil was investigated in two studies. The first study was performed in 3 soils from Europe and one soil from the United States, using [nitroimino-^{14}C] and [thiazolyl-2-^{14}C]-labeled clothianidin. The second study was investigated in 6 soils from the United States, using [thiazolyl-2-^{14}C]-clothianidin. Results indicated that clothianidin degraded only slowly (extrapolated half-lives 143-1328 days, with one not calculated due to very slow degradation) in most soils, though some mineralisation was evident (cumulative $^{14}CO_2$ production at study end was 2-17% of applied radioactivity). A proportion (3.7-12.8% of applied radioactivity) became bound to soil. One major (>10%, MNG) and three minor metabolites (TZNG, TZMU, NTG) were detected.

A further two studies were performed examining the aerobic soil degradation of two of these degradates, MNG and TZNG. These studies resulted in DT_{50} values of between 82-108 days for MNG and 62-111 days for TZNG. In general more than half of the degradates were lost during the study (120 days) either through transformation to other degradates (not identified in the study), binding to organic matter, or complete mineralisation, with the remainder being unchanged parent.

Aerobic aquatic metabolism

The degradation and metabolism of clothianidin was investigated in two natural water and sediment systems collected from ponds in Germany (Hönniger Weiher and Anglerweiher), using [nitroimino-^{14}C]-clothianidin (purity 99.9%). Radioactivity in the water fell fairly rapidly over the test period. By the end of the 100-day study, the amount of the applied radioactivity in the water phase of Hönniger Weiher had decreased to 12.0% and in Anglerweiher it had decreased to 26.0%. The radioactivity in the sediment increased steadily over the test period. In the Hönniger Weiher sediment it reached a maximum of 81.5% on day 58 and remained relatively stable (81.1% on day 100), in the Anglerweiher sediment it reached a maximum of 65.5% on day 100. The bound residues (not extracted) comprised a maximum of 43% of applied radioactivity on day 100 in Hönniger Weiher and 30% on day 58 in Anglerweiher. Half-lives were calculated for the water (Hönniger Weiher: 30.8 days and Anglerweiher: 49.8 days) and for the total system (Hönniger Weiher: 48.0 days and Anglerweiher: 64.8 days).

The main metabolite formed was TMG (21%), which was only found in the sediment. Traces of unknown metabolites (1.3%) were also found in the water phase.

The degradation and aerobic metabolism of clothianidin was also investigated using pond water without sediment from Saskatoon, Saskatchewan. [^{14}C]-labeled clothianidin was stable under the conditions of the test with negligible degradation being observed through 181 days.

Anaerobic aquatic metabolism

The degradation and anaerobic metabolism of clothianidin was investigated using farm pond water and sediment collected from Howe, Indiana, USA. The amount of applied radioactivity rapidly decreased in the water phase from 89.8% on day 0 to 11.9% on day 30, and continued to decrease to <2% after 90 days (1.4% after 360 days). In the sediment, 9.9% of the applied radioactivity was found on day 0, and increased rapidly to 84.2% at day 30, and was greater than 90% from day 59 through the end of the study. The maximum extractable radioactivity in sediment was found on day 14 (46.4% of the applied radioactivity). From day 90 through to the end of the study, 77.0-82.6% of the applied radioactivity remained bound to the sediment, even after the exhaustive extractions. Half-lives were calculated for the water and sediment phases (4 and 11 days), and for binding to sediment in the total system (21 days). No metabolites greater than 5% were formed in the entire system.

Mobility Studies

Volatility

Due to its low vapour pressure, clothianidin has negligible potential to volatilise from soils, and also has negligible volatility from water or moist surfaces.

Adsorption/desorption in soils

The adsorptive and desorptive properties of clothianidin and some of its degradation products were determined in five soils using ^{14}C-labeled clothianidin. The soils ranged in texture from sand to clay loam, and also varied in OM%, pH and cation exchange capacity. Freundlich adsorption constants related to organic carbon content (K_{oc}) for clothianidin ranged from 84 to 345 mL/g, depending on soil type. Using standard mobility classes (McCall *et al* 1980), clothianidin has high mobility in 4 of the soils studied, and medium mobility in the one soil.

The K_{oc} values for the degradates in the same soils were: 5 and 25 for MNG, indicating a very high mobility, 205 to 433 for TZNG, indicating moderate mobility, 46 and 95 for TZMU, indicating high to very high mobility, and 525 to 6159 for TMG, indicating a slight to low mobility.

Freundlich desorption constants related to organic carbon content were higher than the corresponding adsorption constants (Koc) for clothianidin and it's degradates, indicating partially irreversible adsorption to soil.

Potential to reach groundwater

The laboratory adsorption/desorption batch tests in soil suggest that clothianidin has a moderate to high leaching potential in soil. However, the results of lysimeter and soil field dissipation studies did not support the K_{oc} predictions. In the lysimeter studies, only 1.2% of the applied radioactivity (mean of 2 lysimeters) was found in the leachates after 3 years, when clothianidin was applied to grass (160 g ai/ha), while only 0.3% of the applied radioactivity was found in leachate when clothianidin was applied as a seed treatment (100 g ai/ha) for two consecutive years. A maximum annual leachate concentration of 0.35-0.43 µg parent equivalent/L occurred in the second year of the grass study, while a maximum annual concentration of 0.104 µg parent equivalent/L occurred in the third year of the seed treatment study. In both studies, clothianidin was not detected in the leachates. In the grass study, the metabolites MNG and NTG were identified at maximum concentrations of 0.06 µg/L and 0.04 µg/L, respectively (annual mean). In the seed treatment study, an unknown degradation product was detected at a maximum concentration of 0.07 µg parent equivalent/L in the leachate from the third year (annual mean).

Field dissipation studies

Soil dissipation studies conducted at 5 sites in corn and canola growing regions in the USA and Canada using application rates five to six times higher than normal (ie 0.66 kg ai/ha for corn and 0.24 kg ai/ha for canola) found that under field conditions, clothianidin dissipated slowly to moderately in the 0-120 cm layer of soil, with the exception of the Saskatchewan site where little degradation was observed. The dissipation rate constants (k) for each trial were calculated using simple first-order regression. Individual DT_{50} values for the studies ranged between 295 and 838 days (excluding Saskatchewan). No correlation between the soil properties and the dissipation rates were observed. Applications of clothianidin were made to bare soil plots (approximately 0.1 ha) via broadcast spray.

No clothianidin residues were detected below 60 cm (24 inches) at the Ohio and Wisconsin sites, while no residues were found below 46 cm (18 inches) at the North Dakota site, and below 30 cm (12 inches) at the Saskatchewan and Ontario sites. The highest concentrations of metabolites in soil in these field trials were 10 µg/kg for TZNG, 9 µg/kg for TZMU, and 6 µg/kg in the case of MNG (TMG was detected, but average concentrations were less than the detection limits).

The relationship between leaching depth, the amount of rainfall received, and soil texture is not clear-cut. The Wisconsin site received the highest rainfall and had sandiest texture, and also one of the highest leaching depths, while the Saskatchewan site received the lowest rainfall, and has a clay texture, and also had one of the shallowest leaching depths. However, sites receiving rainfall between the two extremes show no clear relationship between these factors.

Accumulation in soil and sediment

Because of its moderate to high persistence in soil, with repeated application year after year clothianidin has the potential to accumulate in soil or sediment. Assuming a worst-case half-life of 838 days based on field dissipation study data, and the recommended application frequencies for the proposed crops (turf, apples, pears, peaches, nectarines and cotton) at the maximum application rates, DEW estimated that soil concentrations in the surface 15 cm could accumulate to between 0.08-25 mg ac/kg soil, and take up to 15 years to plateau.

Bioaccumulation

Based on the low octanol-water partition co-efficient for clothianidin, a low potential for bioaccumulation is expected.

Summary of Environmental Effects Studies

Avian toxicity

With acute oral exposure, clothianidin technical is practically non-toxic to Bobwhite quail (LD50 > 2000 mg/kg bodyweight), and moderately toxic to Japanese quail (LD50 = 430 mg/kg), but there are effects ranging from reduced food consumption and/or bodyweight reduction or clinical signs at lower doses (NOEL <500 mg/kg and 12.5 mg/kg, respectively). With subacute exposure, it is practically non-toxic to Bobwhite quail and mallard ducks (LC50 > 5200 ppm in diet for both species), but again there are various effects at lower doses (NOEC = 325 ppm and 650 ppm, respectively). The NOEC and LOEC for both Bobwhite quail and mallard ducks in avian reproductive toxicity studies were 500 ppm and >500 ppm, respectively, in both cases.

Aquatic toxicity

Fish

Acute toxicity tests based on US EPA/OECD Guidelines found that clothianidin is practically non-toxic to the freshwater species rainbow trout (96 h LC50 > 101.5 mg ai/L) and bluegill sunfish (96 h LC50 > 117 mg ai/L), and to the estuarine/marine species sheepshead minnow (96 h LC50 > 93.6 mg ai/L, the highest concentration tested). A 33 day exposure early life stage study based on US EPA/OECD Guidelines indicated that clothianidin is very slightly toxic to fathead minnow (No Observed Effect Concentration [NOEC] = 20 mg ai/L, the highest concentration tested). Acute toxicity limit tests with the metabolites TMG, MNG and TZNG found that these were all practically non-toxic to rainbow trout.

