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Public Release Summary
on

Evaluation of the new active

PYMETROZINE

in the product

CHESS 250 WP INSECTICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

September 1999

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 (Worksafe Australia) 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.*

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

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

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

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LIST OF ABBREVIATIONS AND ACRONYMS

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

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SUMMARY

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is considereing an application to register the product Chess 250 WP Insecticide. This product contains the new active pymetrozine. This product claims to control green peach aphid, cabbage aphid and blue green aphid in brassicas and potatoes.

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of pymetrozine. Before deciding whether to approve this product for use in Australia, the NRA invites public comment. Comments should be submitted by 30 September 1999, to the NRA at the address indicated on page 1.

The NRA has assessed the data submitted by the applicant in support of the proposed use of pymetrozine and provides the following information for public comment.

Public Health Aspects

Toxicology

Following oral administration to rats the active ingredient of Chess 250 WP Insecticide, pymetrozine, was rapidly and almost completely absorbed and then excreted in the urine and faeces. The compound is extensively metabolised and tissue levels of pymetrozine and its metabolites were low 7 days after administration. Pymetrozine has low acute oral toxicity, causes moderate eye irritation, and slight skin sensitisation by injection into the skin but no skin irritation or skin sensitisation when applied to the skin surface. The product, Chess 250 WP Insecticide, is of low acute oral toxicity, is non-irritating to the skin, is a slight eye irritant and a slight skin sensitiser.

Following repeated oral administration of high doses of pymetrozine, anaemia and liver damage are consistent adverse effects in mice, rats and dogs, with increased cell replication (hyperplasia) in the thyroid in rats after long-term dosing. The liver damage included increased liver weights and liver cell size, mottled appearance and liver cell death. Long-term exposure at high doses produced liver tumours in mice and female rats. However, at low to moderate doses tumours were not observed. Pymetrozine does not damage genetic material, the likely mechanism of tumour formation being through damage to liver cells followed by increased cell division. This process is unlikely to occur at expected levels of human exposure.

Reproduction was not affected in rats and birth defects were not observed in rats and rabbits. Delayed foetal development was seen but only at doses which were toxic in the mother animals, and is considered to be secondary to the maternal toxicity.

Conclusion

Based on an assessment of the toxicology, it was considered that despite significant adverse effects in some species at high dose levels there should be no adverse effects on human health from the proposed use of Chess 250 WP Insecticide in accordance with label directions.

Residues in food and trade aspects

Metabolism studies in tomatoes, potatoes, mice, rats, lactating goats and laying hens were reviewed. The residue definition for pymetrozine is parent pymetrozine, based on the metabolism studies provided.

Analytical methodology

Validated analytical methodology for pymetrozine in the commodities for which registration is sought was provided. Determination of the residue is by HPLC with UV detection at 300 nm. The limits of quantitation in crops such as beans, carrots, cabbages, tomatoes, broccoli, potatoes and cucurbits is 0.02 mg/kg.

Australian trials were conducted in potatoes, broccoli, cabbages, cauliflowers and Brussels sprouts in representative growing areas. In nine potato trials, two sprays of Chess 250 WP Insecticide were applied at a 14 day interval and mature tubers were sampled from 0 to 14 days after treatment. The product was applied at up to four times the maximum label rate. No detectable residues were found in any potato samples taken.

A total of nine residue trials were conducted in broccoli, cabbages, cauliflowers and Brussels sprouts. Two sprays were applied at 14 day intervals and samples were taken immediately before the second spray and at 0, 1, 3, 5, 7 and 14 days after second treatment. The product was applied at up to four times the maximum label rate. Residues in all four crops were below the limit of quantitation at 5 to 14 days after treatment. An MRL of *0.02 mg/kg is recommended with a withholding period of 14 days.

Trade

Major countries to which brassica crops are exported include Singapore, Hong Kong, Malaysia and Japan. The major countries to which potatoes are exported include Mauritius, Singapore, Malaysia, Papua New Guinea and Hong Kong. No information was provided on relevant MRLs in these countries. There are no Codex MRLs established for pymetrozine.However, as non-detectable residues are expected as a result of the use of Chess 250 WP Insecticide, trade issues should not arise.

Registration has been sought in the US for the use of pymetrozine on cucumbers, fruiting vegetables, potatoes and hops.

Occupational health and safety aspects

NOHSC has conducted a risk assessment on Chess 250 WP Insecticide for use on brassicas and potatoes. Chess 250 WP Insecticide can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Pymetrozine is not listed in the NOHSC List of Designated Hazardous Substances. Novartis Crop Protection Australasia Pty. Ltd. has classified pymetrozine as a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances. This classification is based on acute eye irritation and the incidence of carcinogenic effects observed in animals in long term toxicological studies. Chess 250 WP Insecticide was also classified by Novartis Crop Protection Australasia Pty. Ltd. as a hazardous substance based on the concentration of pymetrozine in the formulation in accordance with NOHSC criteria.

Chess 250 WP Insecticide is packaged in 200 g water-soluble sachets. It will be imported in bulk cardboard drums and repacked in Australia. Laboratory staff, store men, process operators, and packers will potentially be exposed to Chess. The product is packed in water-soluble bags using an automated packing machine. Operators involved in loading the product into the hopper will wear personal protective equipment. Transport workers, wharf workers and retailers will only handle the packaged product. Therefore, contamination is only possible if packaging is breached.

Chess 250 WP Insecticide has low acute oral, dermal, and inhalational toxicity. It is a slight eye irritant and slight skin sensitiser, but has no skin irritant properties.

The product is diluted with water, and mixed with a wetting agent in the case of brassicas. The application rate is 400 g product/ha in a total spray volume of 100-800 L/ha. A second application can be made at the same rate 14 to 21 days later.

No worker exposure data was available for pymetrozine or Chess 250 WP Insecticide. The occupational health and safety risk assessment was based on estimates obtained from an exposure model.

