Public Release Summary
on

Evaluation of the new active BUPROFEZIN

in the product

APPLAUD INSECTICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

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Canberra
Australia

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FOREWORD

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

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

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

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals.*

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library, 22 Brisbane Ave, Barton, ACT.

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

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	acceptable daily intake (for humans)
ai	active ingredient
ANZFA	Australian New Zealand Food Authority
bw	body weight
CCPR	Codex Committee on Pesticide Residues
d	day
DM	dry matter
DT_{50}	time for 50% loss, half life
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
F	female
FAO	Food and Agriculture Organisation of the United Nations
GAP	Good Agricultural Practice
GC-MSD	gas chromatography with mass selective detector
h	hour
HPLC	high pressure liquid chromatography *or* high performance liquid chromatography
HPLC-UV	high performance liquid chromatography with ultra-violet detector
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
IOBC	International Organisation for Biological Control
IPM	Integrated Pest Management
JMPR	Joint FAO/WHO Meeting on Pesticide residues
kg	kilogram
Koc	adsorption coefficients based on organic carbon content
L	litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
M	male
mg	milligram
mL	millilitre
MRL	maximum residue limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimate of Dietary Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	no observable effect concentration/level
%OC	percentage organic carbon
PHI	pre-harvest interval
pka	acid dissociation constant
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
s	second
SPE	solid phase extraction

STMR	supervised trials median residue
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TRR	total radioactive residues
T-Value	a value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TGAC	technical grade active constituent
WHO	World Health Organisation
WHP	withholding period

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SUMMARY

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is considering an application to register the product Applaud Insecticide (Applaud). This product contains the new active buprofezin. This product claims to control red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops.

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of buprofezin. Before deciding whether to approve this product for use in Australia, the NRA invites public comment. Comments should be submitted by 31 July 2001, to the NRA at the address indicated on page 1.

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

Public Health Aspects

Toxicology

Buprofezin has low oral toxicity in rats, very low oral toxicity in hamsters and rabbits and very low dermal and inhalational toxicity in rats. Buprofezin is not a skin irritant in rabbits, or a skin-sensitiser in guinea pigs, but is a slight eye irritant to rabbits.

Applaud Insecticide, a product containing 400 g/L buprofezin, has very low oral and low dermal toxicity in rats. The inhalational toxicity of the product was moderate. It is not a skin irritant but is a slight eye irritant in rabbits and is not a skin sensitiser in guinea pigs.

Following ingestion buprofezin is rapidly absorbed, widely distributed in the tissues and rapidly eliminated in rats. Although only about half of an ingested dose is absorbed, it is extensively metabolised and then excreted in bile and urine. Repeat-dose studies indicated that the primary targets for buprofezin toxicity are the liver and thyroid. At high doses, mice, rats and dogs had increased liver and thyroid weight which was accompanied by microscopic changes such as swelling and an increased number of liver and thyroid cells. In dogs there was also an increased concentration of liver enzymes in the blood indicating some liver damage. However, studies on thyroid function revealed no effects on thyroidal enzyme activity even at high doses.

Specific studies indicated that buprofezin does not damage genetic material. Additionally, long-term exposure studies in mice, rats and dogs indicated that buprofezin does not cause cancer. There were no effects on reproductive behaviour or performance in rats and at doses which were not toxic to the mother, there were no developmental effects on the rat or rabbit foetus.

Conclusion:
Based on an assessment of the toxicology, it was considered that there should be no adverse effects on human health from the use of this product when used in accordance with the label directions.

Residues in food and trade aspects

The Applicant provided residue data for citrus fruit from trials conducted in Australia (7), New Zealand (1), Italy (3), Spain (1) and Portugal (1). The residue data which were in accordance with the use pattern proposed by the applicant ranged from 0.05 to 0.69 mg/kg for oranges, lemons and mandarins. The data taken as a whole allowed the establishment of an MRL of 2 mg/kg for citrus fruit.
Data for mangoes were generated from six trials conducted in Australia. Residues in whole fruit ranged <0.01 to 0.045 mg/kg at 28 days after treatment. An MRL of 0.2 mg/kg is recommended for mango.
Evaluation of animal transfer data and predicted dietary burdens indicates that the following animal commodity MRLs are required: meat [in the fat] *0.05 mg/kg, edible offal *0.05 mg/kg and milks *0.01 mg/kg.

The residue definition for monitoring Good Agricultural Practice (GAP) and dietary intake is *buprofezin*.

Registration of Applaud Insecticide will not pose a significant risk to human health.

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

Table 1

Compound	**Food**		**MRL (mg/kg)**
DELETE:			
Buprofezin	FC 0001	Citrus fruits	T 3
	MO 0105	Edible offal (mammalian)	T *0.05
	MM 0095	Meat (mammalian)	T *0.05
	ML 0106	Milks	T *0.01
ADD:			
Buprofezin	FC 0001	Citrus fruits	2
	MO 0105	Edible offal (mammalian)	*0.05
	FI 0345	Mango	0.2
	MM 0095	Meat (mammalian) [in the fat]	*0.05
	ML 0106	Milks	*0.01

* Denotes MRL set at or about the limit of analytical quantitation
T Temporary MRL

Table 4

Compound	Animal Feed Commodity		MRL (mg/kg)
ADD:			
Buprofezin	AB 0001	Citrus pulp, dry	5

The following withholding period statements are recommended in conjunction with the above MRLs:
Harvest

Citrus fruits: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Mango: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Livestock Protection Statement

Do not allow livestock to graze grasses or weeds under treated trees

Based on this assessment, residue related risk is considered low and acceptable.

Occupational health and safety aspects

Buprofezin is not on the NOHSC *List of Designated Hazardous Substances.* Based on the NOHSC *Approved Criteria for Classifying Hazardous Substances,* Buprofezin and Applaud Insecticide are classified as non-hazardous.

Applaud Insecticide will be imported fully formulated and packaged. It will be packed in 1, 5 and 10 L containers.

Applaud Insecticide possesses low acute oral and dermal toxicity. The product is not a skin irritant or a sensitiser but is a slight eye irritant.

Applaud Insecticide is proposed for the control of red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops. It will be applied by oscillating boom or by airblast sprayers. The proposed application rate is 60mL product/100 L.

Worker exposure data was not available for buprofezin or Applaud Insecticide.

Instructions and Safety Directions are provided on the product labels to minimise exposure to the product. Based on the risk assessment, elbow length PVC gloves and cotton overalls are recommended for users of Applaud Insecticide. A re-entry statement is not required for this product.

Environmental aspects

Buprofezin is to be used for control of red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops. Residues are expected to be associated mainly with the surrounding soil, or water bodies via spray drift. While hydrolysis is a possible degradation route in acidic media (pH 5), sunlight is not expected to be a major route of degradation in aqueous media. Aerobic soil metabolism is a route for primary degradation with eventual mineralisation occurring. Measured DT_{50} values of buprofezin in aerobic soils were in the order of 26-220 days with the rate of degradation related to the soil's microbial status. Under aerobic field conditions, the half-lives were of the order of 50 to 70 days and about 36 to 104 days under flooded field conditions. Buprofezin has low to slight soil mobility and did not show any significant leaching in soil with a low organic matter content. Additionally there were no mobile degradation products seen in any significant quality and buprofezin is classified as an unlikely leacher. A field dissipation study in a rice paddy showed that buprofezin residues in the aquatic systems rapidly dissipated. Overall, accumulation in soils is not expected to be a major concern. Buprofezin accumulates moderately in bluegill sunfish with ready depuration on cessation of exposure.

Buprofezin is practically non-toxic to birds in acute and sub-acute dietary studies. Acute exposure of fish to buprofezin showed there was no mortality caused up to the level of the chemical's water solubility. No chronic fish studies with either buprofezin or the formulated product were presented. Buprofezin had a marked adverse effect on *Daphnia magna*, with most of the exposed daphnids immobile after 48 hours exposure to a mean measured concentration of 420 µg buprofezin/L. Under chronic exposure conditions, buprofezin is moderately toxic to young *D. magna* Straus. Acute exposure of the green alga, *Pseudokirchneriella subcapitata* to buprofezin at approximately 150% of the proposed maximum Australian use rate had no effect on growth rate or biomass. A 14 day exposure of duckweed, *Lemna gibba*, to buprofezin as a 70% wettable powder applied at a rate of 4.4 kg buprofezin/ha, resulted in no significant difference in frond numbers in the buprofezin exposed samples and controls leading to the conclusion that the formulated buprofezin product was not toxic to *Lemna gibba* under the test conditions.

Laboratory and field studies indicate that buprofezin is practically non-toxic to honey bees (*Apis mellifera*) by either contact or ingestion. Laboratory and field studies with parasitic wasps indicated no significant harmful effects occurred after treatment with rates of up to 1.8 kg buprofezin/ha (the maximum proposed Australian use rate is ca. 2.9 kg buprofezin/ha). Laboratory studies indicated that oriental ladybirds exposed to formulated product at rates of 12.5 to 50 g buprofezin/100 L showed significant mortality effects at the maximum exposure rate and reduction in viable egg production at rates above 12.5 g/100 L. The proposed Australian use rate maximum is 24 g buprofezin/100 L, a rate which will result in marked adverse effects on the survival of this ladybird species. In contrast, buprofezin was harmless to the steel-blue ladybird with respect to after treatment at 12.5 g buprofezin/100 L. Predatory mites exposed to a 25% WP formulation at 50 g/L of buprofezin, suffered no significant mortality, little oviposition inhibition, nor adverse effects on development.

Laboratory earthworm tests with *Eisenia foetida* indicated that buprofezin had no adverse effects on mortality or behaviour that could be related to the exposure over a 14 day period at concentrations of up to 1000 mg/kg dry soil respectively. There was, however, a statistically significant reduction in the worms' bodyweights after exposure to buprofezin at the 1000 mg/kg dry soil level. A study of the effect of buprofezin on soil microflora indicate that buprofezin should not have long term effects on the microbial populations.

The hazard assessment indicates that buprofezin in the feed supply of birds and mammals will not result in unacceptable adverse effects and it is unlikely that the proposed use of Applaud Insecticide is a hazard to birds or mammals. Direct overspray would present a hazard to fish and daphnids and possibly other aquatic species. There is an indicated hazard at 10% spray drift but use of the Ganzelmeier model shows hazard should be acceptable to fish and *D. magna* with a buffer distance of approximately 15 m. A 1% runoff produces levels of contamination similar to a 10% spray drift. However, the soil mobility metabolism and dissipation studies, plus the use of a suitable buffer distance, show that there is low likelihood of there being any significant transfer to aquatic environments and any hazard should be further reduced by the trapping of runoff in any grassed areas between the treated trees.