Aquatic invertebrates

Acute toxicity tests based on US EPA/OECD Guidelines found that clothianidin is practically non-toxic to the water flea *Daphnia magna* (48 h EC50 > 119 mg ai/L) and the estuarine/marine species eastern oyster (96 h EC50 > 129 mg ai/L), but very highly toxic to the estuarine/marine species mysid shrimp (96 h LC50 = 53 μg ai/L). In a 21 day exposure/reproductive study based on US EPA/OECD Guidelines, clothianidin was found to be slightly toxic to *Daphnia magna* (NOEC = 120 μg ai/L for neonate production). A 39 day exposure/reproductive study with mysid shrimp based on US EPA/OECD Guidelines indicated that clothianidin is highly toxic to mysids (NOEC = 9.7 μg ai/L for reproductive output), but this study deviated significantly from test guidelines in regard to reproduction performance by mysids in the untreated control. Acute toxicity tests with the metabolites TMG, MNG and TZNG found that these were at most slightly toxic to daphnids (48 h EC50 >33.9 mg/L, >100.8 mg/L, and = 41.3 mg ai/L, respectively – ie TMG and TZNG more toxic than the parent substance). An acute toxicity test also showed that leachate water from a lysimeter study was not toxic to daphnids, consistent with the absence of clothianidin and the low levels of metabolites present.

Benthic organisms

Very high toxicity to the chironomid (midge) *Chironomus riparius* was found in an acute test based on US EPA/OECD Guidelines (a standard test not normally used with this species, exposed in water in the absence of sediment – 48 h EC50 = 29 μg ai/L). Similar tests with clothianidin metabolites found MNG, MU and TZMU to be at most slightly toxic (48 h EC50s >100 mg/L, >83.6 mg/L and > 100 mg/L, respectively), but TZNG highly toxic (48 h EC50 in the range 250-500 μg/L), to *Chironomus riparius*.

Standard 28 day benthic studies based on German/OECD Guidelines (spiked water, in the presence of sediment) indicated high toxicity from clothianidin to *Chironomus riparius* (NOEC = 0.56 μg ai/L – the most sensitive aquatic species evaluated), whereas the metabolite TMG was at most slightly toxic (NOEC = 100 μg/L in a limit test - based on nominal initial concentrations for both substances).

Algae and aquatic plants

Studies based on US EPA/OECD Guidelines with the green alga *Selenastrum capricornutum* and the duckweed *Lemna gibba* indicated that clothianidin is at most slightly toxic to these species (96 h EC50 = 56 mg/L for area under the growth curve to >120 mg/L for growth rate, and 14 d EC50 >120 mg/L, respectively, based on nominal initial concentrations). Studies based on US EPA/OECD Guidelines with the metabolites TMG, MNG and TZNG indicated they were at most slightly toxic to the green alga *Selenastrum capricornutum* (96 h EC50s = 10.2 mg/L for cell density to >47.6 mg/L for growth rate, >101.7 mg/L and >105 mg/L, respectively).

Mesocosm

Clothianidin had an acute impact on the mesocosms at the two highest test concentrations (6.3 and 20 μg/L). Emerging insects were especially heavily affected by the application and their population densities showed a strong decrease. The population densities of all affected freshwater insect taxa as well as all insect community parameters completely recovered within 77 days (less than one summer season) even at the highest test concentration, the transient toxic effects at the two highest test concentrations were assessed to be ecologically acceptable. The overall NOEC for all species was found to be at a concentration of 2.0 μg/L TI-435 50 WDG (= 1.0 μg/L TI-435).

Non-target terrestrial invertebrates

Honey bees

Laboratory tests to US EPA/OECD Guidelines with honey bees indicated that clothianidin is very highly toxic to adult worker bees, in fact ranking among the most highly acutely toxic insecticides to bees (acute oral toxicity = 3.79 ng ac/bee, acute contact toxicity = 44.3 ng ac/bee). Similar tests with clothianidin metabolites indicated that TMG, MNG and TZMU are virtually non-toxic to bees (acute oral toxicity >151 μg/bee, >153 μg/bee and >113 μg/bee, respectively), whereas TZNG is moderately toxic to bees (acute oral toxicity = 3.9 μg/bee).

A range of cage, tunnel and field studies were conducted to evaluate the extent of clothianidin residues in flowering *Phacelia tanacetifolia* that had been treated with clothianidin as a water dispersible granule formulation, and to determine effects on bees and hives exposed to such residues or to clothianidin provided in food sources. Such studies are important because of concerns that harmful effects on bees of residues in pollen and nectar of the closely related insecticide imidacloprid may explain serious declines in bee populations allegedly observed in some areas where that insecticide had been used. These studies indicated that fresh residues of clothianidin significantly effected mortality of bees. However, if the applications were made when bees were not actively foraging the aged residues showed a decrease in the effect on mortality.

Predators and parasites

Clothianidin is rated as harmless to ground beetles (*Poecilus cupreus*), moderately harmful to Green lacewing (*Chrysoperla carnea*) and harmful to predatory mite (*Typhlodromus pyri*), rove beetle (*Aleochara bilineata*) the wasps (*Aphidius rhopalosiphi*) and an ER50 of 0.36 g ac/ha for the parasitic wasps (*Trichogramma cacoeciae*) were determined in extended laboratory studies. Note that these effects occurred at application rates well below those proposed for the new products.

A field study indicated that clothianidin showed initial dose related mortality up to 150 g ac/ha for three test species *Typhlodromus pyri*, *Chrysoperla carnea* and *Trichogramma cacoeciae.* However, this response dissipated 3 days after treatment. Examination of the effects on cotton beneficials at 25 and 50g ac/ha indicated moderate negative effect on cotton beneficials.

Soil Invertebrates

Studies based on OECD Guidelines and the earthworm *Eisenia foetida* found 14-day LC50 and NOEC values of 13.2 mg/kg dry soil and <10 mg/kg dry soil, respectively, for clothianidin technical. Similar studies for the formulated product TI-435 50% WDG found 7-day and 14-day LC50 values for of 71.2 mg formulation/kg (35.5 mg ac/kg) and 33.42 mg formulation/kg (16.7 mg ac/kg), respectively. The 14-day NOEC for earthworm weight change was <5.6 mg formulation/kg (<2.8 mg ac/kg) (the lowest dose tested). Hence, clothianidin is rated as moderately toxic to earthworms. Examination of the effects of the WDG formulated product on earthworm reproduction determined a NOEC of 0.53 mg ac/kg soil dw (equivalent to a field application rate of 150 g ac/ha). Similar studies were also reported with the clothianidin metabolites MNG and TZNG. For MNG, the 14 d LC50 and NOEC values were >1000 mg/kg dry soil and 580 mg/kg dry soil, respectively, rating MNG as very slightly toxic. For TZNG, the 14 d LC50 and NOEC values were 970 mg/kg dry soil and 63 mg/kg dry soil, respectively, rating TZNG as slightly toxic.

A 28 day study indicates that clothianidin is highly toxic to collembola. The reproduction LC50 was 0.76 mg ac/kg soil dry weight, and the reproduction NOEC was 0.32 mg ac/kg soil dry. For mortality the results were: LOEC = 1.0 mg ac/kg soil dry weight, LC50 = 1.02 mg ac/kg soil dry weight and the NOEC = 0.32 mg ac/kg soil dry weight.

Toxicity to terrestrial plants

A study was conducted with 10 crop/pasture plant species where seeds were sown in pots and the soil sprayed with a 50 WDG formulation of clothianidin at a rate corresponding to 225 g ai/ha. There were no statistically significant differences in seedling emergence, or on seedling height or weight at 14 days post sowing between this treatment or a corresponding formulation blank application and the untreated control for any of the species tested. A similar study where spray was applied to emerged seedlings found no significant effects on vegetative growth of the 10 test species. Hence, the NOEC to the 10 species tested for clothianidin applied as the 50 WDG formulation was 225 g ac.

Mammals

Clothianidin is moderately to practically nontoxic to small mammals on an acute oral basis (acute LD_{50} for clothianidin technical >5000 mg ai/kg body weight for rats, = 425 mg ai/kg body weight for mice).

Micro-organisms

No significant differences in short-term respiration or nitrate production were found between soils treated with clothianidin and the untreated controls.

Hazards Arising From Use

Risk to aquatic organisms from spraydrift

The application of clothianidin to pome fruit trees (as a soil drench) and bananas (as a stem spray or injection) is not expected to result in significant exposure to the aquatic compartment as a result of spray drift. Consequently, the risk to the aquatic compartment as a result spraydrift from these proposed uses of clothianidin is considered acceptable.

For the other proposed applications the potential chronic risk was determined using AgDRIFT® and the Ganzelmeier tables for spray drift and the mesocosm NOEC. The calculations also included consideration of repeated applications. The potential chronic risk can be mitigated with the use of buffer distances. The proposed downwind buffer distances for the proposed uses are summarised in the following table:

Crop			**Buffer distance**
Fruit trees (apples, pears, peaches and nectarines)	One of 3000 L/ha (600 g/ha clothianidin)		40 m
	Two applications of 2000 L/ha (400 g/ha clothianidin)		50 m
Cotton	– Ground		40 m
	– Aerial	Very Fine-Fine ($D_{v0.5}$ = 137 µm)	>800 m
		Fine ($D_{v0.5}$ = 180 µm)	800 m*
		Fine Medium ($D_{v0.5}$ = 255 µm)	300 m
Turf			10 m

. *Only 300 m is required if only a single application is made.