Instructions and Safety Directions are provided on the product label to minimise exposure to the product. Applicators need to wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow length PVC gloves when using the prepared spray. No re-entry period is recommended for Chess 250 WP Insecticide at this stage. However the applicant has included the following re-entry statement on the product label: 'Do not enter treated area without protective clothing until spray has dried'. Additional information is available on the product Material Safety Data Sheet.

Environment aspects

Pymetrozine is essentially stable at pH 7 and 9, while at pH 5 the DT50 at 25°C was 5-12 d. The substance is fairly to readily degradable by aqueous photolysis at pH 7, with DT50s of 4.3-6.8 days (as natural summer sunlight days at 40-50°N latitude), but the rate of aqueous photolysis may be limited by turbidity in practical situations in Australia. Pymetrozine on

soil (pH ~7.2) was readily degradable through photolysis, with DT50s of 1.6-4.3 days (DT50s 10.4 d and 5.9 d in the dark controls) and DT90s ≥30 d in the various treatments.

Aerobic soil metabolism studies indicate that degradation of this substance is generally biphasic, with DT50 values ranging from 2 d to 29 d in three soils and 96-142 d in a fourth soil (where low microbial activity and %OC and soil moisture maintenance difficulties possibly account for slower degradation). DT90s in these soils ranged from 16 d to >357 d. Continuously anaerobic soil metabolism studies indicated DT50s of 69-108 d, with greater degradation evident after 6-12 months than under continuously aerobic conditions with the same soils, whereas a briefer study (initially aerobic) with different soil indicated that pymetrozine itself was stable under anaerobic conditions, although the major metabolite formed under the aerobic phase of the test underwent further degradation. An aerobic aquatic metabolism study found that pymetrozine dissipated rapidly from the water initially, with a DT50 of 4.8 days in pond water and 6.3 days in river water, but with corresponding DT90s of 31 and 33 days. Degradation in sediment was slow and pymetrozine dissipated slowly from the whole system, with DT50s of 100-143 days (DT90s > 1000 days).

The major metabolites produced from various means of degradation were a hydroxylated form of the parent and various triazinone and pyridine ring products arising following cleavage of this or the parent molecule. Mineralisation to CO_2 also occurred, sometimes to quite significant levels. The level of unextracted residues appeared to depend on the nature of the extraction, with acid extraction leaving significant levels of bound residues, while alkali extraction left very low levels of bound ^{14}C activity.

Pymetrozine is very slightly volatile and unlikely to evaporate significantly from soil or water. K_{OC} values found for adsorption ranged from 246-1290 to 1390-7880 in studies with different soils and methodologies, indicating that pymetrozine may vary from having medium mobility to being immobile in soil. Column leaching studies with freshly applied pymetrozine or aged soil found that pymetrozine and its metabolites generally showed little mobility, though adsorption/desorption studies indicate that some metabolites have potential for high mobility in soil. Calculations of the Gustafson Ubiquity Score (GUS) using available data generally indicate that pymetrozine is an "improbable leacher" (GUS < 1.8).

Field dissipation studies have also revealed biphasic degradation patterns, with DT50s of 26-91 d and DT90s of 285-1009 d (non-linear degradation models) in three US studies. Interim reports of field lysimeter studies with radiolabelled pymetrozine indicated half-lives of 7.9-20.4 d in the initial 14 days after application, and 103-1269 for days 14-180 (studies are continuing). Other soil residue studies indicated DT50s of 11-60 days, with non-first order decay patterns indicating much longer DT90s in most cases. All the field studies have shown little movement of pymetrozine or its metabolites below 10-15 cm. Outdoor confined accumulation rotational crops studies indicated DT50/DT90s of 110/370 days in one study and 13.2/146 days in the other. However, the low rate and frequency of application of this substance mean it is unlikely to accumulate significantly in soil. The characteristics of the substance and its low application rate and frequency indicate that it is unlikely to bioaccumulate in fish.

Pymetrozine TGAC is practically non-toxic to birds by both acute oral exposure and subacute dietary exposure, and an avian reproduction study indicated a NOEL of 300 ppm. The TGAC was found to be practically non toxic and the formulation slightly toxic to fish with acute exposure, and the TGAC very slightly toxic to fish with chronic exposure. With acute (96 h) exposure, pymetrozine was slightly toxic to mysid shrimp and at most moderately toxic to eastern oyster. Acute (48 h) exposure tests indicated that the TGAC was at most slightly toxic and the formulation practically non-toxic to the daphnid *Daphnia magna*, but non-lethal effects suggested greater toxicity and the 21 d NOEC with the TGAC was 94 µg/L in one study and 25.1 µg/L in another, with the latter study showing high mortality by day 4-5 at 234-462 µg ai/L. The TGAC and/or formulation were at most slightly toxic with 72-120 h exposure to algae and 14 d exposure to the duckweed *Lemna gibba*. Major metabolites were found to have at most slight to moderate toxicity to fish, *Daphnia magna* and the alga *Scenedesmus subspicatus*.

Laboratory studies indicate that pymetrozine TGAC and Chess 250 WP Insecticide are virtually non-toxic to honey bees (*Apis mellifera*) and bumble bees (*Bombus terrestris*) with oral and contact exposure. Although high mortality was found in one semi field study with bumble bees, this was considered to be due to design of the study in which affected bumble bees were unable to find the exit from the hive. No harmful effects were found in several other bumble bee studies. Laboratory studies with a wide range of predators and parasitoids indicated that harmful effects due to direct mortality and/or effects on reproduction may occur with some predator and parasite species if they are exposed to high rates of pymetrozine, but that significant direct toxicity is unlikely to arise with most species tested at field rates similar to those proposed in Australia, with the exception of the parasitic wasp *Encarsia formosa*. Glasshouse and field studies confirmed that predators (including *Encarsia formosa*) and parasite populations were generally not affected by use at field rates, with some exceptions which may be due to scarcity of prey, rather than direct toxicity. Laboratory tests with earthworms (*Eisenia foetida foetida*) indicate that the active ingredient and formulation have very slight toxicity to this earthworm species with 14 d exposure.