Buprofezin is most likely to be practically non-toxic to honeybees by either contact or ingestion and the proposed use pattern is not expected to result in an unacceptable hazard. Buprofezin was not hazardous to spiders, silk worms, parasitic wasps, and predacious mites. A laboratory study indicated definite hazard to oriental ladybirds would be expected from the proposed use rates of Applaud Insecticide. In contrast steel-blue ladybirds appeared unaffected by exposure to the active.

Environment Australia concludes that a low hazard to the environment may be predicted provided the product is used according to the proposed label recommendations and Good Agricultural Practice.

Efficacy and crop safety aspects

Buprofezin is a thiadiazine insect growth regulator. It acts by inhibiting cuticle deposition. It also suppresses egg laying in female adults with inhibition of prostoglandin synthesis and has effects on levels of hormones associated with moulting in nymphs.

The data presented supported the claim for control of red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops. The design, analysis and conduct of the efficacy trials were adequate.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical buprofezin (Applaud Insecticide) to control red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops.

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

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

Written comments should be received by the NRA by 31 July 2001. They should be addressed to :

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Applicant

Dow Agrosciences Australia Limited

Product details

Buprofezin will be marketed under the trade name Applaud (containing 400g/L buprofezin) as a suspension concentrate formulation.

Applaud will be formulated overseas and imported into Australia.

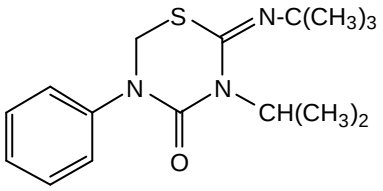
Dow Agrosciences Australia Limited intend to market Applaud in all States and Territories.

CHEMISTRY AND MANUFACTURE

The active constituent, buprofezin, is manufactured in Japan by Nihon Nohyaku Co Ltd.

Chemical Characteristics of the Active Constituent

Common name: Buprofezin (BSI)
Synonyms and code number: NNI-750, ST-29285
Chemical name
(CAS): 2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1,3,5-thiadiazin-4-one
(IUPAC): 2-tert-butylimino-3-isopropyl-5-phenylperhydro-1,3,5-thiadiazin-4-one
(CAS RN): 69327-76-0
Molecular formula: $C_{16}H_{23}N_3OS$
Molecular weight: 305.44 g/mol
Chemical structure:



Physical and Chemical Properties of Pure Active Constituent

Physical state: crystalline solid
Colour: white
Odour: none
MP: 104.2-105.5°C
Density: 1.183-1.187 g/mL at 20°C
Solubility in water: 0.382 mg/L at 25°C
Solubility in organic solvents: 520 g/L in chloroform, 320 g/L in toluene, 240 g/L in acetone, 220 g/L in ethyl acetate, 20 g/L in methanol, 20 g/L in n-hexane.
Vapour pressure: 0.0168 Pa (52°C), 0.163 Pa (72°C), 2.01 Pa (101°C), 8.79 Pa (122°C), 54.8 Pa (151°C).
Octanol/water partition coefficient: log P_{OW} = 4.31 at 20°C
Storage stability: Buprofezin is stable for 14 days at 54°C, and stable to metal ions up to 200°C.
Pesticide group: Insect growth regulator
Chemical family: Thiadiazine derivative

PRODUCT

Distinguishing name or trade name: Applaud Insecticide
Formulation type: Suspension concentrate
Active constituent concentration: 400 g/L

Physical and Chemical Properties of the product

Physical state: Suspension concentrate
Density: 1.09 g/mL (25°C)
Acidity, alkalinity or pH: 6.35
Viscosity: 460 mPa s
Storage stability: Stable for 21 days at 54°C

The source of the technical grade active constituent to be used in the product has been approved by the NRA (approval number 51554).

MSDS for the inactive constituents were provided.

Review of the product chemistry data has been completed. The available data supports the registration of Applaud Insecticide for the proposed use.

TOXICOLOGICAL ASSESSMENT

The toxicological database for buprofezin, which consists primarily of toxicity tests conducted using animals, is quite extensive. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared to likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Metabolism and Toxicokinetics

After oral dosing, buprofezin was rapidly absorbed and widely distributed in the tissues with no evidence of accumulation, and rapidly eliminated. There were no significant sex or dosing regime differences in excretion or metabolism in rats. Most of an orally administered dose (70-80%) was excreted in the faeces rather than the urine (13-21%). Up to 38% had been excreted in the bile after 24 hours. Buprofezin is metabolised mainly by hydroxylation of the phenyl ring, resulting in 4-hydroxy, 3,4-dihydroxy and 3-hydroxy-4-methoxy buprofezin, and oxidation of sulphur to form isopropyl phenyl urea through cleavage of the thiadiazine ring, with much of the excreted material in the form of conjugates. Buprofezin is not changed in the intestinal tract, but bile metabolites are further metabolized in the intestinal tract to form metabolites found in faeces.

Acute Studies

Buprofezin has low acute oral toxicity in rats (LD_{50} M= 2198 mg/kg, F= 2355 mg/kg; no deaths), and very low acute oral toxicity in hamsters (LD_{50} > 10,000 mg/kg; no deaths) and rabbits (LD_{50} >5000 mg/kg; no deaths). Acute dermal (LD_{50} > 5000 mg/kg; no deaths) and inhalational (LC_{50} > 4570 mg/m^3 ; no deaths) toxicity were very low in rats. Buprofezin was not a skin irritant, but was a slight eye irritant in rabbits, and was not a skin sensitiser in guinea-pigs.

The product, Applaud Insecticide, containing 400 g/L of buprofezin, showed very low acute oral (LD_{50} > 5000 mg/kg; no deaths) and low dermal (LD_{50} > 2000 mg/kg; no deaths) toxicity in rats. The product showed an LC_{50} for inhalational toxicity of > 930 mg/m^3 in rats, was not a skin irritant but was a slight eye irritant in rabbits, and was not a skin sensitiser in guinea-pigs.

Short-Term Studies

In rats fed buprofezin at dietary concentrations of 0, 40, 200, 1000 or 5000 ppm for 90 days, body weight gains were slightly suppressed at 5000 ppm. Water intake was increased in males at 5000 ppm. Decreased haematocrit, haemoglobin and red blood cell count were noted in males and haematocrit in females at the highest concentration. At 5000 ppm, activated partial thromboplastin times were prolonged,

serum glucose and triglyceride concentrations were lowered and the concentrations of total cholesterol and phospholipids were elevated.

There were increases in serum beta-globulin, alpha 1-globulin and albumin and a decrease in gamma-globulin in males at 5000 ppm, and increased albumin, alpha 1-globulin, alpha 2-globulin, alpha 3-globulin and beta-globulin in females at this dose. Serum glucose was lowered in males dosed at 200 ppm and above and beta-globulin and alpha 1-globulin were elevated in females receiving 1000 ppm. Both absolute and relative liver and thyroid weights were increased at 5000 ppm in animals of both sexes. In the 1000 ppm group, the relative thyroid weight was increased in males and relative liver weight in females. Enlargement of the hepatocytes in the central to the middle zone of the lobules and thickening and hyperplasia of the follicular epithelial cells of the thyroids were observed in high dose animals and in some animals at 1000 ppm. The NOEL was 40 ppm, equal to 3.4 mg/kg bw/day for males and 4.1 mg/kg bw/day for females, based on decreased serum glucose levels in males at 200 ppm.

In dogs administered buprofezin orally at doses of 0, 2, 10, 50 or 300 mg/kg/day, subdued behaviour and signs of slight ataxia, slight abdominal distension, and lowered body weight gains were observed at the highest dose. Elevated liver weights were seen at 50 and 300 mg/kg/day, with increased levels of plasma alkaline phosphatase activity seen in males at 50 mg/kg/day and in all dogs receiving 300 mg/kg/day, while the normal decline in alkaline phosphatase activity with maturity was less evident in animals receiving 10 mg/kg/day and in females dosed at 50 mg/kg/day. Slightly elevated alanine aminotransferase activity was recorded in five dogs receiving 300 mg/kg/day. Absolute and relative liver weights were increased in all dogs receiving 50 or 300 mg/kg/day, kidney weights were increased in dogs receiving the highest dose, and high thyroid weight was noted in males receiving 50 mg/kg/day and males and females receiving 300 mg/kg/day. Homogeneity of cytoplasm and intracytoplasmic eosinophilic bodies in the hepatocytes were seen in dogs receiving 50 (one female only) or 300 mg/kg/day. The NOEL was 10 mg/kg bw/day based on elevated liver weights, liver enzymes, and thyroid weights at 50 mg/kg bw/day.

Chronic Studies

Mice fed buprofezin at concentrations of 0, 20, 200, 2000 or 5000 ppm for 2 years had retarded growth, decreased specific gravity of urine, reduced levels of protein in the urine, elevation in platelet and lymphocyte count, increased absolute and relative liver weight and an increased incidence of hepatocellular swelling and hepatocellular hyperplasia at the highest dose. The total blood cholesterol was increased at week 52 for females and week 104 for males. At 2000 ppm, growth was slightly retarded, and liver weights and the incidence of centrilobular hepatocellular swelling were increased in both sexes after 52 weeks, with an increased incidence of hepatocellular hyperplasia observed in females. An increase in liver weight was noted in males at week 52 at 200 ppm. Buprofezin was not carcinogenic in mice. The NOEL was 20 ppm equal to 1.82 and 1.89 mg/kg bw/day in male and female mice respectivly, based on increased liver weight in males at 200 ppm.

In rats fed buprofezin at concentrations of 0, 5, 20, 200 or 2000 ppm for 24 months, body weights were lowered at 2000 ppm and relative kidney and heart weights increased in females at 200 and 2000 ppm. Hypertrophy of hepatocytes was seen in males and females at the highest dose, associated with proliferation of smooth endoplasmic reticulum, and the incidence of hyperplastic nodules. Thickening and hyperplasia of the follicular epithelial cells in thyroids were observed in most of the animals at 2000 ppm and in a few animals in the 200 ppm group, and increased incidence of cystitis, chronic nephrosis and interstitial oedema in the heart was observed in females at the highest dose. There was no evidence of carcinogenicity in rodents. The NOEL was 20 ppm, equal to 0.9 and 1.1 mg/kg bw/day for males and females respectively, based on increased kidney and heart weights and thickening and hyperplasia of thyroidal epithelial cells.