The proposed downwind buffer distance for aerial application to cotton using fine-medium sprays is within the recommended distances in the cotton Best Management Practices Manual (BMPM). However, the proposed buffer distances for both very fine-fine and fine sprays exceed the recommended distance.

Risk to aquatic organisms from runoff

Modelling of the run-off for the proposed application indicates that the potential risk is mitigated when untreated areas, foliage interception and adsorption to sediment are considered. In the modelling a period of 48 h between application and the run-off event was allowed to allow for binding of the chemical to the crop and surrounding soil. In order to minimise the potential risk to the aquatic compartment DEW recommends that a warning statement be added to the labels of all three proposed products to avoid application within 48 h of predicted rainfall. DEW notes that the label for Sumitomo Shield Systemic Insecticide already includes an instruction in the critical comments for the banana stem spray stipulating a 24 h gap between application and predicted rainfall.

Risk to groundwater and accumulation in soil and sediment

The laboratory adsorption/desorption batch tests in soil suggest that clothianidin has a moderate to high leaching potential in soil. However, the results of lysimeter and soil field dissipation studies did not support the K_{oc} predictions. These studies indicated minimal leaching of clothianidin and its degradates. Therefore, the use of clothianidin in the proposed products will not negatively impact on groundwater when used at the proposed rates.

Risk to birds

The predicted dietary intakes from consuming treated foodstuffs exclusively are all well below the dietary NOEC values for bobwhite quails (325 ppm) and mallard ducks (650 ppm), except for the use as a soil drench in pome fruit. This application involves the directed application of the product containing the active to cleared soil in a small band at the base of the tree. As the treated area represents a fraction of the area within the orchard and the treated area being bare will not contain significant quantities of foodstuff which foraging birds will find attractive, the avian risk is expected to be acceptable.

Risk to mammals

The predicted TER values indicate that there is an unacceptable risk for the both large (for all food sources except fruit, pods with seeds, large insects) and small mammals (for all food sources) only when clothianidin is applied as a soil drench in pome fruit. As noted above for the risk to birds, the treated area represents a fraction of the area within the orchard and the treated area being bare will not contain significant quantities of foodstuff which foraging mammals will find attractive. Similarly the TER values of predict an unacceptable risk to small mammals for the application to bananas. However, the directed nature of the method of application will limit the quantity of food sources that will be treated with clothianidin. Hence, the proposed uses of clothianidin containing products are not expected to result in an unacceptable risk to mammals.

Risk to terrestrial invertebrates

Bees

Clothianidin is among the most toxic of all insecticides to bees. The risk to bees is high if spraying occurs when they are present in the crop and foliar residues may remain highly toxic to bees for a period after application. Hence the labels for all three proposed products should warn that clothianidin is dangerous to bees and will kill bees foraging in the crop to be treated or in hives that are over-sprayed or reached by spray drift, and that residues may remain toxic to bees for several days after application.

Beneficials

A field study indicated that clothianidin showed initial dose related mortality up to 150 g ac/ha for three test species *Typhlodromus pyri*, *Chrysoperla carnea* and *Trichogramma cacoeciae.* However, this response dissipated 3 days after treatment. In another study, examination of the effects on cotton beneficials at 25 and 50 g ac/ha indicated a moderate negative effect on cotton beneficials.

Given the above information, some adverse effects on beneficials in pome and stone fruit orchards where clothianidin is used could be expected to occur. Thus, DEW recommends that a label statement be included in the labels of the proposed products warning of potential effects on beneficials especially given the higher Australian rates of up to 600 g ac/ha allowed under the proposed use patterns.

Earthworms

The effect ratios predicted for the various crops indicate a risk to earthworms when exposed to soil treated with single or repeated applications of clothianidin when used as a soil drench. While only a small area the orchard will be treated at these rates and immigration from non-treated areas would occur, the persistence of clothianidin in the soil would suggest these treated area are unlikely to be inhabited by earthworms. There also an unacceptable risk for turf and fruit trees, assuming only a single annual application per year to turf and 80% interception respectively, though the risk is only marginal for the latter.

Collembola

An unacceptable risk to collembola is predicted for the repeated application of clothianidin in all crops except cotton. As for earthworms, use as a soil drench will only affect small areas and while collembola may not return to these spots, orchard populations should not be affected overall. Similarly for turf, use it is unlikely that a single chemical will be annually applied to the same area of grass year after year. However, 3 sprays of clothianidin as part of a season long program in pome and stone fruit orchards is predicted to lead to an unacceptable risk to collembola populations in the orchard, though risk from a single spray per season appears acceptable.

Risk to microorganisms

No effect on nitrogen turnover or respiration of micro-organisms was observed for clothianidin, as the formulated material, up to application rates up to 750 g ac/ha. Hence, the proposed use of the products on crops where the application rates are below this (fruit trees, cotton, bananas and turf) is unlikely to present a risk to soil micro-organisms.

The application rate of Sumitomo Samurai Systemic Insecticide as a soil drench is well above the tested rate, consequently, the effect of this rate on soil micro-organisms is unknown. However, as the treated area represents only a fraction of the overall area of orchards there is the potential for recolonisation of the soil from untreated areas if the treatment were to have adverse effects on the micro-organisms.

Risk to non-target terrestrial vegetation

The proposed application rates to fruit trees, pome, turf and bananas are above the NOEC of 225 g ac/ha (the only level tested) of the seedling emergence and vegetative vigour tests, and adverse effects on non-target vegetation can not be completely ruled out. However, efficacy trial on fruit trees (pome and stone) showed no phytotoxic effect at rates up to and including the proposed application rates. Additionally, the exposure of non-target vegetation will be through off site movement (either in the form of spray drift or run-off) which will be at rates below the application rate. Hence, the application of clothianidin at the proposed rates is not expected to have unintended adverse effects on non-target vegetation.

Assessment of clothianidin against PBT criteria

The available information indicates that clothianidin meets the PBT criteria for persistence and toxicity and fails the PBT criteria for bioaccumulation. Therefore, clothianidin is considered to be a persistent and toxic chemical but cannot be regarded as PBT.

Conclusions

Clothianidin is persistent in soil and is among the most toxic of all insecticides to bees. Clothianidin is also highly toxic to collembola and moderately toxic to earthworms.

The current submission is seeking registration in several crops for three products. DEW's recommendations for each of the proposed uses follow:

For **foliar spraying to pome and stone fruit trees**, calculations indicate that with a single foliar application per season at the maximum rate or two applications per season at two thirds the maximum application rate soil clothianidin will not accumulate to levels that pose an unacceptable risk to soil invertebrates. Therefore, provided the that the use of Sumitomo Samurai Systemic Insecticide on Pome and Stone Fruit be limited to a single application of 3000 L/ha (600g/ha clothianidin) with a 40 m downwind buffer or two applications of up to 2000 L/ha (400g/ha clothianidin) with a 50 m downwind buffer and the other label instructions are adhered to, DEW is able to recommend to the AVPMA that it be satisfied that the foliar use of Sumitomo Samurai Systemic Insecticide on pome and stone fruit with a single spray per season would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes.

The proposed use of **Sumitomo Samurai Systemic Insecticide as a soil drench** in pome fruit orchards will present an unacceptable risk to earthworm and collembola within the treated zone. However, it is anticipated that this impact will be localised to the treatment area which will represent only a small proportion of the orchard and overall populations will not be affected. Additionally, DEWs assessment of the risk resulting from run-off of this use relies on a 48 h interval between application and the run off event occurring to allow for adsorption of clothianidin to soil. Consequently, DEW can support the registration of this use and is able to recommend to the AVPMA that it be satisfied that the soil drench use of Sumitomo Samurai Systemic Insecticide in pome fruit orchards would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes, provided the above recommended label statements are added to the label for the product.

The proposed product **Sumitomo Stealth Systemic Insecticide on turf** is not expected to result in an unacceptable risk to the aquatic compartment providing a 10 m downwind buffer is applied. Although an unacceptable risk to collembola is predicted for repeated applications on an annual basis this is expected to be mitigated by the need for less frequent applications if infestations are treated only when they arise. Consequently, if the other label recommendations are accepted DEW is able to recommend to the AVPMA that it be satisfied that the use of Sumitomo Stealth Systemic Insecticide on turf would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes.

The proposed use of **Sumitomo Shield Systemic Insecticide in bananas** will result in very little environmental exposure when used as a stem injection or trunk spray. Consequently, DEW is able to recommend to the AVPMA that it be satisfied that the use of Sumitomo Shield Systemic Insecticide on bananas would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes.

Registration of **Sumitomo Shield Systemic Insecticide is also sought in cotton** for both ground and aerial application. The potential risk for ground application can be mitigated by imposing a 40 m downwind buffer, which is within the 100 m buffer recommended in the cotton BMPM for ground application. For aerial application the potential risk is also mitigatable within the recommended 300 m buffer distance of the cotton BMPM provided a fine-medium spray quality is used with successive applications. Consequently, DEW is able to recommend to the AVPMA that it be satisfied that the use of Sumitomo Shield Systemic Insecticide on cotton for both ground and aerial application would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes, provided the above recommended label statements are added to the label for the product.

If a fine spray quality needs to be used, DEW is able to recommend to the AVPMA that it be satisfied that the use of Sumitomo Shield Systemic Insecticide on cotton for aerial application would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment under Section 14 subsection 1 of the Agvet Codes, only if a single spray per season is used, or an 800 m downwind buffer is applied if 2 fine sprays are to be made per season.