No laboratory tests have been performed on Australian native plant species, but a herbicide screening test showed no herbicidal or morphological effects on any of the species tested, and practical and research experience has not revealed adverse effects on succeeding crops, adjacent crops or treated plant products to be used for propagation. Studies of the effects of pymetrozine TGAC and formulation on respiration and ammonification/nitrification in soils indicate at most minor and transient effects, and activated sludge respiration inhibition tests with the parent substance and major metabolites indicate that these substances are non-toxic to bacteria.

Thus chronic toxicity to daphnids is the most sensitive aquatic toxicity indicator for this substance, and is also appropriate to acute exposure situations because of the high mortality found in the chronic test with just 4-5 days exposure. Pymetrozine appears to have a high degree of specificity in its toxicity to arthropods, though some non-target species may be harmed with exposure to high application rates, and populations of predators or parasites may fall where the substance causes a large decline in the target species and the latter constitutes their major food source.

The use of pymetrozine on brassica vegetables and potatoes as proposed presents no expected hazard to birds, mammals, plants, terrestrial invertebrates such as earthworms, or soil micro-organisms, nor to fish or aquatic invertebrates such as mysid shrimp and eastern oyster. The only aquatic species for which a hazard was identified was the aquatic invertebrate *Daphnia magna*, with direct overspray of a shallow waterbody. Use of pymetrozine is also not expected to result in a direct hazard to non-target terrestrial invertebrates such as bees or insect and mite predators and parasites. 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

The data presented supported the claims of control of cabbage aphid and green peach aphid on brassica vegetables (cauliflowers, broccoli and Brussels sprouts) and the control of green peach aphid on potatoes.

Chess 250 WP Insecticide produced no phytotoxic effects on brasssica vegetables or potatoes in the trials reported.

There is justification for use of pyetrozine due to its low impact on benificial insects compared with some currently registered insecticides used for aphid control. Its use will be appropriate in IPM programs and will also be beneficial for use in resistance management as it will reduce selection pressure on the currently registered products. There is however, a potential for development of resistance to pymetrozine if its use is not properly managed.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical pymetrozine as an insecticide for the control of green peach aphid, cabbage aphid and blue green aphid in brassicas and potatoes.

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 pymetrozine, 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 8 October 1999. They should be addressed to :

Applicant

Novartis Crop Protection Australasia Limited

Product details

Pymetrozine will be marketed under the trade name Chess 250 WP Insecticide containing 250g/kg pymetrozine as a wettable powder.

Chess 250 WP Insecticide will be imported fully formulated and packed in Australia.

Novartis Crop Protection Australasia Limited intends to market Chess 250 WP Insecticide in all States and Territories for the control of green peach aphid and cabbage aphid in brassica vegetables and green peach aphid in potatoes.

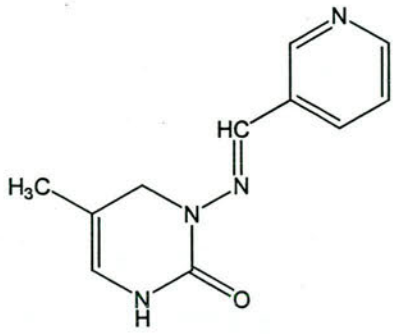
CHEMISTRY AND MANUFACTURE

Active constituent

The chemical active constituent pymetrozine has the following properties:

Common name (ISO):	pymetrozine
Chemical name:	(E)-6-methyl-4-[(pyridin-3-ylmethylene)-amino]-4,5-dihydro-2H-[1,2,4]triazin-3-one.
Product name:	Chess 250 WP Insecticide
CAS Registry Number:	123312-89-0
Empirical formula:	$C_{10}H_{11}N_5O$
Molecular weight:	217.2
Physical form:	granule
Colour:	white to beige
Odour:	odourless
Melting point :	217°C (decomposition)
Density (at 20°C):	1.37g/cm3
Octanol/water partiti coefficient (K_{ow}):	
	at pH 5 log Pow = -0.24
	at pH 7 log Pow = -0.19
	at pH 9 log Pow = -0.20
	pure water log Pow = -0.18
Vapour pressure at 25°C	< 4x10-6 Pa

Structural formula:



TOXICOLOGICAL ASSESSMENT

The toxicological database for pymetrozine, 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 which 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 produced in humans. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

Pymetrozine is rapidly and almost completely absorbed following oral administration in rats. Over half of the dose is excreted in the urine, with up to 30% of the dose excreted in the faeces. It was extensively metabolised, with unchanged pymetrozine accounting for less than 3% of the dose at low doses (0.5 mg/kg bw). Saturation of metabolism occurred at high doses (100 mg/kg bw), resulting in a higher amount of unchanged pymetrozine excreted in the urine (20%). Repeated administration of pymetrozine did not significantly alter the pattern of metabolism or excretion. Tissue levels of pymetrozine or its metabolites were low 7 days after dosing.

Acute Studies

Pymetrozine had low acute oral toxicity in rats (LD_{50} = 5820 mg/kg) and mice (LD_{50} = 1732 mg/kg in males and 3043 mg/kg in females). No deaths or clinical signs were seen in rats dermally treated with 2000 mg/kg pymetrozine. The inhalation LC_{50} in rats was greater than 1800 mg/m^3 (no deaths), the highest achievable concentration. Pymetrozine was not a skin irritant, but was a moderate eye irritant in rabbits. It was a skin sensitiser in guinea pigs following injection into the skin, but not after applications to the skin surface.