In dogs administered buprofezin orally at doses of 0, 2, 20 or 200 mg/kg bw/day for two years, body weight gain was suppressed in both sexes and food consumption was slightly lower in males at the highest dose. Increased plasma alkaline phosphatase activity was seen at 20 and 200 mg/kg/day, and an increase in plasma alanine amino-transferase activity was recorded at 200 mg/kg/day. Reduced serum thyroxin was noted in dogs at 200 mg/kg/day. Bromosulfophthalein retention was increased in females receiving 20 or 200 mg/kg bw/day. Liver and thyroid weights were increased at 20 and 200 mg/kg bw/day. Enlargement of centrilobular hepatocytes and bile duct hyperplasia in the liver was seen in dogs receiving 20 and 200 mg/kg bw/day. The NOEL was 2 mg/kg bw/day, based on liver and thyroid effects at 20 mg/kg bw/day.

Reproduction and Developmental Studies

In reproduction studies in rats fed buprofezin at doses of 10, 100 and 1000 ppm, body weight gains were reduced in F1 and F2 males at the highest dose and also at lower doses, especially in F1 animals. Survival of F0 pups was decreased during days 0-4 of the lactation period at 10 and 1000 ppm, respectively. In addition, lower mean live pup weight in all dosed groups at first mating, a decrease in the number of delivered and live pups in the 100 and 1000 ppm groups from F1 2nd mating (F2b), and a decrease in body weights of the pups during lactation in the top-dose, most pronounced in F1a and F2a animals, were observed in all dose groups in F2a. Foetal weight was decreased in the second mating of F0 (F1b) in all dose groups, but this effect was not dose-related and was not observed in the analogous F2 animals. The absolute and relative liver weights were increased in F0 males and females at 1000 ppm. No effects on reproduction function were observed. The NOEL was 10 ppm, equal to 0.6 mg/kg/day in males and 0.9 mg/kg/day in females.

In a single-generation study in rats fed buprofezin in the diet at 10, 100 or 1,000 ppm, reduced pup-weight gain and increased relative liver weight were observed in animals of both sexes at 1000 ppm. The NOEL in this study was 100 ppm, equal to 6.4 mg/kg bw/day and 8.9 mg/kg bw/day for males and females respectively.

In a developmental study in rats given buprofezin from day 6 to 15 of gestation at oral doses of 0, 50, 200 or 800 mg/kg bw/day, maternal toxicity was evidenced by reduced food intake, decreased body weight, loose faeces, urogenital staining, lethargy, hunched posture, thin appearance and piloerection at 800 mg/kg. Water consumption was increased at 200 or 800 mg/kg bw/day. Four females showed total embryonic resorption at 800 mg/kg bw/day and in females which carried live young to term, increased early post-implantation loss and reduced litter size and foetal weight were noted. Foetuses in the 800 mg/kg dose group showed an increased incidence of subcutaneous oedema and signs of slight foetal immaturity including reduced mean foetal weight. There was no indication of teratogenic potential. The NOEL for maternal toxicity was 38 mg/kg bw/day and for embryotoxicity was 175 mg/kg bw/day in rats.

Rabbits were given buprofezin orally from day 6 to 19 of gestation at doses of 0, 10, 50 or 250 mg/kg bw/day. Animals at 250 mg/kg/day lost weight initially following onset of treatment, and overall body weight gain during gestation was reduced. Food consumption was reduced from the commencement of the treatment period until day 13 of gestation in the 250 mg/kg group. Two females receiving 250 mg/kg bw/day showed resorption of the entire litter. Buprofezin gave no indication of teratogenic potential. The NOEL for maternal toxicity in rabbits was 50 mg/kg bw/day.

Genotoxicity Studies

Buprofezin showed a positive result (aneuploidy) at high concentrations in an *in vitro* cell culture system in Syrian hamster embryo cells without DNA damage and the product, Applaud Insecticide, caused chromosomal damage in bone marrow cells of male Swiss mice, but not in spermatocytes. Buprofezin was not genotoxic in the following *in vitro* and *in vivo* mutagenicity studies at the level of genes and chromosomes : 2 Ames tests using bacteria *S. typhimurium*, reverse mutation with *E. coli*, mouse lymphoma forward mutation assay, *in vivo* in BDF1 mice, DNA repair assay (*B. subtilis* H17 & M45), *in vitro* cytogenetics (human lymphocytes), unscheduled DNA synthesis in primary hepatocytes from male rats and mouse micronucleus test. The negative results for *in vivo* and *in vitro* studies with metabolic activation suggest that buprofezin is not genotoxic *in vivo.*

Other studies (effect of buprofezin on duodenal ulcer induction and thyroid function in rats)

Rats were administered a single oral dose of buprofezin at 0, 613, 1036, 1751, 2959 or 5000 mg/kg. Four males and 8 females in the 2959 mg/kg group and 9 males and 10 females in the 5000 mg/kg group were found dead or killed *in extremis*. Behavioural effects observed at most doses included tremor, subdued behavior, diarrhoea, gait disturbance, piloerection, lacrimation, soiled fur, chromodacryorrhoea and eyelid closing. Decreased body weight was shown in surviving animals at 1751 mg/kg and above. At necropsy there was congestion, red or white spots and/or perforated foci in the proximal duodenum in males treated at 2959 mg/kg and above and in females at 1751 mg/kg and above. Ulcerous lesions in the duodenum were detected in one male treated at 1751 mg/kg, in 5 males and 8 females at 2959 mg/kg and in all males and females at 5000 mg/kg.

In male rats treated orally with buprofezin at doses of 100, 300 or 1000 mg/kg/day for 7 days, dose-related decreases in serum tri-iodothyronine (T3) and thyroxine (T4) concentrations were observed.

Rats were fed a diet containing buprofezin at concentrations of 200, 1000 and 5000 ppm, or 5000 ppm propyl-thiouracil (PTU) for 1, 3 or 6 months. At 5000 ppm of buprofezin the levels of serum T3 and T4 decreased to 30% and 70% of each control level, respectively and then recovered. In the rats treated with PTU the decreases of the serum levels of T3 and T4 were more marked than those in rats treated with buprofezin at 5000 ppm and the recoveries of those thyroid hormone levels were not observed.

Body weight gain was strongly depressed by 15 days after commencement of the treatment in rats dosed with 500 mg buprofezin/kg bw/day or 30 mg PTU/kg bw/day by oral gavage for 15, 30 or 60 days. Absolute and relative thyroid weights were increased in the treated groups, serum T4 was lowered and thyroidal peroxidase activity was elevated. All the changes in PTU-dosed animals were more pronounced than those of the buprofezin dosed animals. In buprofezin- and PTU-dosed animals, vacuolation of cells was scored moderate to severe in anterior pituitary.

No effect of Buprofezin was observed in an *in vitro* study of buprofezin in which PTU and potassium cyanide were added to a reaction mixture of thyroidal peroxidase at concentrations up to 7.2 x 10-5 M.

The potency of buprofezin for thyroid inhibition was checked in a comparison of the effect of buprofezin on serum protein-binding iodine (PBI) in rats, mice, hamsters, guinea pigs and rabbits. Buprofezin had lower potency for thyroid inhibition than PTU and the rat appears to be more sensitive to this effect than mice, hamsters, guinea pigs and rabbits.

A potential metabolite, 1-isopropyl-3-phenylurea was not mutagenic in bacterial strains, *Salmonella typhimurium* and *E. coli* WP2 uvr A, in the presence and absence of metabolic activation.

The effects of buprofezin in humans have been reported by a manufacturer of technical material. Medical surveillance of workers who routinely handled buprofezin in a factory has been undertaken, revealing no effects which could be attributable to exposure to buprofezin.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

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

On the basis of its low toxicity, the NDPSC recommended that buprofezin be scheduled S5 in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first aid directions on the product label.

NOEL/ADI

The lowest overall NOELs for buprofezin were 1 mg/kg bw/day established in a 2-year rat study, based on increased kidney and heart weights and thickening and hyperplasia of thyroidal epithelial cells, and 0.9 mg/kg bw/day in a two generation reproduction study in rats, based on maternotoxicity and foetotoxicty at the next highest dose. A safety factor of 100 is considered appropriate for the ADI, due to the extensive, good quality toxicology database for buprofezin. This results in an ADI of 0.01 mg/kg bw/day.

RESIDUES ASSESSMENT

As part of the residues evaluation of this application, metabolism of buprofezin in plants and animals, analytical methodology in citrus fruit and animal tissues, a transfer study in dairy animals, storage stability in crops and animal tissues and residues data for citrus fruit and mango were considered.

Metabolism

Lemon trees received single or double applications of [^{14}C-U phenyl] buprofezin at either 75 days before harvest or 75 and 14 days before harvest. Up to 91% and 97% of the radioactivity was recovered for the single and double applications, respectively. The radioactivity was primarily present in the surface wash (16% and 65%, single and double application) and peel (74% and 32%, single and double application) of the fruit. Less than 2% of the recovered radioactivity was present in the pulp. Non-extracted radioactivity accounted for 9% and 3% of the Total radioactive residues (TRR) following single and double applications, respectively.

TRR in whole fruit were primarily composed of parent buprofezin following the double application and a ring-opened form of the parent compound (Metabolite A) following single application. Other transformation products formed by hydroxylation at the phenyl ring and oxidative cleavage were present at less than 10% of TRR.

In rats, buprofezin is readily eliminated via excreta within 48 hours after administration (>86% of the administered dose), with faeces being the major route of elimination. After 96 hours, the highest levels of radioactivity were present in liver, kidney and fat. Further characterisation of the metabolites in liver revealed that *p*-OH buprofezin (BF2) and a sulphoxide form of buprofezin (BF10[)]) were the major components of the radioactivity. In an accumulation study where high doses of buprofezin were fed to rats (up to 1000 mg/kg bw), fat was found to be the target tissue, compared to liver and kidney.