Recommendation

Based on a review of the information provided by the applicant, the registrations of *Sumitomo Samurai Systemic Insecticide*, *Sumitomo Shield Systemic Insecticide* and *Sumitomo Stealth Systemic Insecticide* are supported from an environmental perspective.

EFFICACY AND SAFETY ASSESSMENT

Proposed Use Pattern, Justification and Mode of Action

Three new products containing clothianidin as their only active constituent are proposed for the control of various insect pests on a range of crops and use patterns.

Sumitomo Samurai Systemic Insecticide (Samurai) as a 500g/kg water dispersible product to control:

- Woolly aphid, longtail mealybug, tuber mealybug and codling moth in apples and pears;
- Oriental fruit moth and green peach aphid in peaches and nectarines.

Samurai offers good control of several major insect pests of pome and stone fruit in the one product. It is compatible with IPM programs and can provide an effective alternative for inclusion in resistance management programs.

Sumitomo Shield Systemic Insecticide (Shield) as a 200g/L suspension concentrate product to control:

- Cotton aphid and green mirid in cotton;
- Weevil borer and rust thrips in bananas.

Shield offers an alternative product for judicious use in IMP in cotton and a very effective alternative for protection of banana suckers (pseudostems).

Sumitomo Stealth Systemic Insecticide (Stealth) as a 500g/kg water dispersible product to control:

- First instar larvae of African black beetle (ABB) in turf.

Stealth provides for excellent alternative control of ABB to currently registered products with more soil mobility, greater residual activity, superior environmental and operator safety and with a potentially wider pest control spectrum.

Clothianidin is a chloronicotinyl nitroguanidine in the neonicotinoid class (Group 4) of insecticides. These compounds are acetylcholine receptor agonists/antagonists. Their mode of action is through the binding to the acetylcholine receptor and thus interfering with nerve transmission. Insects are exposed by either contact or ingestion.

Evaluation of Efficacy and Safety

Samurai

The data submitted included 26 trials with Samurai applied at various rates in commercial orchards, including four further trials to assess safety and compatibility with integrated pest management (IPM) systems in widespread use in the industry. The design of the trials, data collection, analysis and validation were acceptable. All orchard trials were based in eastern states of Australia and were subject to prevailing pest insect pressure as well as weather and climatic conditions at the time. Efficacy was determined by reduction of insect numbers and/or damage to fruit, and was compared with untreated trees and at least one standard treatment of another appropriate registered insecticide.

The trials established that Samurai typically reduced populations of woolly aphid and both species of mealybug by 80-90%, and under certain conditions provided extended control of woolly aphid into the next season. Samurai gave significant knockdown of mealybug on foliage and tree limbs, as claimed, but not complete control. In the case of high numbers of codling moth in pome fruit orchards, Samurai typically reduced infestations in fruit from over 30% in untreated fruit to 6%, or less where pest pressure was lower. In stone fruit orchards where Oriental fruit moth was a major problem, Samurai reduced infestations in untreated fruit from over 40% to 3% or less, and also virtually eliminated populations of green peach aphid when applied at the lower rate proposed for this pest.

Samurai did not contribute to any obvious pest-mite flare, indicating that IPM systems utilising *Typhlodromus* beneficials were not disrupted. Samurai is intended to be a component of a season-long program in which it would be used twice only on the same moth generation. Other moth generations in the season would be controlled with other insecticides to minimise any resistance development. A trial of various programs incorporating Samurai reduced damage by 6-17% and demonstrated that the product could be integrated into current commercial practice. In addition the submission provides evidence that Samurai is safe to apple and pear trees provided that surfactant additions are limited to 0.05%v/v. It is therefore expected that when used in accordance with amended label directions, Samurai will be effective in the limitation of the sucking insects as claimed on the label, and will give substantial control of the two major moth pests of pome and stone fruit orchards.

In normal commercial practice, existing registered products are used judiciously in IPM and resistance management programs. IPM includes use of beneficial organisms such as predatory mites (*Typhlodromus* spp), hence insecticides that have minimal impact on these and other beneficials are preferred. Resistance management measures include alternation of insecticides to minimise repeated exposure of insect populations to the same insecticide or group. Samurai is intended to be part of this wider system, but with added advantages of a broader spectrum of effectiveness than some currently registered products, and no evidence of encouraging pest mite flares.

Apples and pears – Aphids and mealybugs

Efficacy data presented for control of aphids and mealybugs by foliar spraying supports the claims for use that Samurai "will give significant knockdown of these pests on foliage and tree limbs". Complete control is not claimed, nor was it demonstrated. This is consistent with the behaviour of these cryptic insects, which tend to shelter from direct contact with applied insecticide. The data support the claim for control subject to the caveats listed on the label. In particular, the minimum spray rate is set at 1500L/Ha, and the mode of spraying is to use the full dilution in the Table to achieve thorough coverage rather than a higher concentration with proportionately lower coverage. Most lower rates of Samurai achieved control levels that were statistically similar to the proposed label rate (20gai/100L), suggesting that the extent of coverage was likely to be of greater importance than the amount of insecticide applied.

Orchard programs which optimise the use of insecticides in IPM and other management systems have been implemented widely in the industry. Samurai is intended to complement these existing practices, hence sprays with Samurai are limited to two

The efficacy data presented for control of woolly aphid by soil drench supports the claim that Samurai at the rates indicated would give substantial control in the first season. The data also confirmed that the higher rate would also extend control to the early part of the next season. Application of treatment was at late petal fall in most trials but was delayed in the other because of weather conditions. The timely application of Samurai appears to be important.

Apples and pears – Codling moth

The data are adequate to support the claim that Samurai maintains control of a generation of the target insect. In all trials the use of Samurai at the label rate reduced damage to fruit significantly, and in some cases almost completely. Adverse seasonal conditions lowered the effectiveness in at least one trial but the efficacy of standard treatments was also affected to a similar extent. Effectiveness generally increased with rate of

Samurai applied, and in most cases rates of less than the label rate were not as effective. The data are consistent with the label rate of 20gai/100L being optimal for control of this pest.

Peaches and nectarines – Oriental Fruit Moth (OFM) and Green Peach Aphid (GPA)
The data for OFM are adequate to support the claim of control of this insect in peaches. The overall effectiveness of Samurai was usually statistically similar when the applied rates were equivalent to 15gai/100L or higher, or 20gai/100L for on-tree fruit in 1 of 3 trials. The influence of rate on effectiveness was sometimes clouded by parameters such as high variability in pest pressure in the orchard, so that the proposed label rate of 20gai/100L is accepted as optimal for control of this pest. All were equivalent to the best standard.

GPA was much more sensitive to Samurai than OFM, and although it was significantly affected even by the lowest rates tested, control was achieved more rapidly with 5gai/100L. This rate is therefore appropriate for use when GPA is the only target.

Safety to target crops.
Possible phytotoxic effects of Samurai with or without surfactant were assessed in all trials. In most cases on apple and pear (numerous trials) no adverse effects of treatments were found with the exception of slight surface russeting on apples when the treatment included Maxx surfactant at 0.1%v/v and one case of significant russeting on pear variety Sensation. The label restraint of using Maxx at no more than 0.05% was therefore included and is considered adequate.

Safety to non-target crops.
The proposed formulation of Samurai had no general adverse phytotoxic effect on ten plant species of various families when applied at a concentration slightly above the proposed label rate. Differences in seedling vigour and growth and other possible indicators of phytotoxicity were minor and not statistically different from those of untreated samples. The assessments were appropriate to assess general effects on plants but excluded the specific hosts on the proposed label. The issue of safety to following crops is not relevant in an orchard situation.

Shield

The application for the registration of clothianidin for the control of aphid and green mirid in cotton is supported by fourteen trials specifically targeting aphids and/or mirid and three trials involving other pests and beneficial insects. Four of these trials, specifically targeting cotton aphid (two trials) and green mirid (two trials) in cotton, were conducted in Queensland. Five trials were conducted in NSW with three specifically targeting aphid and two targeting green mirid in cotton. One of these trials used aerial application of treatments.

The remaining five trials were conducted at Kununurra in WA with two trials using handheld spraying equipment targeting cotton aphid and one involving aerial application of the treatments for cotton aphid in cotton. A single trial using a high clearance spray boom targeted green mirid in cotton. A single trial conducted in Zucchini evaluated treatments for the control of cotton aphid, green mirid, leafhoppers and beneficial insects in this crop.

Of all the above trials, four involved measurements/observations on the treatment effects on beneficial insects. A single trial specifically targeted jassids in cotton in NSW.A further trial conducted in NSW examined treatment effects on beneficial insects and some insect pests in cotton.

Label claims for the control of weevil borer and rust thrip in bananas by stem inject or basal stem spraying are supported by five trials, all conducted at the same site/region at Kennedy, Queensland in the period 2003 to 2005.

Cotton trials were conducted under commercial cotton growing conditions with treatments generally applied by hand held spraying equipment or in a couple of instances with tractor mounted motorized sprayers. The exceptions being the aerial application of treatments in two trials conducted in WA and NSW.

Treatments were laid out as randomised complete blocks, invariably with four replicates in small to medium sized plots (2 -6 rows wide by 10-20m in length). Aerial trials had a plot size of 12 -15 beds wide by 100 - 150m in length. Application equipment varied from hand held compressed gas sprayers to tractor mounted sprayers and to aircraft using micronaire or a JARBA boom.