The product Chess 250 WP Insecticide was of low acute oral, dermal and inhalation toxicity in rats. The oral and dermal LD_{50}s were greater than 2000 mg/kg (no deaths), and the inhalation LC_{50} was greater than 5062 mg/m^3 (no deaths). Chess 250 WP was not a skin irritant, but was a slight eye irritant in rabbits and was a slight skin sensitiser in guinea pigs.

Short Term Studies

Application to the skin at up to 1000 mg/kg bw/day of pymetrozine for 4 weeks (6 h/day, 5 days/week) did not produce observable toxicity in rats.

Rats were administered 0, 10, 100 or 600 mg/kg bw/day pymetrozine for 4 weeks. At 600 mg/kg bw/day animals ate less, drank more, gained less weight, were anaemic, had enlarged and mottled livers, mottled lungs, smaller thymus glands, and evidence of decreased sperm counts and sperm formation. At 100 mg/kg bw/day and above animals had enlarged liver cells, thymus atrophy, slight cell number increases in the spleen (hyperplasia), increased liver, kidney and spleen weights, decreased thymus weight, blood chemistry changes indicating liver dysfunction (increased; protein, albumin, bilirubin and cholesterol levels and alkaline

phosphatase activity), and possibly also some evidence of kidney dysfunction (decreased plasma chloride level in both sexes, decreased plasma potassium level in females and increased urinary SG in males). No effects were seen at 10 mg/kg bw/day.

Long Term Studies

In mice treated at 0, 1000, 3000 or 7000 ppm (equivalent to 150, 450, 1050 mg/kg bw/day) pymetrozine in the diet for 3 months, liver toxicity at all treatment levels, consisting of increased liver weight and size of liver cells, liver cell death and the presence of a large number of lymphocytes were seen. Slight anaemia and increased spleen weight and red cell production in the spleen (a normal rodent response to anaemia) were observed at 3000 and 7000 ppm. A NOEL was not established in this study.

Oral administration of 0, 50, 500 or 5000 ppm (equivalent to 3.5, 33, & 365 mg/kg bw/day) pymetrozine in the diet for 3 months in rats caused anaemia, liver damage, and reduced body weight gain and food consumption at the highest dose only. Liver damage was manifested by increased liver weight and size, increased liver cell size, mottled appearance of the liver, increased plasma alkaline phosphatase (an enzyme released from damaged bile duct, bone or kidney cells) and bilirubin and cholesterol levels, and the presence of bilirubin in the urine. Other changes included increased spleen weight and number of cells in the spleen (hyperplasia) and decreased thymus weight and smaller thymus cells. Sperm production was decreased in males at 600 mg/kg bw/day. Most of the effects, excluding organ weight changes, were found to be reversible over a 4 week recovery period. The NOEL was 33 mg/kg bw/day.

Dogs were treated with 0, 100, 500 or 2500 ppm (equivalent to 0, 3.2, 14, & 57 mg/kg bw/day) pymetrozine in the diet for 3 months. Dogs treated with 57 mg/kg bw/day pymetrozine developed severe anaemia and increased immature red blood cells; one dog died and some were weak and unable to stand, lost weight and ate less. Liver toxicity was seen at 14 and 57 mg/kg bw/day. Effects on the liver were similar to those observed in rats, with additional changes in plasma enzymes that reflect liver damage (increased alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transferase) at 57 mg/kg bw/day. Animals at 57 mg/kg bw/day also had increased spleen weight, production of red blood cells and pigment deposition in the spleen and liver, decreased thymus weight and cell size, reduced testis weight and sperm production, and lower thyroid weight. Inflammatory changes were detected in the skeletal muscle, gastrointestinal tract, salivary gland, prostate, heart and autonomic nerve ganglions. The NOEL was 3.2 mg/kg bw/day.

Dogs were treated with 0, 20, 200 or 1000 ppm pymetrozine in the diet for 12 months (equivalent to 0, 0.57, 5.2 or 28 mg/kg/day). There were no effects at 0.57 mg/kg bw/day. At 5.2 mg/kg bw/day and above slight anaemia, increased blood clotting time, increased plasma cholesterol and phospholipid levels, were observed. At 28 mg/kg bw/day evidence of liver damage (increased plasma alkaline phosphatase and alanine aminotransferase, and bile duct hyperplasia), deposition of iron stores in the liver and spleen (haemosiderosis), and myopathy of smooth and skeletal muscles were observed. The NOEL was 0.57 mg/kg/day.

Chronic/Carcinogenicity Studies

Mice were treated with 0, 10, 100, 2000 or 5000 ppm (equivalent to 1.2, 12, 250 & 675 mg/kg bw/day) pymetrozine in the diet for 18 months. No effects were observed at 1.2 and 12 mg/kg bw/day. At 675 mg/kg bw/day females ate less, both sexes gained less weight, the survival rate amongst males was increased and males were anaemic. At 250 mg/kg bw/day and/or above; liver, adrenal and spleen weights were increased, masses and nodules in, and enlargement of the liver were seen, enlarged spleen and pituitary, increased liver cell numbers (hyperplasia), red cell formation and iron deposition in the spleen and increased activity in the bone marrow were noted. The incidence of hepatocellular carcinoma was increased in both sexes at 675 mg/kg bw/day and in the males at 250 mg/kg bw/day and hepatoma was increased in the females at 675 mg/kg bw/day. The NOEL was 12 mg/kg/day.

In rats treated for 2 years with pymetrozine in the diet at 0, 10, 100, 1000, or 3000 ppm (equivalent to 0.43, 4.5, 47, & 154 mg/kg bw/day), anaemia was seen at 154 mg/kg bw/day, benign liver tumours were present in female rats and in both sexes increases in liver weight, cell size and liver cysts, and mottled appearance were observed at 47 mg/kg bw/day and above. Liver toxicity was further demonstrated by increased plasma bilirubin, cholesterol and phospholipid levels and decreased glucose levels and alanine aminotransferase (an enzyme released by damaged liver cells) activity. Other organ toxicity included increased spleen weight, nodules in the uterus and ovaries and an increased number of thyroid follicular epithelial cells at 47 and/or 154 mg/kg bw/day. The NOEL was 0.43 mg/kg bw/day.