A lactating cow was orally dosed with [^{14}C-U phenyl] buprofezin for 7 days. Approximately 66% of the administered dose was recovered, of which 64% was excreted; 1.6% was present in tissues and 0.09% was present in milk. In tissues, the majority of the radioactivity was found in liver, kidney and milk. Further characterisation of the radioactivity in liver, kidney and milk was reported; approximately 55% and 30% of the TRR in liver and kidney, respectively remained unextractable. In kidney, metabolite BF2 (*p*-OH buprofezin) was the predominant component of the radioactivity and in milk BF23 (*p*-acetaminophenol) was the major component of the radioactivity. In liver and milk, all metabolites were present at less than 10% of the recovered radioactivity; BF2 was present in liver at 18% of the recovered radioactivity.

Analytical methods

A validated method for the determination of buprofezin and *p*-OH buprofezin in citrus was provided. Buprofezin and *p*-OH buprofezin are acetylated and determined by GLC as two separate chromatographic peaks. The limits of quantitation were 0.1 mg/kg for buprofezin and 0.05 mg/kg for *p*-OH buprofezin. Acceptable recoveries were reported. In the mango trials conducted in Australia, the Limits of Quantitation were 0.01 – 0.02 mg/kg in both mango pulp and peel.

In a modified method provided by the applicant, residues of buprofezin are determined by LC-MS/MS following solid phase clean up. The Limits of Quantitation are 0.02 mg/kg in pulp, peel and whole fruit.

[)] BF10 = 2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one 1-oxide.

A method for determination of buprofezin, BF12[▶] and BF23 (*p*-acetaminophenol) in milk was provided. Residues are determined using GC/NPD following clean-up using SPE cartridge. The Limit of Quantitation is 0.01 mg/kg; appropriate recoveries were reported. In tissues, residues of buprofezin, BF12 and BF2 are determined using GC/MS; the Limits of Quantitation are 0.05 mg/kg in muscle, fat, liver and kidney. Acceptable recoveries were reported for each tissue. Chromatograms indicate that separate peaks are observed for each compound.

Storage stability

Buprofezin residues in orange homogenate were shown to be stable for up to 6 months upon storage at –18° C. The study is for an acceptable period, as whole fruit samples in the Australian trials were analysed within 3 to 4 months after collection.

The stability of buprofezin in milk, beef liver and beef fat was determined up to 371 days, following storage at –10 to -–20° C. Concurrent recoveries were conducted at each storage interval. The data showed that buprofezin residues in milk, beef fat and beef liver remain stable up to 300 days. The study was conducted for an acceptable period, as samples in an animal transfer study were analysed within 7 months of collection.

Residue definition

The parent compound is considered appropriate for the purposes of monitoring Good Agricultural Practice (GAP) and estimation of dietary intake. The residue definition will therefore be as follows:

Buprofezin buprofezin

Although in the dairy cow metabolism study, other transformation products or metabolites may form the predominant component of the residues in animal tissues, less than 10% of the recovered radioactivity in liver and milk was composed of these metabolites. The analytical methodology allows for determination of buprofezin, BF2 and BF12 in tissues and buprofezin, BF12 and BF23 in milk, however very low levels of residues were found in the transfer study, and therefore the contribution of these metabolites to the overall residues was negligible. Hence a complex definition is not considered appropriate.

Residue trials

The proposed use pattern in citrus is a maximum of two applications at 24 g ai/100 L, with a 21 – 28 day re-treatment interval and a withholding period of 28 days. Data for oranges, lemons and mandarins were provided from trials conducted in Australia, New Zealand, Italy, Spain and Portugal. The data points which were considered to match GAP are: 0.05, 0.05, 0.067, 0.119, 0.24, 0.33, 0.395 and 0.69 mg/kg. An STMR of 0.18 mg/kg is estimated for citrus fruit. The data set supports the establishment of an MRL of 2 mg/kg for citrus fruit. Residues in pulp ranged from <0.01 to 0.084 mg/kg and residues in peel ranged from 0.17 to 1.60 mg/kg.

[▶] BF12 = (N-(4-hydroxyohenyl)-N'-isopropylurea.

The proposed use pattern for mango is a maximum of two applications per season at 24 g ai/100 L with a 28 day re-treatment interval and a withholding period of 28 days. Data for mangoes were provided from trials conducted in Australia and Taiwan. The Taiwan data were not considered in the establishment of an MRL, as the trials did not match the proposed Australian GAP. The data points which were considered to match GAP are: <0.01, <0.01, 0.02, 0.02 and 0.045 mg/kg for whole fruit. An STMR of 0.02 mg/kg is recommended for mango. The data support an MRL of 0.2 mg/kg. Residues in mango pulp ranged from no detectable residues to <0.01 mg/kg. An STMR of 0.01 mg/kg is recommended for mango pulp for dietary intake purposes.

Processing studies

In a US study, oranges trees received an exaggerated treatment of buprofezin, i.e. 10× the rate proposed in Australia. Treated fruit were processed into fractions including juice, oil and dry pulp. Processing factors of 0.17, 43 and 4 were calculated for juice, orange oil and dry pulp, respectively.

Animal feed commodity MRLs

Using the processing factor for dry pulp and maximum residues in whole citrus fruit, a maximum level of 2.86 mg/kg is estimated for dry pulp. On the basis of this estimate, an MRL of 5 mg/kg is recommended for citrus pulp, dry.

The use of mango pulp as a feed commodity was also considered by the Applicant. Maximum residues in whole fruit were 0.045 mg/kg. Residues in mango peel however, were 5× greater than in whole fruit. Using residues in peel as a 'worst case' situation, levels of 0.3 mg/kg are estimated as the likely exposure. As estimated levels of buprofezin in dry citrus pulp are higher than in mango fruit, the citrus pulp forms the basis for the establishment of animal commodity MRLs.

Animal commodity MRLs

Feed levels investigated in a dairy transfer study were 5, 15 and 50 ppm. Residues below the limits of quantitation were found in muscle and kidney following dosing at all three levels. One finite value of 0.05 mg/kg buprofezin was found in a liver sample following dosing at 50 ppm; there were no detectable residues of BF12 or BF2 in any of the other 8 liver samples.

Residues of buprofezin and BF12 above the limit of quantitation of 0.01 mg/kg were not found in any milk samples following dosing at 5 or 15 ppm. Residues of buprofezin up to 0.02 mg/kg were found in milk taken from one animal dosed at 50 ppm. Residues in cream ranged 0.01 – 0.05 mg/kg buprofezin following dosing at 15 and 50 ppm; no residues were present in cream following feeding at 5 ppm.

In fat, residues of buprofezin were found only following dosing at 50 ppm. Residues were 0.07, 0.11 and 0.12 mg/kg. Although buprofezin is considered to be a lipophilic compound, no residues were found in fat following feeding at 5 and 15 ppm.

Using the MRL of 5 mg/kg for dry citrus pulp as an estimated exposure level, MRLs for meat [in the fat], edible offal and milk are recommended on the basis of 5 ppm feeding level in the transfer study. Residues in milk and tissues were below the limits of quantitation of 0.01 mg/kg in milk and 0.05 mg/kg in liver, kidney, muscle and fat, following feeding at 5 ppm for 28 days. Therefore MRLs of *0.01 mg/kg for milk and *0.05 mg/kg for edible offal (mammalian) and meat (mammalian)[in the fat] are recommended. It should be noted that the animal commodity MRLs allow 100% feeding of citrus pulp at the MRL, which is considered to be a conservative exposure.

Estimated dietary intakes

The chronic dietary risk is estimated by the National Estimated Daily Intake calculation (NEDI) encompassing all registered/temporary uses of the chemical and dietary intake data from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with the *Guidelines for Predicting Dietary Intake of Pesticide Residues (revised)* (WHO, 1997). The calculation has been revised to reflect the *expected* residue levels in commodities (STMRs) rather than the *maximum* residue levels (MRLs). This is consistent with the principles for assessing chronic dietary intake which is considered to occur through a lifetime of exposure.

The refined NEDI for buprofezin is equivalent to approximately 2% of the ADI. It is concluded that the chronic dietary exposure is small and the risk is acceptable.

Bioaccumulation potential

Buprofezin has a log P_{OW} value of 4.3. According to the FAO definition[#] the compound should therefore be designated as fat soluble and has been defined as such by the JMPR.
In the dairy metabolism study, TRR in muscle and fat were comparable; there was no clear indication that fat was a target tissue, compared to liver and kidney.

In the 28 day animal transfer study, buprofezin residues were present in fat following dosing at 50 ppm. In muscle, kidney and liver, residues of buprofezin were generally less than LOQ. The propensity for buprofezin residues to be magnified with dose was not determined as residues were only found at the highest feeding level.

Tissue residues (mg/kg) were not magnified when compared to the dose rates (mg/kg bw) administered in the feeding study.

[#] FAO Manual on the Submission and Evaluation of Pesticide Residues Data, Food and Agriculture Organisation of the United Nations, Rome, 1997, p 36.

Recommendations

Registration of the product:

Registration of Applaud Insecticide for use on citrus fruit and mango is supported on the basis of evaluation of the residue data.

Recommended amendments to the MRL Standard:

Table 1

Compound	Food		MRL (mg/kg)
DELETE:			
Buprofezin	FC 0001	Citrus fruits	T 3
	MO 0105	Edible offal (mammalian)	T *0.05
	MM 0095	Meat (mammalian)	T *0.05
	ML 0106	Milks	T *0.01
ADD:			
Buprofezin	FC 0001	Citrus fruits	2
	MO 0105	Edible offal (mammalian)	*0.05
	FI 0345	Mango	0.2
	MM 0095	Meat (mammalian) [in the fat]	*0.05
	ML 0106	Milks	*0.01

* Denotes MRL set at or about the limit of analytical quantitation

T Temporary MRL

Table 4

Compound	Animal Feed Commodity		MRL (mg/kg)
ADD:			
Buprofezin	AB 0001	Citrus pulp, dry	5

The MRL recommendations indicated above will be conveyed to the Australia and New Zealand Food Authority (ANZFA) for consideration for incorporation into Standard A14 of the Food Standards Code and consequent adoption into the State/Territory food legislation.

Withholding periods:

Harvest

Citrus: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Mango: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Livestock Protection Statement

Do not allow livestock to graze grasses or weeds under treated trees

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Trade Implications

Commodities exported and main destinations

Citrus fruits are mainly exported to Malaysia, Singapore, Hong Kong, USA, Indonesia, Japan, New Zealand and the Phillippines. Mangoes are predominantly exported to Hong Kong and Singapore. Many of these countries do not have MRLs or tolerances in place for buprofezin.