Banana trials treatments were applied to banana suckers (pseudostems) in commercial crops, after adult plant removal and when about 1.5m in height. Four to six plants were treated per treatment, which was probably an inadequate number due to losses in destructive sampling and natural attrition over the duration of the trials (8 months). Stem injection treatments were applied using a forestry injection gun and coarse needle to a depth of 40-5-mm into the stem at about 150mm above ground level. Butt drenching for the application of 'standards' was with a backpack sprayer with treatment application 300 mm up and around the base of the plant. Trunk spraying of Shield was to the lower stem of the plant using 10 ml of solution applied through a cone nozzle fitted to a forestry injection gun.

Cotton trials

Insecticide treatments comprised a range of rates of clothianidin and 'standard' insecticide treatments together with an untreated control. Rates of clothianidin ranged from 8 -200 g ai/ha. The proposed label rates were mostly represented in all trials.

All trials made general observations and/or comments about phytotoxicity or more particularly the lack of damage symptoms to the cotton.

Two aerial trials in cotton, targeting aphid, were conducted. All trials included one or more standards as appropriate and an untreated control. With respect to sites and seasons the trials were adequate in number to evaluate the efficacy of clothianidin against cotton aphid and green mirid in cotton.

Trial data submitted indicated that predators, particularly some species such as predatory beetles, bugs and lacewings are susceptible to Shield at the proposed **IPM** label rate. Indeed, overall, the product was rated to be 'Moderate' in its ranking for impact on beneficial insects at the IPM rate, an identical ranking to the standard comparison insecticides.

Cotton trials specifically targeting cotton aphid and green mirid in cotton crops demonstrated the efficacy of Shield at a range of rates against these cotton pests. Generally, Shield performed at a similar level to the standards used although acetamiprid did demonstrate a longer residual effect on aphid in two trials. Invariably, better efficacy and longer term control of both pests was achieved at rates of Shield at and above 50g ai/ha. At this rate and above it was mostly equivalent to or better than most of the standards.

Banana trials

Stem injection treatments and trunk spray treatments comprised clothianidin and imidicloprid (2 trials at 0.6

g) which was applied over a rate range from 0.15 to 0.9 g ai per stem. Butt spraying of the standards comprised Imidicloprid at 0.6 g ai/stem, Fipronil at 0.15 g ai and Prothiofos at 2.5 g ai. The trials include untreated control plants.

Weevil borer and rust thrip were assessed prior to treatment application and by destructive sampling of stems, at four and eight months after treatment in the case of borers and every month from one to eight months after treatment by destructive sampling of the fifth or sixth leaf for the presence of rust thrip.

Banana trials were restricted to one site (plantation) in the period 2003-2005 inclusive. All of the five trials experienced only low to moderate pest infestations, particularly weevil borer damage, and a lack of uniformity in pest distribution between banana plants. It appears that rainfall soon after treatment application may have impacted adversely on stem/butt spray treatments in some of the trials. All trials included one or more standards and an untreated control. Despite the above limitations, the trials were adequate to evaluate the efficacy of clothianidin applied by stem injection and stem spraying for the control of weevil borer and rust thrip in bananas.

Stem injection of Shield was clearly demonstrated to be superior to basal stem or trunk spraying for the control of both insect pests. Both the degree of control and duration of control were mostly superior to all stem spraying treatments including standard butt spraying treatments. Higher rates of Shield as a stem spray were effective but could not match the duration of control achieved by stem injection. It was suggested that rainfall soon after treatment application in several trials may have 'diluted' the stem spraying and butt drenching treatments hence reducing the longevity of control.

Stealth

The application for the registration of clothianidin for the control of ABB in turf is supported by five trials specifically targeting ABB at the larvae and adult stage of the life cycle.
Three of these trials were conducted in the metropolitan area of Perth, Western Australia. A fourth trial was conducted at Murray Bridge in country South Australia and the fifth trial at Moorebank in the western suburbs of Sydney, New South Wales. The trials were all conducted in the period of summer 2003/4 to autumn 2005 under equivalent commercial conditions.

Trials were conducted 'in situ' on golf course fairways comprising either couch (*Cynodon dactylon*), kikuyu grass turf or a combination of both turf grass species.
Treatments were laid out as randomised complete blocks with either four or five replicates in small to medium sized plots.

Application equipment varied from a motorbike mounted compressed air sprayer for the larger dimension plots to a hand held sprayer for the smaller dimension trials. Treatments were applied to moist turf situations and overhead irrigation applied at 10 - 15mm of water immediately after completion of the treatment application.

Insecticide treatments comprised a range of rates of clothianidin and 'standard' insecticide treatments together with an untreated control.

Appropriate statistical analysis involving analysis of variance and comparison of means was conducted on the data relating insect number or percentage control for each of the applied treatments.

All trials made general phytotoxicity observations about the lack of damage symptoms to the turf involved.

The range of Clothianidin rates covering the proposed label rates and the inclusion of one or more 'standards' in all trials were deemed to be appropriate.

With respect to sites and seasons one of the five trials was directed at the control of adult ABB rather than the first instar larvae as specified on the proposed label. This in itself is not a problem since a range of life cycle stages is likely to exist in some situations and the efficacy against adult ABB needs to be known. The trial conducted at Moorebank, Sydney NSW had only a low population of larvae at treatment time, which initially increased then declined over the three month duration of the trial. The remaining three trials had a reasonable pest challenge and gave excellent results with clothianidin, at a range of application rates, equal or superior to the standards in the control of ABB larvae.

The trials were adequate to examine the safety to turf, albeit only two turf grass species were involved.

Three of the five trials relied on for this assessment clearly demonstrated that Stealth, if used in accordance with the label recommendations, is effective in controlling larvae stages of African black beetle in turf.
A fourth trial, on low numbers of ABB larvae gave good control at the highest recommended label rate and above but only after a period of two to three months following treatment application.

Overall Conclusions

The large amount of data submitted from numerous trials in pome and stone fruit orchards demonstrated the efficacy of Samurai in controlling a range of orchard insect pests including woolly aphid, longtail mealybug, tuber mealybug, codling moth, Oriental fruit moth and green peach aphid. In addition the submission provides evidence that Samurai is safe to apple and pear trees, and is compatible with the IPM and other management systems that are widely used in the industry. It is therefore expected that when used in accordance with amended label directions, Samurai will be effective in the limitation of the first three insects as claimed on the label, and in substantial control of the remaining insects.

Proposed label claims for the efficacy of Shield at 250 ml/ha plus 0.2% v/v. Maxx surfactant against cotton aphid and green mirid in cotton are supported by the trial data presented. Application by ground spraying equipment for aphid and green mirid and air for aphid control is supported.

The label recommendations and rates for stem injection of neat Shield and stem spraying of Shield for weevil borer and rust thrip and their respective methods of application in banana plants are appropriate and supported.

The data submitted to support the Stealth application was of sufficient quality to demonstrate reliable control, at the top end of the proposed label rates and above, with equivalence to commercial standard treatments. Based on this evidence, it is expected that when applied in accordance with the proposed label directions (after due consideration to the suggested amendments) the product will be effective in satisfying the label claims and with safety to turf grass species.

LABELLING REQUIREMENTS

Draft text labels for *SUMITOMO SHIELD SYSTEMIC INSECTICIDE*, *SUMITOMO SAMURAI SYSTEMIC INSECTICIDE* and *SUMITOMO STEALTH SYSTEMIC INSECTICIDE* are attached. Labels contain text as recommended by the APVMA's advisors.

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

SUMITOMO SAMURAI® SYSTEMIC INSECTICIDE

ACTIVE CONSTITUENT: 500 g/kg CLOTHIANIDIN

GROUP	4A	INSECTICIDE

For the control of mealybug, woolly aphid and codling moth in apples and pears, and green peach aphid and oriental fruit moth in peaches and nectarines.

CONTENTS: 2.5 kg, 5 kg

SUMITOMO CHEMICAL

Sumitomo Chemical Australia Pty Ltd
501 Victoria Avenue
Chatswood NSW 2067
Tel: 02 9904 6499
A.B.N. 21 081 096 255

® Registered trademark of Sumitomo Chemical Co., Japan

DIRECTIONS FOR USE

Restraints

MAXX surfactant may cause russeting on pears and apples. Do not use MAXX surfactant on pears and apples in conditions such as high humidity where russeting may be caused. Do not use MAXX surfactant at more than 50 mL/100 L water. Do not use MAXX surfactant within 7 days of applying copper based or nutritional products to fruit.

Do not apply more than 2 foliar sprays per season. Do not apply more than 1 foliar spray per season if water volumes are greater than 2000 L/ha.

CROP	PEST	RATE	CRITICAL COMMENTS
Apples	Woolly apple aphid	**Dilute foliar spray** 40 g / 100 L	These sprays may be timed to coincide with the spray timing required for codling moth control. Ensure thorough coverage. Woolly apple aphid should be sprayed at the first signs of infestation but after petal fall. Some woolly apple aphid may survive the first spray in sheltered spots such as cracks in the bark. From here they will multiply again. If this occurs a second spray may be required two or more weeks later. SAMURAI should be applied as part of a season long program with other chemical group sprays to provide control. The addition of MAXX Organosilicone Surfactant at 50 mL/100 L water may improve efficacy. Refer to **Restraints** and the Application/Wetting Agent section. Concentrate spraying is not recommended because thorough coverage is essential for good control of these insects.