Reproduction and Developmental Studies

Continuous dietary administration of pymetrozine to rats at 0, 20, 200 or 2000 ppm (equivalent to 1.9, 19 & 190 mg/kg bw/day) for 2 successive generations did not affect reproduction. Toxicity in parental animals at 200 and 2000 ppm was similar to that observed in the repeat dose studies described above. Effects on pups were observed at the highest dose only, including delayed eye opening and reduced litter weights. The NOEL for parental toxicity was 1.9 mg/kg bw/day, and the NOEL for effects on offspring was 19 mg/kg bw/day.

No foetal malformations were observed in rats following oral administration to the pregnant dam of 0, 30, 100 or 300 mg/kg bw/day pymetrozine during the period of foetal organ formation. Dams ate less and gained less weight at 100 and 300 mg/kg bw/day. Minor abnormalities and delayed formation of bones were observed in the foetuses of the 300 mg/kg bw/day group only. The NOELs for maternal and foetal toxicity were 30 and 100 mg/kg bw/day, respectively.

Pregnant rabbits were orally treated with 0, 10, 75 or 125 mg/kg bw/day pymetrozine during the period of foetal organ formation. No adverse effects were observed at 10 mg/kg bw/day. At higher doses, dams at less and gained less weight, an increased number of embryos died, and litters were smaller. The foetuses of these groups showed increased incidences of minor anomalies of one or both front legs (flexure of the wrist) and an additional (13th) rib, and delayed formation of the bone. The NOEL for maternal and foetal toxicity was 10 mg/kg bw/day.

Genotoxicity

Pymetrozine did not induce gene mutation in *Salmonella typhimurium*, *Escherichia coli* or Chinese Hamster V79 lung cells with or without metabolic activation *in vitro*. No structural chromosome changes were demonstrated in Chinese hamster ovary cells *in vitro* or in mouse bone marrow cells *in vivo*. It did not induce unscheduled DNA synthesis in rat primary hepatocytes *in vitro*.

Other Studies

Pymetrozine was a liver enzyme inducer in mice (100 ppm and above) and rats (1000 ppm and above) following dietary administration for up to 42 days. Increased replicative DNA synthesis in the hepatocyte was demonstrated in mice at 2000 ppm and above, and plasma thyroid hormones were increased in rats. The changes were reversible.

PUBLIC HEALTH STANDARDS

Poisons Schedule

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

The NDPSC recommended that pymetrozine be listed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The most sensitive species tested was the rat with a NOEL of 0.43 mg/kg bw/day in a 2-year dietary study. In order to calculate an Acceptable Daily Intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation from animal data to humans, variation within the human population, the quality of the experimental data, and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.004 mg/kg bw/day was established for pymetrozine.

RESIDUES ASSESSMENT

Novartis Crop Protection Australasia Limited has applied for registartion of Chess 250 WP Insecticide for the control of aphids in brassica vegetables and potatoes.

The applicant provided an extensive data package in support of registration. The data package included residue and metabolism studies in accordance with the *Requirements for Clearance of Agricultural and Veterinary Products.*

RESIDUES IN FOOD COMMODITIES

Metabolism Studies/Residue Definition

Metabolism studies in tomatoes, potatoes, mice, rats, lactating goats and laying hens were reviewed. The residue definition for pymetrozine is parent pymetrozine, based on the metabolism studies provided.

Analytical methodology

Validated analytical methodology for pymetrozine in the commodities for which registration is sought was provided. Determination of the residue is by HPLC with UV detection at 300 nm. The limits of quantitation in crops such as beans, carrots, cabbages, tomatoes, broccoli, potatoes and cucurbits is 0.02 mg/kg.

Residue Studies

Australian trials were conducted in potatoes, broccoli, cabbages, cauliflowers and Brussels sprouts in representative growing areas. In nine potato trials, two sprays of Chess 250 WP Insecticide were applied at a 14 day interval and mature tubers were sampled from 0 to 14 days after treatment. The product was applied at up to four times the maximum label rate. No detectable residues were found in any potato samples taken.

A total of nine residue trials were conducted in broccoli, cabbages, cauliflowers and Brussels sprouts. Two sprays were applied at 14 day intervals and samples were taken immediately before the second spray and at 0, 1, 3, 5, 7 and 14 days after the second treatment. The product was applied at up to four times the maximum label rate. Residues in all four crops were below the limit of quantitation at 5 to 14 days after treatment. An MRL of *0.02 mg/kg is recommended with a withholding period of 14 days.

Dietary Intake

Dietary intake calculations indicate that the maximum intake of pymetrozine from brassica vegetables, potatoes and stone fruit is approximately 3 % of the Australian ADI for pymetrozine (0.004 mg/kg bodyweight/day).

MRL Standard

The following amendments will be made to the MRL Standard:

Table 1

Compound		Food	MRL (mg/kg)
Pymetrozine			
Delete:	VB 0040	Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas	T0.1
	VR 0589	Potato	T*0.02
Add:	VB 0040	Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas	*0.02
	VR 0589	Potato	*0.02

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

Brassicas: DO NOT HARVEST FOR 14 DAYS AFTER APPLICATION

Potatoes: NOT REQUIRED WHEN USED AS DIRECTED.

Trade Implications

Overseas registration status

Registration has been sought in the US for the use of pymetrozine on cucumbers, fruiting vegetables, potatoes and hops. The tolerance sought for potatoes is 0.02 mg/kg (Federal Register, May 1998)

Relevant MRLs or tolerances in other countries are given below:

Country	**Commodity**	**MRL(mg/kg)**
Czech Republic	Cabbage	0.05
Switzerland	Brassica vegetables	0.10
	Cabbage	0.02
EU (proposed)	Cabbage, potato	0.05
Japan	Other vegetables (excluding fruiting vegetables)	1.0
	Potato	0.1

In all of the above cases, the residue definition (or proposed residue definition) is the parent compound.