Commodity	Importing Country	Export 1997/1998 (tonnes)	$, 000 value 1997/1998
Mango	Hong Kong	2,540	6,169
	Singapore	950	2,526
	Japan	197	1,873
	Saudi Arabia	274	725
	UAE	145	383
Citrus fruit	Malaysia	33,302	23,781
Oranges	Singapore	22,156	16,766
	USA	21, 378	32, 458
	Hong Kong	11,997	9.491
	Japan	7,618	11,171
	New Zealand	6,677	5,122
Mandarins	Indonesia	5, 937	10,880
	Hong Kong	2,302	3,679
	Singapore	1,103	1,589
	USA	1,040	1,776
	New Zealand	901	933
Lemon/lime	Japan	2,839	4,463
	Hong Kong	427	601
	Singapore	353	394
Grapefruit	Singapore	111	134
	New Zealand	50	41

Although the Australian MRL for citrus fruit will be set at 2 mg/kg, highest residues in oranges and mandarins from trials conducted according to GAP were 0.119 mg/kg and 0.33 mg/kg, respectively. Therefore the limit recommended by JMPR (see CODEX Alimentarius Commission MRLs) for oranges would be appropriate for countries which adopt CODEX MRLs for importation, namely Hong Kong, Singapore and Malaysia.

The time-limited tolerances in the US for citrus fruit, milk, meat and offal are similar to the recommended Australian MRLs. Therefore export of treated citrus fruit and animal commodities to the US should not pose trade problems in the immediate term.

Overseas registration status

Applaud Insecticide is registered for use on citrus in Argentina, Barbados, Brazil, Chile, China, Cyprus, Dominican Republic, Ecuador, Greece, Guatemala, Italy, Japan, Jordan, Lebanon, Nicaragua, Oman, Peru, Portugal, South Africa, Spain, Syria, Trinidad and Tobago, Turkey, UAE, Uruguay. It is used under a Section 18 emergency exemption in the US.
It is registered for use on mango in Taiwan only. Relevant MRLs are tabulated below:

Country	Commodity	MRL (mg/kg)
Japan	Mandarin, orange	0.3
	Other citrus fruit	2
Netherlands	Other food commodities	*0.05
New Zealand	Citrus fruit	0.5
Peru	Mandarin	0.3
Poland	Fruits and vegetables	0.5
Scandinavia	Citrus	0.2
Spain	Citrus	0.2
USA *	Citrus fruit	2
	Citrus pulp, dry	10
	Cattle fat, goat fat, hog fat, horse fat, sheep fat	0.02
	Cattle meat, goat meat, hog meat, horse meat, sheep meat	0.02
	Meat by-products	0.5
	Milk	0.03
Taiwan	Mango	1
CODEX (JMPR 1999)	Oranges, sweet sour	0.5

* Time-limited tolerances, expiry date 21/12/2001.

CODEX Alimentarius Commission MRLs

Buprofezin has been reviewed by JMPR and the proposed MRL of 0.5 mg/kg for oranges (sweet, sour) was considered by CCPR in April 2001. It was recommended that the MRL be elevated to Step 8 of the process. The MRL will be considered by Codex Alimentarius Commission in July 2001 and pending acceptance it should then have full CXL status (i.e. a Codex Maximum Residue Limit). There are no CODEX MRLs (or proposed MRLs) for mango or animal commodities.

Potential risk to Australian export trade

Residues of buprofezin in milk, meat and edible offal of animals which have fed on processing waste of treated fruit, are unlikely to be above the Limits of Quantitation, therefore the potential for these commodities to 'unduly prejudice trade' is minimal.

Treated citrus fruit will contain finite residues of buprofezin (MRL 2 mg/kg; STMR 0.18 mg/kg). Major export destinations for citrus fruit, predominantly oranges are Malaysia, Singapore, USA, Hong Kong and Japan. As there are time-limited tolerances in place for buprofezin in the US, which are comparable to the recommended MRLs, the US does not pose significant concern. The other major markets however do observe CODEX MRLs. The proposed CODEX limit of 0.5 mg/kg could be adequately met if label directions are followed, as maximum residues of 0.2 mg/kg were found in oranges treated in the Australian trials in accordance with GAP. However, until the CODEX limit is ratified (decision to be taken in July 2001) a potential for prejudice to Australia's export in oranges exists.

Similarly with mangoes, there is only a relevant tolerance for buprofezin in Taiwan of 1 mg/kg. This tolerance is five times the recommended MRL for mango, which is 0.2 mg/kg. However for countries importing mangoes and citrus fruits other than oranges, which do not have existing tolerances, a potential for prejudice to Australia's export in these fruits exists. The proposed label is to contain advice for citrus and mango growers, that information on overseas residue tolerances for buprofezin and extended withholding periods which should be observed for fruit intended for export is available from Dow Agrosciences Australia Limited. This will provide mitigation of the potential to prejudice trade.

As part of the Public Consultation Period prior to registration of the product, relevant grower groups and citrus and mango fruit exporters are requested to provide comment on the trade aspects of the proposed use.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Buprofezin is not on the NOHSC *List of Designated Hazardous Substances.* Based on the NOHSC *Approved Criteria for Classifying Hazardous Substances,* Buprofezin is classified as non-hazardous.

Buprofezin is in the form of an off-white viscous liquid. It has low oral, dermal and inhalation toxicity in rats and rabbits. It is a slight eye irritant but neither a skin irritant in rabbits nor a skin sensitiser in guinea pigs.

Applaud Insecticide cannot be classified as hazardous according to NOSHC criteria based on the information supplied to NOHSC.

Applaud Insecticide is a suspension concentrate formulation. It is expected to possess low acute oral and inhalation toxicity and low acute dermal toxicity. The product is not likely to be a skin irritant but may be irritating to eyes. The product will be supplied in 1, 5 & 10 L containers.

Formulation, transport, storage and retailing

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

End use

Applaud Insecticide is proposed for the control of scale insects, mealybugs and jassids/leafhoppers in citrus and mango scale in mango crops. It will be applied by oscillating boom or by airblast sprayers. The proposed application rate is 60mL product/100 L.

The main routes of exposure to the product are inhalational and dermal. The product is a suspension concentrate formulation, however workers are still likely to be exposed to some concentrate while loading spray equipment. Workers may also be exposed to spray mist from the product spray. Functions that can lead to exposure to the product include opening containers, mixing/loading, application, cleaning up spills, cleaning/maintaining equipment.

Re-entry statement

A re-entry statement is not recommended based on the toxicity of the product and its use pattern, but may be included on the label if required.

Recommendations for safe use

Workers involved in transport, storage and retailing should be protected by safe work practices and training. End users should follow the instructions on the product label. Elbow-length PVC gloves and cotton overalls are recommended for users of Applaud Insecticide.

The personal protective equipment recommended should meet the relevant Standard Australian standards specified below:

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

AS 3765-1990 Clothing for Protection Against Hazardous Chemicals

Conclusions

Applaud Insecticide can be used safely if handled in accordance with the instructions on the product label.

Environmental Assessment

Introduction

Dow AgroSciences Australia Limited has made an application for registration of the new technical grade active constituent, buprofezin, a new insecticide for control of a narrow spectrum of sucking insect pests in citrus and mangoes. Buprofezin is a thiadiazine insect growth regulator with contact and stomach action and probably inhibits prostaglandin and chitin synthesis.

Environmental Fate

Buprofezin will be applied to citrus and mango trees through use of high volume orchard sprayers. Spray drift could be significant, and the main non-target contamination of soil and water is likely to be through drift and run-off to a lesser degree. The company's data package is relatively complete except for a formal aerobic aquatic study which would have allowed a better estimation of the rate of movement to the sediment.

Based on the Mensink classification, buprofezin has moderate volatility while the water solubility classifies buprofezin as slightly soluble. The log *n*-octanol/water coefficient value confirms the water solubility and indicates a potential for bioaccumulation, soil sorption, and toxicity.

- **Hydrolysis/Photolysis**

While stable at pHs 7, and 9, buprofezin is hydrolysed at pH 5 at 25^{o}C with a half-life of 57.6 days. In a second experiment, in acid (pH 2.0-2.4) and basic solutions (pH 7.0 to 12.0), buprofezin had half-lives in excess of 50 days. In weaker acids and organic acid/salt systems (pHs from 3.4 to 5.0), the half-lives were about 12 or 13 days. In all cases 1-isopropyl-3-phenyl urea was the major degradation product. Hydrolysis is a possible degradation route in acidic media. Photolytic degradation of buprofezin in an aqueous pH 9 solution is slow with a calculated half-life of 38 days and parent the main material in the aqueous phase after ca. 166 hours. The aqueous photolytic half-life in the environment was estimated as 84 days and sunlight is not expected to be a major route for buprofezin degradation in the aqueous environment. No information on degradation of buprofezin on soil was presented based on the very limited photodegradation seen under aqueous conditions.

- **Soil metabolism**

  - ***aerobic soils***

When a US sandy bam and sandy clay loam were treated with buprofezin (ca. 1.8-1.9 mg/kg dry soil) under aerobic conditions for 181 and 364 days respectively, DT_{50} values were 26.3 and 69.6 days respectively with DT_{90} values of 98.2 and 305 days, indicating buprofezin has slight to fair aerobic soil degradability. Buprofezin was the major extractable metabolite over the study period with total buprofezin making up 4.1% of the applied soil radioactivity [0.08 ppm] in the sandy loam and 9.8% [0.18 ppm] in the sandy clay loam soil after 181 and 364 days respectively. Volatile radioactivity at the study's finishing times was 60 [sandy loam soil] and ca. 49% [sandy clay loam soil] of the applied radioactivity with the radioactivity confirmed as >99% $^{14}CO_2$. Four minor degradation products and four unknowns were

detected, in no case did any of these exceed 2% of the applied radioactivity. The study showed extensive mineralisation of buprofezin occurred once the parent was modified.