		Soil drench 2.5 – 5 g per tree applied in 1 L of water to the soil around the base of the tree.	Apply between green tip and late petal fall. The higher rate will give longer control. Control may be achieved in the season of application. It is however recommended that trees with infestations in autumn are marked so that they can be treated at green tip the following season. The speed of control from this application depends on how fast the product enters the root zone and is taken up by the tree actively growing. The diluted product needs to be applied to give thorough coverage around the trunk to a distance of 15 cm from the trunk. Ensure that mixture penetrates the soil around the trunk base and does not run off. If in doubt about penetration, irrigation or rain is required after application to take the chemical into the root zone. Remove trash and weeds from application zone before spraying.

Apples and Pears	Longtailed mealybug Tuber mealybug	**Dilute foliar spray** 40 g / 100 L	The first spray should be as soon as crawlers are seen but after petal fall. Ensure thorough coverage. Two sprays 14 days apart will give significant knockdown of these pests on foliage and tree limbs, however some mealybug may survive in sheltered spots and multiply again from these. They then migrate to the calyx of the fruit where they are very difficult to control, so these sprays should be applied as part of a season long program with other chemical group sprays to keep them under control. The addition of MAXX Organosilicone Surfactant at 50 mL/100 L water may improve efficacy. Refer to **Restraints** and the Application/Wetting Agent section. Concentrate spraying is not recommended because thorough coverage is essential for good control of these insects.
	Codling moth	**Dilute foliar spray** 40 g / 100 L **Concentrate spraying** Refer to the Mixing / Application section.	Apply once pest monitoring indicates that a generation egg hatch is taking place. Ensure thorough coverage. Apply two consecutive sprays 14 days apart to maintain control of a generation. It is recommended this be part of a season long control program. Further sprays for this generation, or the next should be from a different chemical group. The addition of MAXX Organosilicone Surfactant at 50 mL/100 L water may improve efficacy. Refer to **Restraints** and the Application/Wetting Agent section.

Peaches and Nectarines	Oriental fruit moth	**Dilute foliar spray** 40 g / 100 L **Concentrate spraying** Refer to the Mixing/ Application section.	Apply once pest monitoring indicates that a generation egg hatch is taking place. Apply two consecutive sprays 14 days apart to a generation. Further sprays for this generation, or the next should be from a different chemical group. SAMURAI should be used as part of a season long control program. The addition of MAXX Organosilicone Surfactant at 50 mL/100 L water may improve efficacy. Refer to the Application/Wetting Agent section.

	Green peach aphid	**Dilute foliar spray** 10 g / 100 L **Concentrate spraying** Refer to the Mixing/ Application section.	Apply once monitoring indicates that chemical control is necessary. Ensure that a reasonable amount of leaf is present at spraying to enhance uptake.

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

WITHHOLDING PERIODS:

Apples, Pears, Peaches, Nectarines: Do not harvest for 21 days after application.
Do not graze treated area or cut treated area for stock feed.

Treated fruit for export to particular destinations outside Australia may require a longer interval before harvest to comply with residues standards of importing countries. Please contact your industry body, exporter or Sumitomo Chemical Australia before using Sumitomo SAMURAI Systemic Insecticide.

GENERAL INSTRUCTIONS

INSECTICIDE RESISTANCE WARNING

GROUP	4A	INSECTICIDE

For insecticide resistance management Sumitomo SAMURAI Systemic Insecticide is a Group 4A insecticide. Some naturally occurring insect biotypes resistant to SAMURAI 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 SAMURAI or other Group 4A insecticides are used repeatedly. The effectiveness of SAMURAI on resistant individuals could be significantly reduced. Since the occurrence of resistant individuals is difficult to detect prior to use, Sumitomo Chemical Australia Pty Ltd accepts no liability for any losses that may result from the failure of this product to control resistant insects. SAMURAI may be subject to specific resistance management strategies. For further information contact your local supplier, Sumitomo Chemical Australia Pty Ltd representative or local agricultural department agronomist.

CROP MONITORING

Effective pest control depends upon regular monitoring of crops during the season at 3-5 day intervals.

MIXING

Measure the required amount of product to a partially filled spray tank and then add the remainder of the water. Ensure agitation is maintained during tank filling and whilst spraying. Do not let prepared spray solution sit in spray tank overnight.

COMPATIBILITY

It is advised to test water quality, which may vary considerably with location, as well as all mixtures prior to mixing commercial quantities.

APPLICATION

This product may be applied by ground equipment only. Ensure equipment is calibrated to give good coverage at correct volume.

Do not apply more than 2 foliar sprays per season. Do not apply more than 1 foliar spray per season if water volumes are greater than 2000 L/ha (see **PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT**).

Dilute Spraying:

- Use a sprayer designed to apply high volumes of water up to the point of run-off and matched to the crop being sprayed.
- Set up and operate the sprayer to achieve even coverage throughout the crop canopy. Apply sufficient water to cover the crop to the point of run-off. Avoid excessive run-off.
- The required water volume may be determined by applying different test volumes, using different settings on the sprayer, from industry guidelines or expert advice.
- Add the amount of product specified in the Directions for Use table for each 100 L of water. Spray to the point of run-off.
- The required dilute spray volume will change and the sprayer set up and operation may also need to be changed, as the crop grows.

Concentrate Spraying: Do not use less than 1000 L per hectare of water once trees reach medium size (2.5 m high).

- Use a sprayer designed and set up for concentrate spraying (that is a sprayer which applies water volumes less than those required to reach the point of run-off) and matched to the crop being sprayed.
- Set up and operate the sprayer to achieve even coverage throughout the crop canopy using your chosen water volume.
- Determine an appropriate dilute spray volume (see **Dilute Spraying** above) for the crop canopy. This is needed to calculate the concentrate mixing rate.

The mixing rate for concentrate spraying can **then** be calculated in the following way:

EXAMPLE ONLY:

1. Dilute spray volume as determined above: **for example** 2000 L/ha
2. Your chosen concentrate spray volume: **for example** 1000 L/ha
3. The concentration factor in this example is: 2X (that is, 2000 L ÷ 1000 L = 2)
4. If the dilute label rate is 40 g/100 L, then the concentrate rate becomes 2 X 40, that is, 80 g/100 L of concentrate spray.

- The chosen spray volume, amount of product per 100 L of water, and the sprayer set up and operation may need to be changed as the crop grows.
- For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training and follow industry Best Practices.

Wetting Agent

Add MAXX Organosilicone Surfactant at the rate of 50 mL/100 L (0.05%) of spray. Do not exceed this rate (see **Restraints**). Other surfactants may be acceptable but their effectiveness, safety to trees and fruit, or compatibility with SAMURAI cannot be guaranteed.

PROTECTION OF LIVESTOCK

Dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift, and residues may remain toxic to bees several days after application.

Risks to non-target insects – Clothianidin may have adverse effects on some non-target beneficials, in particular where IPM is practiced, to foliage dwelling predators.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT apply under weather conditions, or from spraying equipment, that may cause spray drift onto nearby or adjacent areas, particularly wetlands, waterbodies or watercourses. This product is highly toxic to aquatic invertebrates. DO NOT contaminate streams, rivers or waterways with the chemical or used containers. DO NOT apply when there are aquatic and wetland areas including aquacultural ponds or surface streams and rivers downwind from the application area and within the mandatory no-spray zone shown in the table below.

FOR GROUND APPLICATION		
Maximum Application Rate	**Applications per Season**	**Downwind No-Spray Zone**
2000 - 3000 L/ha (600 g/ha clothianidin)	One	40 metres
up to 2000 L/ha (400 g/ha clothianidin)	Two	50 metres

DO NOT apply if heavy rains are expected within 48 hours.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area, away from direct sunlight. 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.

SAFETY DIRECTIONS

Poisonous if swallowed. Wash hands after use.

FIRST AID

If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia Tel. 131126; New Zealand 0800 764 766.

MSDS

Additional information is listed in the Material Safety Data Sheet (MSDS).

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD OR RAIL	
In a Transport Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 024 973** ALL HOURS - AUSTRALIA WIDE

EXCLUSION OF LIABILITY

Unless otherwise expressly stated in writing neither Sumitomo Chemical Australia Pty Ltd nor the distributor has any knowledge of the particular use to which the buyer proposes to put this product. In purchasing this product the buyer must rely solely upon their own skill and judgement as to its suitability for the particular purpose for which it is required. Except to the extent that exclusion or denial of liability is prohibited under the Trade Practices Act or any relevant state legislation, Sumitomo Chemical Australia Pty Ltd and the distributor expressly exclude any warranty as to the quality or fitness of any goods sold for any purpose whatsoever and deny all responsibility in contract tort negligence or otherwise for any harm or damage resulting from the use of such goods or from acting on the advice or recommendations as to such use given in good faith by any representative of Sumitomo Chemical Australia Pty Ltd or the distributor. If these conditions are unacceptable to the buyer, the goods should be returned to Sumitomo Chemical Australia Pty Ltd unopened within seven (7) days for refund of purchase price.

APVMA Approval No.: 60687/2.5kg/0108
APVMA Approval No.: 60687/5kg/0108

Batch No:
Date of Manufacture:

MAXX Organosilicone Surfactant™ is a tradename of Sumitomo Chemical Australia Pty Ltd

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

SUMITOMO STEALTH® SYSTEMIC INSECTICIDE

ACTIVE CONSTITUENT: 500 g/kg CLOTHIANIDIN

GROUP	4A	INSECTICIDE

For the control of African black beetle larvae in turf.