Major countries to which brassica crops are exported include Singapore, Hong Kong, Malaysia and Japan. The major countries to which potatoes are exported include Mauritius, Singapore, Malaysia, Papua New Guinea and Hong Kong. No information was provided on relevant MRLs in these countries. There are no Codex MRLs established for pymetrozine.However, as non-detectable residues are expected as a result of the use of Chess 250 WP Insecticide, trade issues should not arise.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Pymetrozine is not listed in the NOHSC List of Designated Hazardous Substances. Novartis Crop Protection Australasia Pty. Ltd. has classified pymetrozine as a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances. This classification is based on acute eye irritation and the incidence of carcinogenic effects observed in animals in long term toxicological studies. .

The following risk phrases are allocated to pymetrozine:

R36	Irritating to eyes
R40	Possible risk of irreversible effects

Substances are hazardous when they contain concentrations of ≥1% pymetrozine.

Pymetrozine is a light to dark grey powder with non-specific odour. It is of low acute toxicity by all routes. It is not a skin irritant in rabbits, but is a skin sensitiser in guinea pigs and a moderate eye irritant in rabbits.

Chess 250 WP Insecticide is classified by Novartis Crop Protection Australasia Pty. Ltd. as a hazardous substance based on the concentration of pymetrozine in the formulation in accordance with NOHSC Approved Criteria for Classifying Hazardous Substances.

Chess 250 WP Insecticide is a wettable powder. It is of low acute toxicity by all routes. It is a slight eye irritant in rabbits and slight skin sensitiser in guinea pigs, but has no skin irritant properties in rabbits.

The product will be imported fully formulated and repacked in Australia.

Transport, storage and retailing

Chess 250 WP Insecticide is packaged in 200 g water-soluble sachets. It will be imported in bulk cardboard drums and repacked in Australia. Laboratory staff, store men, process operators, and packers will potentially be exposed to Chess. The product is packed in water-soluble sachets using an automated packing machine. Operators involved in loading the product into the hopper will wear personal protective equipment. Transport workers, wharf workers and retailers will only handle the packaged product. Therefore, contamination is only possible if packaging is breached.
Advice on safe handling of the product during routine use is provided in the Material Safety Data Sheet (MSDS) for Chess 250 WP Insecticide.

End use

Chess 250 WP Insecticide is to be used for the control of green peach aphid and cabbage aphid in brassica vegetables and greeen peach aphid in potatoes. It is diluted in water, mixed with a wetting agent in the case of brassicas, and applied as a ground spray. The application rate is 400 g product/ha in 100 L/ha, minimum spray volume (0.4 % (w/v) product, 0.1% (w/v) pymetrozine).

A maximum of 2 applications/crop is recommended with at least 14 to 21 days between the two applications.The withholding period (WHP) for harvesting brassicas is 14 days; no WHP is specified for potatoes.

Exposure of end users will be predominantly through the dermal route during ground application and clean-up procedures. Inhalation exposure to spray mist may occur. Given the product is non-volatile and is packed in water-soluble sachets, inhalation exposure to product mist or dust is not expected to be significant. The undiluted product is a slight eye irritant and slight skin sensitiser. Given the high dilution of product in the working strength solution (0.4 % w/v), the prepared spray is not expected to be irritating to the eyes or sensitising to the skin.

No worker exposure data was available for pymetrozine or Chess 250 WP Insecticide. The risk assessment was based on exposure estimates from the UK Predictive Operator Exposure Model. The risk assessment conducted using data from this model indicated that the risk was acceptable for mixer/loaders, applicators, and workers performing combined tasks wearing gloves during application.

The risk assessment indicated that cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow length PVC gloves are recommended when using the prepared spray.

Entry into treated areas or handling treated crops

Workers re-entering treated crops may come into contact with product residues. Workers are not likely to re-enter treated crops immediately after spray application. Given the low acute systemic toxicity and topical hazards of the product, and the high dilution in the final spray, a re-entry period is not recommended at this stage.

The applicant has included the following re-entry statement on the draft label: "Do not enter treated area without protective clothing until spray has dried'. This statement should appear on the final product label and MSDS.

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 and Safety Directions on the product labels. Safety Directions include the use of cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow-length PVC gloves when using the prepared spray.

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

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

AS 3765-1990 Clothing for Protection Against Hazardous Chemicals

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

Conclusions

Chess 250 WP Insecticide can be used safely if handled in accordance with the instructions on the product label. Additional information is available on the MSDS for Chess 250 WP Insecticide.

Environmental Assessment

Novartis Crop Protection Australasia Pty Ltd has applied for registration of a new end-use product, Chess 250 WP Insecticide, containing the new technical grade active constituent (TGAC) pymetrozine sufficient to give 250g/kg. It is to be used to control aphids in brassica vegetables and potatoes. Pymetrozine is an asymmetric triazinone which blocks feeding through neural inhibition which prevents stylet penetration.

Environmental Fate

Hydrolysis

Three experiments were performed which indicated that pymetrozine was essentially stable at pH 7 and 9. The half-life (25°C) at pH 5 was 5-12 d and 2.8 h at pH 1, but tended to slow as an equilibrium was established with the hydrolysis product. The major products, CGA 300407 (pyridine-3-carbaldehyde) and CGA 215525 (4-amino-6-methyl-4,5-dihydro-2H-(1,2,4)-triazin-3-one), resulted from cleavage of the bridge between the two rings. Higher temperatures predictably shortened the half-lives.