- ***upland and flooded soils***

A soil metabolism study was conducted on a silty clay loam paddy soil (pH 6.4[water]) under "oxidative" and "reductive" flooded conditions and on a sandy loam upland soil (pH 7.0 [water]) treated with buprofezin to give soil concentrations of 10 ppm. Sterile soils were treated similarly. After incubation at 30°C for up to 150 days, calculated half-lives in the oxidative and reductive flooded soils were respectively 37 and 113 days and in the upland soil, 60 days with half-lives under aerobic conditions being up to 2.5 to 3.5 longer in the sterile soils. In the same study, four soils (silty clay loams, sandy loam, and silty loam with one of the silty loams and the sandy loam being the same soils as above), were treated with phenyl ring U-^{14}C buprofezin at concentrations of 1.6 ppm buprofezin in flooded soils and 2.5 ppm in upland soils at 25°C for up to 150 days. Buprofezin was the principal radioactive residue found in the soils over the 150 day period with metabolites not being individually present at more than 5% of the applied radioactivity. Calculated DT_{50} times in the upland conditions were 220 days (silty clay loam, pH 6.8 [water]) and 80 days (sandy loam, pH 7.0 [water]). In the flooded soils, DT_{50}s were 110 days (silty clay loam, pH 7.0 [water]), 95 days (silty clay loam, pH 6.4 [water]), and 150 days (silty loam, pH 5.9 [water]). Significant amounts of radioactivity not accounted for were put down to losses as ^{14}C-carbon dioxide which was not trapped in the course of the study. This was confirmed when the degradation of ^{14}C-buprofezin in silty clay loam under flooded conditions resulted in about 17% of the applied radioactivity after 150 days being associated with trapped carbon dioxide. Carbon dioxide was the only volatile substance of significance.

The studies showed that buprofezin hydrolyses in soil with eventual conversion to carbon dioxide. Oxidative flooded conditions gave the shortest DT_{50}, 37 days, while under upland conditions, the shortest DT_{50} was 60 days (incubation at 30°C). The longest DT_{50} for upland conditions was 220 days, but this was an extrapolated value and needs to be viewed with some caution. Microbial action appears to be important in the degradation of buprofezin.

The results of the aerobic phases of this study were similar to those found for the US aerobic soil study (half-lives indicating slight to fair degradability, extensive mineralisation and degradation of buprofezin over relatively short time intervals).

- **Mobility**

- ***adsorption/desorption***

Batch equilibrium studies of adsorption of buprofezin in one study of four acidic and three basic soils using 24 hours for equilibration, found organic carbon adsorption constants (K_{OC}) of 2150 to 4742 and one value of 19800 for buprofezin, rating it as having low to slight mobility in soil (K_{OC} = 2000-5000) or of being immobile (K_{OC} > 5000). Calculations of the Gustafson Ubiquity Score (GUS) using the available data indicate that buprofezin is an "improbable" leacher (GUS <1.8), i.e. it is unlikely to reach groundwater before degrading.

- ***leachability***

After aerobically aging a German standard soil (classified as a "sand") treated with ^{14}C-buprofezin for 60 days at 19-23°C, approximately 31% of the applied radioactivity was present as trapped carbon dioxide, with 33% of the total radioactive residue solvent extractable and 30-40% present as residual soil residues. The aged soil was then leached with distilled water through 30 cm columns. A mean of 2.7% of the applied radioactivity was found in the leachate, with approximately 43% of the originally applied radioactivity retained on the columns and about 39% lost as volatile (carbon dioxide) radioactivity.

Buprofezin was not identified in any of the leachate material while in the column segments, the principal radiolabelled component was ^{14}C-buprofezin (ca. 6% of the applied radioactivity) with no other metabolites characterised. On the columns, the majority (98%) of the retained radioactivity was found in the top segment. The study showed that aged residues of buprofezin did not significantly leach in low organic matter soil and that no mobile degradation products were produced in any significant quality.

- **Field dissipation**

In a Japanese field dissipation study, four applications of buprofezin as a granular or 50% WP formulation were made to rice in paddy fields at intervals of 10 to 37 days and, as a 25% WP, to oranges in upland soils at intervals of 28 to 33 days. Application rates in the paddy soils were 1.6 kg of buprofezin/ha, and in the upland soils, 2.5 kg buprofezin/ha. The half-lives in flooded soils were between 36 and 104 days, and in the upland soils, 52 and 66 days. Laboratory studies with the same soils gave half-lives of 35 to 172 days for flooded soils and 45 and 110 days for the upland soils. The study showed degradation of buprofezin occurred in the soil. In a second dissipation study conducted in Japan, rice plants growing in paddy fields were given a single treatment with 375 g buprofezin/ha at the pannicle formation or booting stages. In the rice, buprofezin concentrations decreased steadily with the half-lives in rice calculated as 2 and 2.8 days. Concentrations in paddy water were ca. 0.07 ppm immediately after treatment and diminishing to less than 0.01 ppm at 14 days after treatment. In the paddy environment, buprofezin is not expected to be persistent in either treated plants or the aquatic environment.

- **Accumulation/Bioaccumulation**

Because buprofezin has relatively limited persistence in both soils and water and does not produce any significant quantities of metabolites or degradation products, soil accumulation is not expected, as confirmed by modelling. Buprofezin accumulates moderately in bluegill sunfish exposed to a nominal 0.04 mg buprofezin/L for 14 days under flow-through condition with maximum bioconcentration factors of 537 in whole fish, 846 in non-edible portions and 86 for edible tissue. Plateau concentrations in tissues were reached after seven days exposure followed by ready depuration from whole fish, viscera and edible portions after 7 days (98, 99 and 92% depuration).

Environmental Toxicity

Conclusions from the avian acute and oral dietary studies

Bobwhite quail and mallard ducks were used in both acute and sub-acute oral dietary studies. The LD_{50} determined was greater than 2000 mg buprofezin/kg bodyweight for both species in the acute studies while the LC_{50} for the 5 d sub-acute dietary studies were >5243 mg/kg, again for both species. These studies indicate that by US EPA classifications, buprofezin is practically non-toxic to bobwhite quail and mallard ducks by both acute oral exposure (LD_{50} > 2000 mg ai/kg bw) and subacute dietary exposure (LC_{50} > 5000 ppm in diet).

Conclusions from the aquatic toxicity studies

The acute aquatic toxicity of buprofezin as the pure active to rainbow trout (*Oncorhynchus mykiss*), bluegill (*Lepomis macrochirus*) and *Daphnia magna*, was assessed in separate studies. No chronic

aquatic toxicology studies were presented. The data package presented for the assessment of aquatic toxicity was limited.

- **Fish**

In the acute studies with fish, the measured LC_{50}s were greater than 260 µg buprofezin/L under static conditions and greater than 330 µg buprofezin/L in flow-through conditions. Buprofezin is shown by these studies to be non-toxic to fish to the limit of its water solubility.

- **Aquatic invertebrates**

A daphnid acute toxicity studies with buprofezin was carried out under static conditions. There was no mortality reported and an EC_{50} value of >420 (48 h) µg buprofezin/L proposed. However, there was lethargy in all the exposed daphnids and 77% of the daphnids were immobile after 48 hours, indicating that buprofezin exposure has adversely affected the daphnids. This is a clear indication of sub-lethal toxicity and a cause for difficulty in the hazard assessment. Under chronic exposure conditions and based on a reproduction NOEC of 0.08 mg/L and an LC_{50} of greater than 0.36 mg/L, buprofezin is moderately toxic to *D. magna* Straus. This does confirm the acute LC_{50} is greater than approximately 400 µg/L but that there are effects on young daphnids.

- **Algae and aquatic plants**

Acute exposure of the green alga, *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*) to a nominal 2.94 mg buprofezin/L, equivalent to a rate of 4.4 kg buprofezin/ha [approximately 150% of the proposed maximum Australian use rate], had no effect on growth rate or biomass in two tests. Exposure of duckweed, *Lemna gibba,* for 14 days to a buprofezin formulated as a 70% wettable powder applied at a rate of 4.4 kg buprofezin/ha, resulted in no significant difference in frond numbers in the buprofezin exposed samples and controls, resulting in the conclusion that the formulated buprofezin product was not toxic to *Lemna gibba* under the test conditions.

Conclusions for non-target invertebrates

- **Honey bees**

Single oral doses of up to 100 µg buprofezin.bee^{-1} and spraying of bees with buprofezin at rates of up to 2 kg/ha caused no increased mortality compared to similarly treated controls. Field studies using buprofezin at 25 g/100 L showed no adverse effects on worker bees in or leaving the hive nor were there adverse effects seen on the development of eggs, larvae, and cocoons exposed to the buprofezin. Direct spraying of hives and swarming colonies was also without adverse effects. As a result of these observations it is concluded that buprofezin is most likely to be practically non-toxic to bees by either contact or ingestion. Laboratory studies not seen by Environment Australia also suggest low toxicity.

- **Spiders**

No mortality occurred amongst spiders or spider larvae after exposure to buprofezin at concentrations of up to 2000 ppm.

- **Silkworms**

Mortalities in silkworms fed mulberry leaves treated with buprofezin at 1000 and 2000 ppm were similar to those seen in untreated controls over similar time periods and did not exceed 5%.

- **Parasitic wasps**

When nymphs or larval forms of predatory wasps were exposed to buprofezin at 125 and 250 ppm, there was either no mortality seen at either level or the mortality rates were similar to those of untreated controls. There were no adverse effects on the reproductive ability of the species tested. Greenhouse and field trials with buprofezin formulations (including Applaud* Insecticide at a rate of 1.8 kg buprofezin/ha) did not appear to have serious adverse effects on wasp predation.

- **Ladybirds**

In a laboratory study, larvae of the oriental ladybirds (*Chilocorus circumdatus*) exposed to buprofezin as a 400 g/L flowable concentrate at rates of 0.125 to 0.5 g buprofezin/L showed that that treatments of 0.25 and 0.5 g/L seriously disrupted development of the larvae and that the 0.5 g/L level resulted in a 60% reduction in adult ladybirds. At 0.125 g/L, there were no statistical differences from the controls in the number of treated larvae reaching maturity. Although the mean numbers of larvae produced after exposure of adult ladybirds to buprofezin at the 0.125 and 0.25 g/L levels were not statistically different from untreated controls, there was a decline in the number of larvae produced. At the proposed maximum Australian use rate of 24 g/100 L, adverse effects on the populations of oriental ladybirds may be expected. In contrast, predation by steel-blue ladybirds (*Orchus chalybeus*) was unaffected by buprofezin (as an Applaud formulation) after exposure to a rate of 12.5 g buprofezin/100 L. The draft label protection of wildlife etc. states notes that Applaud Insecticide is known to be toxic to early instars of the ladybird, *Cryptolaemus montrouzieri, and* to affect egg hatching for some days of use. The data to support such statements were not provided with the application.

- **Predacious mites**

The information provided, although not detailed or extensive, indicated that exposure of predacious mites to buprofezin formulations at concentration of up to 50 g buprofezin/100 L did not result in any significant increases in mortality compared to untreated controls and that oviposition was also not adversely affected.