CONTENTS: 1 kg, 2.5 kg

SUMITOMO CHEMICAL

Sumitomo Chemical Australia Pty Ltd
501 Victoria Avenue
Chatswood NSW 2067
Tel: 02 9904 6499
A.B.N. 21 081 096 255

®Registered trademark of Sumitomo Chemical Co., Japan

DIRECTIONS FOR USE:

Restraint:

DO NOT use on fine textured compacted clay soils without amelioration prior to treatment application.

Situation	Pest	Rate	Critical Comments
Turf grass, Lawns	First instar larvae of African black beetle	Apply by boom spray or watering can at 500 - 700 g/ha or 5 - 7 g/100 m² Apply in sufficient water to achieve good coverage.	Monitor the presence of adult beetles and apply at peak egg hatch, generally in spring to early summer or when small larvae are present. Thorough coverage is important. For best results mow the turf prior to treating. Spraying should preferably be on to wet or dewy grass. Irrigate with 10 mm of water within one hour of application.

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

WITHHOLDING PERIOD:

Do not graze treated turf or lawn, or, feed turf or lawn clippings from any treated area to poultry or livestock.

GENERAL INSTRUCTIONS

INSECTICIDE RESISTANCE WARNING

GROUP	4A	INSECTICIDE

For insecticide resistance management Sumitomo STEALTH Systemic Insecticide is a Group 4A insecticide. Some naturally occurring insect biotypes resistant to STEALTH 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 STEALTH or other Group 4A insecticides are used repeatedly. The effectiveness of STEALTH on resistant individuals could be significantly reduced. Since the occurrence of resistant individuals is difficult to detect prior to use, Sumitomo Chemical Australia Pty Ltd accepts no liability for any losses that may result from the failure of this product to control resistant insects. STEALTH may be subject to specific resistance management strategies. For further information contact your local supplier, Sumitomo Chemical Australia Pty Ltd representative or local agricultural department agronomist.

MIXING

Measure the required amount of product to a partially filled spray tank and then add the remainder of the water. Ensure agitation is maintained during tank filling and whilst spraying. Do not let prepared spray solution sit in spray tank overnight.

APPLICATION

This product may be applied by ground equipment only. Ensure equipment is calibrated to give good coverage at correct volume.

COMPATIBILITY

It is advised to test water quality, which may vary considerably with location, as well as all mixtures prior to mixing commercial quantities.

PROTECTION OF LIVESTOCK

Dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift, and residues may remain toxic to bees several days after application.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT apply under weather conditions, or from spraying equipment, that may cause spray drift onto nearby or adjacent areas, particularly wetlands, waterbodies or watercourses. This product is highly toxic to aquatic invertebrates. DO NOT contaminate streams, rivers or waterways with the chemical or used containers. DO NOT apply when there are aquatic and wetland areas including aquacultural ponds or surface streams and rivers downwind from the application area and within 10 m downwind of the application area. DO NOT apply if heavy rains are expected within 48 hours.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area, away from direct sunlight. 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.

SAFETY DIRECTIONS

Poisonous if swallowed. Wash hands after use.

FIRST AID

If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia Tel. 131126; New Zealand 0800 764 766.

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet (MSDS).

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD OR RAIL	
In a Transport Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 024 973** ALL HOURS - AUSTRALIA WIDE

EXCLUSION OF LIABILITY

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APVMA Approval No.: 60688/1kg/0108
APVMA Approval No.: 60688/2.5kg/0108

Batch No:
Date of Manufacture:

CAUTION
KEEP OUT OF REACH OF CHILDREN

SUMITOMO

SHIELD®

SYSTEMIC INSECTICIDE

ACTIVE CONSTITUENT: 200 g/L CLOTHIANIDIN

GROUP	4A	INSECTICIDE

For the control of aphids and mirids on cotton; rust thrips and weevil borer on bananas.

CONTENTS: 5 L, 20 L

Sumitomo Chemical Australia Pty Ltd
501 Victoria Avenue
Chatswood NSW 2067
Tel: 02 9904 6499
A.B.N. 21 081 096 255

®Registered trademark of Sumitomo Chemical Co., Japan.

DIRECTIONS FOR USE:

RESTRAINTS:
For cotton do not apply more than 2 sprays per season and these should alternate with a pesticide from a different group.
For bananas it is recommended that SHIELD is not applied in consecutive crop cycles but rather alternated with a product from a different group to reduce the possibility of rust thrips developing resistance. Do not apply the stem spray application to bananas if rain is expected within 24 hours.

CROP	PEST	RATE	CRITICAL COMMENTS
Cotton	Cotton aphid Green mirid	125 - 250 mL/ha plus MAXX Organosilicone Surfactant™ at 2 mL/L of water.	**Aphids** Apply when aphid numbers are low but starting to build. For example before there are more than 2 leaves per plant with honeydew. **Mirids** Regular pest monitoring is necessary to determine pest numbers. Apply when numbers reach threshold levels requiring treatment. **For both aphids and mirids** Use the higher rate when heavy infestation is expected and longer control is required. Treated insects may still be on the plant 2 or 3 days after application but will have stopped feeding.
Banana	Weevil borer Rust thrips	**Stem Injection** 3 mL per pseudostem injected at the base. **Stem Spray** 4.5 mL per pseudostem sprayed onto the base, in a total water volume of 10 mL.	**Timing** Apply to pseudostem of the main daughter plant when it is a height of 1.5 m to the base of the central cigar leaf, preferably within one month of the bunch on the mother plant being harvested. **Stem Injection** Injection should be angled such that it is not in the centre of the plant but rather under the outside leaf base about 40 mm deep. See Application section for further information. **Stem Spray** Ensure the stem spray is applied to green growing stem. See Application section for further information.

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

WITHHOLDING PERIODS:

Cotton

Harvest:	DO NOT harvest for 5 days after application.
Grazing/Cotton trash:	DO NOT GRAZE TREATED COTTON CROPS OR CUT FOR STOCKFEED. DO NOT FEED COTTON TRASH TO LIVESTOCK.
Bananas	Not required when used as directed.

GENERAL INSTRUCTIONS

INSECTICIDE RESISTANCE WARNING

GROUP	4A	INSECTICIDE

For insecticide resistance management Sumitomo SHIELD Systemic Insecticide is a Group 4A insecticide. Some naturally occurring insect biotypes resistant to SHIELD 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 SHIELD or other Group 4A insecticides are used repeatedly. The effectiveness of SHIELD on resistant individuals could be significantly reduced. Since the occurrence of resistant individuals is difficult to detect prior to use, Sumitomo Chemical Australia Pty Ltd accepts no liability for any losses that may result from the failure of this product to control resistant insects. SHIELD may be subject to specific resistance management strategies. For further information contact your local supplier, Sumitomo Chemical Australia Pty Ltd representative or local agricultural department agronomist.

CROP MONITORING

Effective pest control depends upon regular monitoring of crops during the season at 3-5 day intervals.

MIXING

Measure the required amount of product to a partially filled spray tank and then add the remainder of the water. Ensure agitation is maintained during tank filling and whilst spraying. Do not let prepared spray solution sit in spray tank overnight.

COMPATIBILITY

It is advised to test water quality, which may vary considerably with location, as well as all mixtures prior to mixing commercial quantities.

APPLICATION

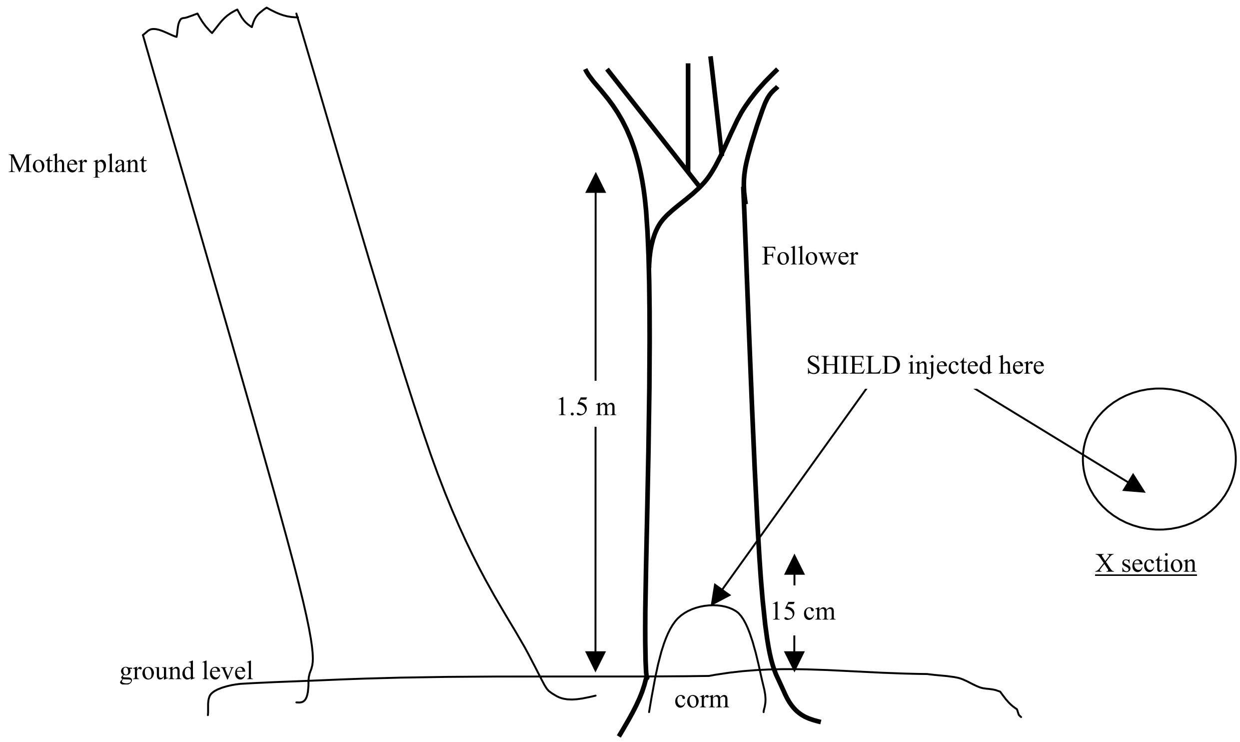
Cotton This product may be applied by air or ground equipment.