Photolysis

Various studies reported the quantum yield for aqueous photolysis, and degradation rate and metabolites produced with aqueous and soil photolysis. Aqueous photolysis is complicated by the fact that at neutral pH, irreversible photochemical and thermal degradation takes place via the *Z*- rather than *E*-isomer. The Z-isomer forms in a reversible reaction in the presence of light, and then may degrade irreversibly to other substances, whereas the *E*-isomer is stable at pH 7 and higher and is formed from the *Z*-isomer in the absence of light. Thus while initial $E \rightarrow Z$ photoisomerisation was found to be very rapid (half-life of 5-7 minutes at 40-50°N under clear skies in mid-spring), at pH 7 the abiotic half-life in surface waters exposed to sunlight is limited by the half-life for the irreversible thermal decay of the *Z*-isomer, which is estimated to be 4.4 h at 20°C.

The aqueous half-life for photolysis from other studies in pH 7 buffer with an artificial light source was 4.3 d (^{14}C-pyridine label) and 6.8 d (^{14}C-triazinone label; natural summer sunlight at latitude 40°N), indicating that pymetrozine was fairly to readily degradable. The major aqueous photolysis products were the same as those resulting from hydrolysis and reached high peak concentrations (CGA 300407 reaching 90% of initial radioactivity on day 30, and CGA 215525 reaching 71% of initial radioactivity after 7 days). Identified products reaching lower concentrations were CGA 249257 (deaminated CGA 215525) and CGA 180777 (nicotinic acid – from oxidation of CGA 300407).

Pymetrozine on soil (pH ~7.2) was readily degradable through photolysis, with the DT50s for soil photolysis similar or faster to those for aquatic photolysis, at 4.3 d and 1.6 d (40°N) for the pyridine and triazinone label studies, respectively. Metabolism still occurred in the dark controls, with DT50s of 10.4 d and 5.9 d (40°N) for the pyridine and triazinone label studies, respectively. Some slowing again occurred, with DT90s ≥30 d in the various treatments. The

hydroxylated pymetrozine product CGA 359009 (with the bridge between the rings still intact) was identified in both the ^{14}C-pyridine and ^{14}C-triazinone soil photolysis studies, and appeared to be subject to photolytic degradation (DT50 of 27.2 d and 12.6 d (40°N) in the pyridine and triazinone label studies, respectively). Its degradation probably resulted in the formation of CGA 300407 (the aldehyde of the pyridine ring resulting from cleavage of the bridge between the rings) and CGA 294849 (a triazin-3,5-dione derivative), identified in the respective studies. A significant level (22-26% applied radioactivity) of $^{14}CO_2$ was also produced over the incubation period with light exposure, compared to only 2-6% of applied radioactivity as $^{14}CO_2$ in the dark over the same period. Bound residues also increased through the experiment to a maximum level of 45-52% applied radioactivity.

Soil and Water Metabolism Studies

Ready biodegradability

Ready biodegradability studies with pymetrozine and some of its major metabolites indicated that the parent, CGA 215525 and CGA 249257 were not classifiable as readily biodegradable, but were not inhibitory to the growth of sewage micro-organisms. The metabolite CGA 300407 was classified as readily biodegradable.

Aerobic soil metabolism

For aerobic soil metabolism, 5 studies were performed at 20-25°C in the dark using 4 different soils, with ^{14}C-pyridine or triazinone-labelled pymetrozine. The results indicated a range of DT50s, from 2 d to 142 d (the latter by an unusual $^{3}\sqrt{}$time model: evidently biphasic, with ~3 days of relatively rapid degradation, degradation then slowing greatly), and DT90s from 16 d to >357 d. The 2 studies (2 radiolabels, 2 pymetrozine application rates – DT50 = 96-142 d with a $^{3}\sqrt{}$time model, or = 8.4-12.6 d over days 0-3 and 277-347 days over days 3-357 by simple exponential models) using a sandy loam with only 0.2%OC and pH 7.4 indicated DT50s and DT90s much longer than the other 3 studies (3 soils, 2 labels – mean overall DT50 = 4.1, 3.0 and 29 d, respectively, for a silt loam, sandy loam and sand, %OC = 1.9-2.3%, pH = 6.6-7.3). Possible reasons for the large difference in degradation rate include differences in microbial activity and %OC and soil moisture maintenance difficulties affecting one soil, and to a minor degree, harsher extraction which may have removed bound parent material in the studies with that soil. The soils were all near neutral in pH, hence abiotic hydrolysis occurring under acidic conditions does not appear a likely explanation for DT50 differences. The mean DT50 values indicated above indicate that pymetrozine ranges from readily degradable (DT50 < 20 d) to fairly (DT50 = 20-60 d) or slightly (DT50 = 60-180) degradable in soil. The one sterile control (one soil, one label) evaluation indicated a DT50 and DT90 of 33 d and 110 d, respectively (the corresponding viable soil/label treatment had a DT50 and DT90 of 3 and 29 d).

The major initial metabolite produced was CGA 359009, the hydroxylated form of the parent (peak concentrations in the various studies ranged from 5-54% of applied radioactivity). Other metabolites were then formed through hydrolysis of the diazo bond and oxidation of the carbon-5 atom in the triazinone ring and deamination of the triazinone ring. Mineralisation to CO_2 also occurred, sometimes to quite significant levels (eg 19% after 122 d and 31% after 1

y). The level of unextracted residues appeared to depend on the nature of the extraction, which were harsher in US studies and included an alkali extraction step.

The overall DT50 estimated for pymetrozine in the dark control of the soil photolysis study was 5.9-10.4 days (~30 days incubation), consistent with the aerobic soil metabolism results for the same soil. Extrapolating from data from 5 or 30 d incubation in four aged soil column leaching studies, pymetrozine DT50s were of the order of a few days in two soils where degradation was also relatively rapid in the above studies, and 62-158 d for DT50s for four other soils, one of which had relatively slow degradation in the soil metabolism studies. Similar major metabolites to the above were identified in these studies.