- **Earthworms**

In tests with buprofezin the 14 day LC_{50} was reported as greater than 1000 mg/kg. While mortality at the 1000 mg/kg level was not considered different from that of the untreated controls, there was a statistically significant decline in the bodyweights of the worms at that level. While a very slight toxicity to earthworms is indicated, there does appear to be some effect with regard to bodyweight reduction after exposure to buprofezin at 1000 mg/kg.

- **Soil micro-organisms**

Following treatment a clay loam soils with buprofezin at 1 to 100 ppm and incubations at 29^{o}C, the numbers of bacteria, fungi, and actinomycetes over a 45 day period showed increase in all their numbers compared to untreated control soil. After the 45 days, the levels of buprofezin had declined to 60-80% of the initial values. Although the supporting data is meagre, buprofezin is not expected to have any serious deleterious effects on soil micro-organisms.

Prediction of Environmental hazard

It is proposed that Applaud Insecticide be used on citrus trees to control certain scales and mealybugs and jassids and on mango trees for scale control. The proposed label recommends a maximum of two applications per season, each at a rate of 30 or 60 mL of product per 100 L in high volume spraying. A maximum of 12000 L spray mixture per hectare is to be used. These rates are equivalent to application of 1.44 to 2.88 kg of buprofezin per hectare. Application is as required by insect populations. Applications are generally 21 to 28 days apart. The product is to be sprayed by oscillating booms or airblast sprayers. Applaud Insecticide is not to be applied by aircraft.

Residues would be expected in the sprayed area on soil with spray drift and run-off potential means of contamination of adjacent areas and surface water. Spray drift and soil residues are expected to persist for sometime before eventual dissipation occurs, mainly through aerobic soil metabolism processes.

Laboratory adsorption/desorption and leaching studies indicate that buprofezin is likely to have low to slight mobility in the soil and to be an unlikely leacher. While residues of buprofezin may persist for some time in the soil, the frequency of application and buprofezin's steady degradation and mineralisation indicate that residues of these chemicals are unlikely to accumulate to give unacceptable soil concentrations.

Hazard to birds and mammals

Estimated residues on feed at the maximum proposed rate are likely to be well below the acute oral LD_{50}s and 5 day dietary exposure NOECs for bobwhite quail and mallard duck and also for the first generation reproduction NOEC for bobwhite quail. Hence, buprofezin used in accordance with label recommendations is not likely to present a hazard to birds ingesting these residues. Acute or chronic hazard to mammals is also highly unlikely.

Aquatic hazard

The hazard presented from direct overspray of a shallow (15 cm deep), lentic waterbody with a single application (i.e. ca. 2.9 kg buprofezin/ha) was evaluated for representative aquatic species for which toxicity data were available. While a hazard was indicated for all species, fish and daphnids appeared the most sensitive. Spray drift reaching a similar waterbody at 10% of the direct overspray rate also gave indications of hazard. Modelling of spray drift for evergreen trees using both Ganzelmeier and AgDRIFT models showed an acceptable hazard to fish and *Daphnia magna* was indicated provided a down-wind buffer distance of 15 metres was maintained. This takes into account that acute toxicity is not observed up to the limit of buprofezin's water solubility. However, the active is more toxic to young daphnids and a chronic hazard can not be entirely ruled out due to lack of data on rates of dissipation to sediment. Hazard to algae and aquatic plants is expected to be low.

Hazard to groundwater and to surface water from runoff

A 1% runoff produces an estimated level of contamination similar to the 10% spray drift scenario and clearly identifies the need to minimise water contamination by this route.

The hazard from runoff should be reduced as the proposed label provides detailed information of spray applications that could be expected to result in minimal runoff. Additionally, the draft label of the Applaud Insecticide states it is not to be allowed to contaminate streams, rivers, or waterways.

To minimise the risks of direct runoff or of contamination via heavy rainfall or irrigation shortly after application inadvertently washing the pesticide into the water system before it became bound to the soil, the company has agreed to a label statement saying that buprofezin "may be toxic to crustaceans", that runoff from treated areas should be prevented from entering waterways, that application should not occur if heavy rains were imminent and that irrigation should not take place within 24 hours of spraying.

Hazard to terrestrial invertebrates and soil micro-organisms

The proposed use of Applaud Insecticide should be harmless to honeybees by either contact or ingestion. Buprofezin was not hazardous to spiders, parasitic wasps, and predacious mites but can be expected to have a disruptive effect on some species of ladybirds by increased mortality in the population and adversely affecting egg laying.

The expected environmental concentration in the top 10 cm of soil of buprofezin when applied at 2880 g/ha to a hectare of citrus or mango orchards would be approximately 1.9 mg/kg (assuming a soil density of 1.5 g/cm^3). This concentration is about $1/500^{th}$ of the 14 day LC_{50} level to earthworms (>1000 mg/kg buprofezin). Consequently the proposed use pattern is not expected to have adversely impact on earthworm mortality in or near treated citrus or mango trees. After treatment of a clay loam soil with buprofezin at up to 100 mg of buprofezin/kg soil there were no adverse effects seen on the soil's microbiological numbers of bacteria, fungi, or actinomycetes. Consequently, the Australian environmental concentration remaining in the soil after use on citrus and mango trees is not expected to adversely affect soil microorganisms.

Hazard to Desirable terrestrial vegetation

Hazard to non-target vegetation is not anticipated in view of the reported use of buprofezin in other crops. Environment Australia has noted the label warning directing that spray drift onto adjacent corps, crop lands, pastures and livestock is to be avoided.

Conclusion

Environment Australia concludes that a low hazard to the environment may be predicted provided the product is used according to the proposed label recommendations and Good Agricultural Practice.

From an environmental perspective registration is supported.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Buprofezin is a thiadiazine insect growth regulator. It acts by inhibiting cuticle deposition. It also suppresses egg laying in female adults with inhibition of prostoglandin synthesis and has effects on levels of hormones associated with moulting in nymphs.

Mode of action: It is a probable chitin synthesis inhibitor and prostoglandin inhibitor, which has a hormone disturbing effect, leading to suppression of ecdysis. It acts as a persistent insecticide and acaricide and has both contact and stomach action. It is not translocated in the plant. It inhibits moulting of nymphs and larvae, leading to death, and suppresses oviposition by adults. Treated insects lay sterile eggs.

Applaud Insecticide is proposed for use for control of red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops and mango scale in mango crops.

Justifications for the proposed uses of Applaud Insecticide in citrus are sound. Jassids in particular require an effective insecticide. Applaud Insecticide offers potential benefits for the maintenance of natural enemies of insect pest species and Integrated Pest Management (IPM) in citrus, compared with most currently registered alternative products approved for this crop.

Currently, control of the most serious mango pest, mango scale, relies on methidathion and to a lesser extent on carbaryl, chlorpyrifos and petroleum oil. These insecticides, except for petroleum oil, are very disruptive to beneficials. Petroleum oil requires repeat high volume applications and is unsuitable for use during the fruiting season because it causes fruit blotching. The repeated use of non-selective insecticides is preventing the implementation of IPM practices in the mango industry. Due to its selectivity, Applaud Insecticide will be most useful when used to reduce scale populations to the point where thay can be successfully maintained below action thresholds by beneficials in a strategic IPM program.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Applaud Insecticide is proposed for use for control of red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugsand citrophilous mealybugs in citrus crops and mango scale in mango crops. Use is proposed for all States and Territories.

Applaud Insecticide is proposed for application by oscillating booms (citrus only) and airblast sprayers. The product will not be applied aerially. The maximum rate of application proposed is 60 mL/100 L water.

It is proposed the product will be available in 1, 5 and 10L pack sizes.

The following withholding periods are recommended for the product:

Citrus, Mango: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Evaluation of efficacy

Citrus
Applaud Insecticide was tested in a large number of trials in NSW, SA and Queensland. In general, trial design was satisfactory with respect to the provision of controls, treatment sizes, comparison with industry standard treatments, number of replicates and range of rates tested. The trials were conducted competently and in the main, analysed appropriately. The data presented supported the claims for control of red scale and white louse scale at the rate of 30-60 mL/100 L subject to the level of activity of beneficial organisms. Similarly, rates of 30-60 mL/100 L are supported for control of longtailed, citrus and citrophilous mealybugs with two applications required subject to the level of infestation. A rate of 30 mL/100 L for the control of jassids is supported.

Mango
Initially, three trials conducted in Qld were provided in support of the claim for control of mango scale in mangoes. The trials were conducted in commercial orchards and insect pressure was significant. Of the three trials it was considered that only one was useful for establishing efficacy and the rate and timing of application. In both the buprofezin and methidathion treatments there was a large degree of unexplained variability which the authors attributed to the presence/absence of beneficials. No identification or counts of the beneficials was undertaken. It was considered that additional trial work was required to confirm the adequacy of the proposed usepattern.

Additional data were presented from trials conducted in Nth Qld. The data confirmed the rate proposed (60mL/100 L), and issues raised with the species of mango scale controlled and number of applications required (two) were resolved. Residual concerns were expressed at the degree of variability shown in both the original and confirmatory trials. It was considered that this could be due to an inherent variability due to the mode of action of buprofezin and that pest pressure could also be a factor. It was considered that the data were lacking in sufficient rigor to confirm the source of the variability. None the less, the trials indicated that buprofezin, at the rate proposed, did give effective control of mango scale – scale numbers were significantly reduced and fruit quality was significantly improved by the use of Applaud Insecticide.

Although some concerns have been raised about the absolute efficacy of Applaud Insecticide for the control of mango scale, it is apparent from the trials conducted in Nth Qld that this product is almost as effective as, and no less variable in its efficacy than, the widely used industry standard methidathion. Applaud Insecticide is certainly much less disruptive and more IPM friendly than the currently available products. Growers currently use repeat applications of broad-spectrum insecticides which aggravate mango scale problems by reducing the natural complement of predators and parasites. As a consequence, control levels are usually inadequate due to the resurgence of the scale, particularly late in the season when fruit damage occurs.

It is considered that whilst trials have indicated less than 100% control of mango scale, the level of control achieved is sustainable for the mango industry. Applaud Insecticide also offers considerable benefits to the industry in terms of introduction of an effective IPM system for mangoes and provides another tool in the management of insecticide resistance in this crop, providing it is used judiciously and label restraints on the maximum number of applications allowed (two), are observed.