Ground: Apply in a minimum spray volume of 100 L/ha.

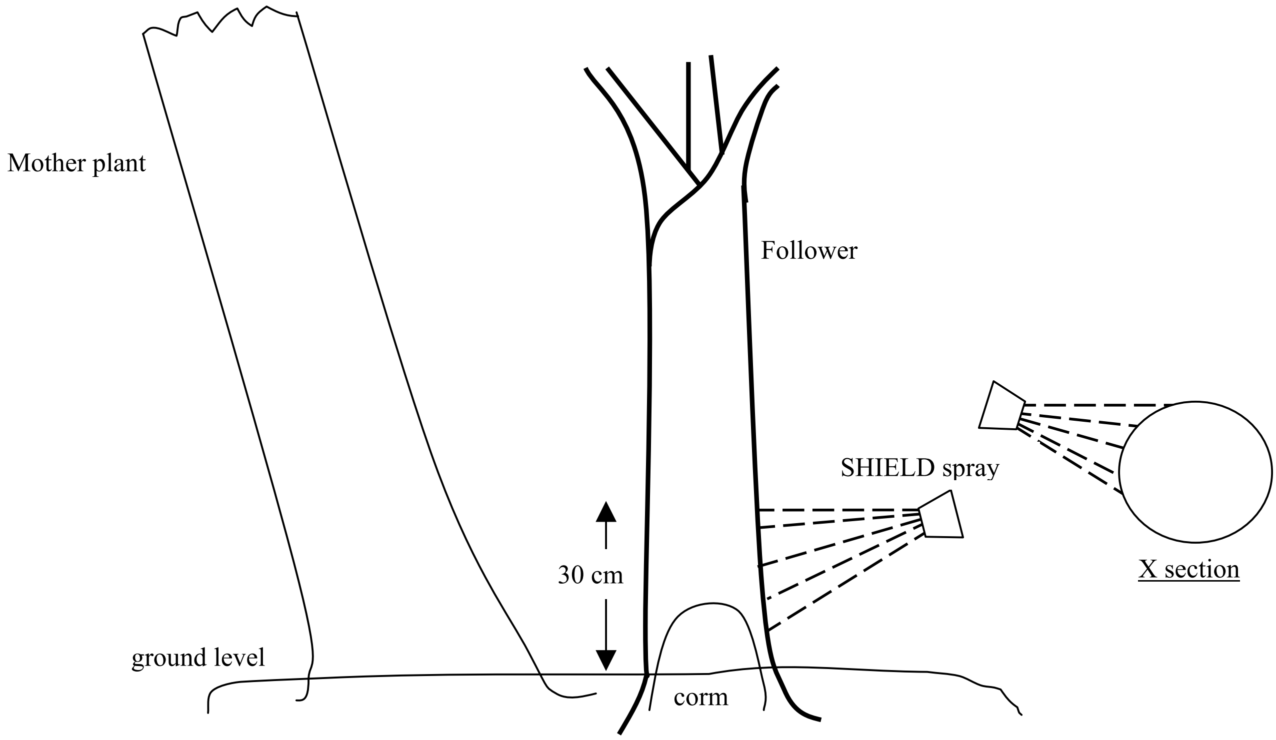
Aerial: Apply in a minimum spray volume of 30 L/ha. A strategy to minimize spray drift should be employed at all times when aerially applying sprays to, or near, sensitive areas. Such a strategy is illustrated by the cotton industry's Best Management Practice Manual.

Bananas This product may be applied by stem injection or stem spray.

Stem Injection: Injection treatments should be applied at 150 mm above ground level angled down towards the base. The needle should go in 100 mm before being drawn back slightly and the liquid injected. The injection should be angled such that it is not in the centre of the plant but rather under the outside leaf base about 40 mm deep. No dilution is required. Chemical should not emerge from the injection site.



Stem Spray: The trunk spray should be applied with a full cone nozzle directed at the base of the stem and up to a height of 300 mm, so that it covers around 40% of that area of the stem. The spray should be calibrated so it delivers 10 mL of mixture per stem. Do not spray on to old leaf bases. Ensure the stem is still green where the spray is applied.



PROTECTION OF LIVESTOCK

Dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift, and residues may remain toxic to bees several days after application.

Risks to non-target insects – Clothianidin may have adverse effects on some non-target beneficials, in particular where IPM is practiced, to foliage dwelling predators.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT apply under weather conditions, or from spraying equipment, that may cause spray drift onto nearby or adjacent areas, particularly wetlands, waterbodies or watercourses. This product is highly toxic to aquatic invertebrates. DO NOT contaminate streams, rivers or waterways with the chemical or used containers. DO NOT apply when there are aquatic and wetland areas including aquacultural ponds or surface streams and rivers downwind from the application area and within the mandatory no-spray zone shown in the table below.

FOR AERIAL APPLICATION		
Applications per Season	Spray Quality	Downwind No-Spray Zone
One	**Fine**	**300 metres**
Two	**Fine**	**800 metres**
One or Two	**Fine-Medium**	**300 metres**
FOR GROUND APPLICATION		
Downwind No-Spray Zone		
40 metres		

DO NOT apply if heavy rains are expected within 48 hours. A strategy to minimise drift should be employed at all times when aerially applying sprays to, or near, sensitive areas. Such a strategy is illustrated by the cotton industry's Best Management Practice Manual.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area, away from 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.

For refillable containers: Empty contents fully into application equipment. Close all valves and return to point of supply for refill or storage.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia Tel. 131126; New Zealand 0800 764 766.

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet (MSDS).

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD OR RAIL	
In a Transport Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 024 973** ALL HOURS - AUSTRALIA WIDE

EXCLUSION OF LIABILITY

Unless otherwise expressly stated in writing neither Sumitomo Chemical Australia Pty Ltd nor the distributor has any knowledge of the particular use to which the buyer proposes to put this product. In purchasing this product the buyer must rely solely upon their own skill and judgement as to its suitability for the particular purpose for which it is required. Except to the extent that exclusion or denial of liability is prohibited under the Trade Practices Act or any relevant state legislation, Sumitomo Chemical Australia Pty Ltd and the distributor expressly exclude any warranty as to the quality or fitness of any goods sold for any purpose whatsoever and deny all responsibility in contract tort negligence or otherwise for any harm or damage resulting from the use of such goods or from acting on the advice or recommendations as to such use given in good faith by any representative of Sumitomo Chemical Australia Pty Ltd or the distributor. If these conditions are unacceptable to the buyer, the goods should be returned to Sumitomo Chemical Australia Pty Ltd unopened within seven (7) days for refund of purchase price.

APVMA Approval No.: 60689/5L/_____
60689/20L/_____

Batch No:
Date of Manufacture:

MAXX Organosilicone Surfactant™ is a tradename of Sumitomo Chemical Australia Pty Ltd

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 partitioning 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.

REFERENCES

Felton, J.C., Oomen, P.A. & Stevenson, J.H. 1986, ‘Toxicity and hazard of pesticides to honeybees: harmonisation of test methods’, *Bee World*, vol. 67, no. 3, pp. 114-24.

Goring, C.A.I. et al. 1975, ‘Principles of pesticide degradation in soil’, in *Environmental Dynamics of Pesticides*, edited by R. Haque and V.H. Freed, Plenum Press, New York, pp 135-72.

Matthews, G.A. 1992, *Pesticide Application Methods*, 2nd ed., Longman, London.

Australian Pesticides and Veterinary Medicines Authority 2007, *Agricultural Manual of Requirements and Guidelines for Agricultural and Veterinary Chemicals [AgMORAG]*, APVMA, Canberra (see footnote below).

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, APVMA, Canberra. (See footnote below)

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

APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of clothianidin in the products Sumitomo Shield Systemic Insecticide, Sumitomo Samurai Systemic Insecticide, and Sumitomo Stealth Systemic Insecticide, please fill in this form and send it, along with payment of $30 to:

Public consultation - clothianidin
Pesticides Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
Public consultation - clothianidin at (02) 62104776.

Name (Mr, Mrs, Ms, Dr)____
Position ____
Company/organisation ____
Address ____
Contact phone number (___) ______________________________________

I enclose payment by cheque, money order or credit card for $__________

Make cheques payable to 'Australian Pesticides and Veterinary Medicines Authority'.

___ Bankcard ___ Visa ___ Mastercard

Card number ______/______/______/______ Expiry date ...../....../......

Signature___________________________________ Date ______________