Registration is supported.

Safety to Beneficial Organisms

The results of a range of overseas studies were presented which indicated that Applaud Insecticide has low to nil toxicity to a wide range of beneficial organisms, including honey and bumble bees and various species of hymenopteran parasitoids and predacious mites.

In several independently-conducted Australian studies Applaud Insecticide was shown to be toxic to larval *Chilocorus circumdatus* ladybirds, but at the proposed label rate was considered by the investigators to be sustainable for the populations. In related studies Applaud Insecticide was non-toxic to adult *Cryptolaemus montrouziere* ladybirds and adult and immature stages of two wasp parasitoids, but was toxic to larval *C. montrouzieri* and may have affected egg hatch in this species for 2-3 weeks following application.

On this evidence Applaud Insecticide may cause some short-term disruption to ladybird populations, but is likely to be considerably less disruptive to the biological control of most pests compared to the currently registered alternatives.

Crop Safety

There are no recorded instances either in Australia or internationally of Applaud Insecticide causing phytotoxicity to citrus or mango crops.

Resistance management

The draft label includes a resistance note (see page 34) and in addition includes the statement that to minimise the risk of resistance developing, a total of no more than two applications of Applaud Insecticide should be made on a crop per season.

The introduction of Applaud Insecticide will provide the opportunity for mango growers to establish a resistance management program using buprofezin, methidathion/carbaryl and petroleum oil.

LABELLING REQUIREMENTS

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Applaud*

Insecticide

ACTIVE CONSTITUENT: 400 g/L BUPROFEZIN

Mode of Action

GROUP	17A	INSECTICIDE

For the control of Red scale and White Louse scale, Jassids (leafhoppers) and Longtailed, Citrus and Citrophilous mealybugs in Citrus crops and mango scale in Mango crops as specified in the Directions For Use table.

Important: Read the attached booklet before use

Dow AgroSciences Australia Limited A.B.N. 24 003 771 659
20 Rodborough Road FRENCHS FOREST NSW 2086
www.dowagrosciences.com.au

CUSTOMER SERVICE TOLL FREE 1-800 700 096 ***Contents: 1, 5, 10 Litres***

NRA Approval No.:

* Trademark of Nihon Nohyaku Co. Ltd.

STORAGE AND DISPOSAL

- Store in the closed, original container in a cool well-ventilated area. Do not store for prolonged periods in direct sunlight.
- **DO NOT** store near foodstuffs, fertilisers or seed.
- 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.

SMALL SPILL MANAGEMENT

- Wear protective equipment (see Safety Directions). Apply absorbent material such as earth, sand, clay granules or cat litter to the spill. When absorption is completed, sweep up material and contain in a refuse vessel for disposal (see Storage and Disposal Section). If necessary wash the spill area with an alkali detergent and water and absorb the wash liquid for disposal as described above.

SAFETY DIRECTIONS

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

FIRST AID

- If poisoning occurs, contact a doctor or Poisons Information Centre. (Ph.: 13 1126)

MATERIAL SAFETY DATA SHEET

Additional information is listed on the Material Safety Data Sheet for Applaud Insecticide which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1-800 700 096.

NOTICE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under off-label permits not endorsed by Dow AgroSciences, or under abnormal conditions.

EMERGENCY RESPONSE
(All Hours)
RING FROM ANYWHERE IN AUSTRALIA
1-800 033 882
(LOCAL CALL FEE ONLY)

IN A TRANSPORT EMERGENCY ONLY
DIAL 000
FOR POLICE OR FIRE BRIGADE

Barcode for stock identification

NRA Approval No.:
GMID

D.O.M./Batch No.:

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Dow AgroSciences™

Applaud*

Insecticide

ACTIVE CONSTITUENT: 400 g/L BUPROFEZIN

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GROUP	17A	INSECTICIDE

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DIRECTIONS FOR USE

RESTRAINT: DO NOT apply by air.

CROP	INSECT PEST	RATE/100 L water	CRITICAL COMMENTS
Citrus including: Oranges Lemons Mandarins Grapefruit Limes	red scale white louse scale longtailed mealybug citrus mealybug citrophilous mealybug	30-60 mL►	To minimise the risk of resistance selection, no more than two applications of Applaud Insecticide should be made on a crop per season. **citrus scales:** Apply Applaud Insecticide when there is heavy crawler emergence, particularly in late summer. • Where the infestation is severe, a second application may be required 14-28 days later. • Works best in an integrated pest management (IPM) programme where parasites such as *Aphytis* spp. are active. **mealybugs:** Apply Applaud Insecticide if thresholds are exceeded in spring-summer. Repeat after 21-28 days if necessary. ► **Rate:** Use the high rate when heavy infestations occur and/or where IPM systems have not effectively managed pest populations. A second application 21-28 days later gives best control.
	Jassids (leafhoppers)	30 mL	**Jassids:** Apply Applaud Insecticide when thresholds are exceeded in January and again in February if required. Apply when juvenile stages predominate.
Mangoes	mango scale	60 mL	**mango scale:** Monitor scales and apply when the majority of crawlers have emerged. This usually coincides with tree flushing after harvest and in spring when fruit are 1.5 to 2.0 cm across. A repeat application within 14 -28 days may be necessary. DO NOT use mineral oils as fruit blotching may occur.

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

WITHHOLDING PERIODS:

Citrus, Mango: DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION.

Some crops for export to particular destinations may require a longer harvesting withholding period. For up-to-date and specific advice, contact Dow AgroSciences Toll Free on 1-800 700 096.

GENERAL INSTRUCTIONS:

APPLICATION:

Apply Applaud Insecticide in sufficient water to ensure complete wetting of all surfaces.

- **Oscillating booms (citrus only)**
  A spray volume of 7,000 to 12,000 L water/ha should be used for trees up to 5m high.

  To optimise control the following application procedures are recommended:

a) ground speed	2.3 to 2.75 km/h
b) pump pressure	3000 to 5000 kPa
c) oscillation rate	90-110 oscillations per minute
d) spray pattern	adjacent cones marrying at about 1.75m (i.e. narrow cone angle, but the maximum angle consistent with good tree penetration)
e) agitation	1 large paddle per 500L; paddles should clear the bottom of the vat by about 10 mm and should have the same orientation
f) boom set	set angle of top to match tree size.

- **Airblast sprayers**
  Airblast sprayers may be used for control of Jassids/leafhoppers, but are less suitable for control of scales and mealy bugs.

  For Jassid control, use spray volumes of approximately 5000 L/ha.

COMPATIBILITY

- Applaud Insecticide is compatible with most commonly used Insecticides and Fungicides with the exception of those which are highly alkaline or highly acidic. For more information, contact your supplier or Dow AgroSciences representative.

CLEANING SPRAY EQUIPMENT:

- After using Applaud Insecticide, empty the tank completely and drain the whole system. Thoroughly wash inside the tank using a pressure hose, drain the tank and clean any tank, pump, line and nozzle filters.
- After cleaning the tank and filters as above, quarter fill the tank with clean water and circulate through the pumps, lines, hoses and nozzles. Drain and repeat the rinsing procedure twice.
- **Rinse Water should be discharged onto a designated disposal area, or if this is unavailable, onto unused land away from plants and water courses.**

INSECTICIDE RESISTANCE WARNING ***Mode of Action***

GROUP 17A INSECTICIDE

For insecticide resistance management Applaud is a Group 17A insecticide.

To minimise the risk of resistance developing, a total of no more than two applications of Applaud Insecticide should be made on a crop per season.

Some naturally occurring insect biotypes resistant to Applaud and other Group 17A insecticides may exist through normal genetic variability in any insect population if Applaud or other Group 17A insecticides are used repeatedly. The effectiveness of Applaud on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Dow AgroSciences accepts no liability for any losses that may result from the failure of Applaud to control resistant insects.

Applaud may be subject to specific resistance management strategies. For further information contact your local supplier, Dow AgroSciences representative or call Customer Service Toll Free on 1-800-700-096.

PRECAUTIONS:

Re-entry Period:
Do not enter treated areas without protective clothing until the spray has dried.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS:

- DO NOT apply under weather conditions, or from spraying equipment, that may cause spray to drift onto nearby plants/crops, cropping lands or pastures.

PROTECTION OF LIVESTOCK:

- DO NOT ALLOW STOCK TO GRAZE GRASSES OR WEEDS UNDER TREATED TREES.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT:

- Applaud Insecticide at label rates of 30 to 60 mL/100 L water has been demonstrated to be safe to a range of predatory and beneficial insects including bumblebees and honeybees, parasitoid wasps such as *Aphytis lignanensis, Leptomastix dactylopii* and *Encarsia* spp., predatory mites such as *Phytoseiulus persimilis* and *Typhlodromus occidentalis*. Applaud Insecticide has no significant effect on adult ladybirds but is known to be toxic especially to early instars of both *Cryptolaemus montrouzieri* and *Chilocorus circumdatus*. Applaud Insecticide may also affect egg hatch of these species for 2 to 3 weeks after application.
- May be toxic to crustaceans. Runoff from treated areas should be prevented from entering waterways.
- DO NOT apply if heavy rain is imminent.
- Irrigation should not take place within 24 hours of treatment.

STORAGE AND DISPOSAL:

- Store in the closed, original container in a cool well-ventilated area. Do not store for prolonged periods in direct sunlight.
- **DO NOT** store near foodstuffs, fertilisers or seed.
- 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.

SMALL SPILL MANAGEMENT:

- Wear protective equipment (see Safety Directions). Apply absorbent material such as earth, sand, clay granules or cat litter to the spill. When absorption is completed, sweep up material and contain in a refuse vessel for disposal (see Storage and Disposal Section). If necessary wash the spill area with an alkali detergent and water and absorb the wash liquid for disposal as described above

SAFETY DIRECTIONS

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

FIRST AID:

- If poisoning occurs, contact a doctor or Poisons Information Centre. (Ph.: 13 1126)

MATERIAL SAFETY DATA SHEET

Additional information is listed on the Material Safety Data Sheet for Applaud Insecticide which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1 800 700 096.

GLOSSARY

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

Suggested Further Reading

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

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

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

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

NRA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of buprofezin in the product Applaud Insecticide, please fill in this form and send it, along with payment of $30 to:

Mr David Hutchison
Agricultural Evaluation
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to the contact officer above at (02) 62723218.

Name (Mr, Mrs, Ms, Dr)_____

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