Anaerobic soil metabolism

For anaerobic metabolism, 3 studies were performed – 2 of these under the same conditions as the aerobic studies that returned the longer DT50s (ie at 25°C on one soil and two radiolabels, but continuously under water and anaerobically maintained), the other one under the same conditions as the aerobic studies that returned a very short DT50, but over a 90 d period after 10 days of aerobic conditions (and only one soil and one label). In the studies with continuously anaerobic conditions, the DT50s were 69-108 d (simple exponential decay without an initial period of more rapid degradation - "*slightly degradable*"), with greater degradation, but less mineralisation evident after 6-12 months than under continuously aerobic conditions with the same soils. The pyridine bridge cleavage metabolite (CGA 180777) was found at higher concentrations than in the corresponding aerobic soil metabolism study, and two triazinone bridge cleavage metabolites were found which had not been identified in any other studies. In contrast, the briefer aerobic/anaerobic study indicated that pymetrozine was stable, although the major metabolite that was formed under the aerobic phase of the test, CGA 359009, underwent further degradation, with cleavage of the bridge between the two rings to form similar metabolites to those found under aerobic conditions.

Aerobic aquatic metabolism

An aerobic aquatic metabolism study was conducted using ^{14}C-pyridine labelled pymetrozine and two water/sediment systems, from a pond and from the Rhine River. Conditions were aerobic in the water, but anaerobic in the sediment, and water pH in both cases was >8, hence abiotic hydrolysis was likely to have been insignificant. Pymetrozine dissipated rapidly from the water initially, then dissipated more slowly, with a dissipation DT50 of 4.8 days in pond water and 6.3 days in river water, but with corresponding DT90s of 31 and 33 days.

Degradation in sediment was slow and pymetrozine was only slightly degradable in the whole system, with DT50s of 100 and 143 days (DT90s > 1000 days) in the pond and river systems, respectively (bi-exponential models were fitted in all cases). Two metabolites were identified in both systems (CGA 359009 and the cleavage product CGA 300407), and several other unidentified metabolites were detected at low concentrations.

Mobility studies

Chemical and physical data indicate that pymetrozine is very slightly volatile and unlikely to evaporate significantly from soil or water, and this was confirmed with soil and plant/soil volatilisation studies.

Batch equilibrium studies of adsorption and desorption of pymetrozine on various soils indicated K_{OC} values for adsorption ranging from 246-1290 (5 soils in a Swiss study) to 1390-7880 (5 different soils in a US study), the differences possibly being associated with differences in methodology and the storage treatment of the soils. These data indicate that pymetrozine may vary from having medium mobility to being immobile in soil. While the pK_a of the substance ($pK_a = 4.1$) suggests that there may be greater adsorption in acid soils, this was not the explanation for the large differences in K_{OC} between the soils tested.

Adsorption/desorption studies with various metabolites (full reports not seen by Environment Australia) indicated that based on the K_{OC} for adsorption, CGA 359009 had medium mobility potential in soil, CGA 180777, CGA 249257 and GS 23199 had very high mobility, while CGA 300407 and CGA 215525 were too unstable in the test system to evaluate satisfactorily. Column leaching studies with freshly applied ^{14}C-triazinone labelled pymetrozine (leaching with 20 cm water in 4 soils common to the Swiss batch equilibrium study, or 51 cm water in 4 different soils common to the US batch equilibrium study) indicated that little movement of the substance occurred below 10 cm (leaching with 20 cm water) or 16 cm (leaching with 51 cm water) depth in the column. Negligible residues were also found in leachate, with the exception of one soil where ~5% applied ^{14}C-radioactivity reaching leachate was apparently due to by-pass flow along the column wall. Based on the calculated relative mobility factors (RMFs) compared to monuron in the 51 cm leachate studies, pymetrozine was classified as having little mobility (RMF <0.54 to 0.75).

Aged soil column leaching studies were conducted with both ^{14}C-triazinone and ^{14}C-pyridine labelled pymetrozine, including Swiss studies with 2 soils in common to the corresponding studies above (5 d aging, leached with 20 cm water) and a US study with the same 4 soils as the corresponding studies above (30 d aging, leached with 51 cm water). Negligible radioactivity was collected in leachate, except for the study with the triazinone label and the greater leaching volume, where >50% of the low amount of radioactivity present (<5% of applied) was attributed to the metabolite CGA 294849, with <10% attributable to the parent substance. Approximately 80% of radioactivity was recovered in soil extracts, 66-74% as parent and 1.5-8.4% as CGA 359009 in the US study and 34-47% as parent and 31-41% as CGA 359009 in the Swiss study, where other minor metabolites were also identified. The depth to which significant levels of radioactivity were recovered in soil extracts varied with the soil and volume of water applied, from no deeper than 15 cm with 3 soils and 25 cm with one soil following application of 51 cm water, and no deeper than 12 cm with both soils following application of 20 cm water. In all cases the majority of radioactivity was recovered from the top 4-5 cm of the column. Thus pymetrozine and its metabolites generally showed little mobility in these aged soil column mobility studies, despite the potential for very high mobility in soil found in individual adsorption/desorption studies.

Calculations by *Environment Australia* of the Gustafson Ubiquity Score (GUS) using available data corresponding as far as possible to the same soil type generally indicate that pymetrozine is an "improbable leacher" (GUS < 1.8).

Field dissipation

Reports of three 532-543 day field dissipation studies conducted in the USA were provided, with the substance applied as a 50 WP (504 g ai/kg) formulation to bare soil at rates of 1850 g ai/ha. These revealed biphasic degradation patterns, with models fitted by Environment Australia indicating DT50s of 26-91 d and DT90s of 285-1009 d. Little downward movement of pymetrozine or its metabolites below 15 cm soil was detected. Interim reports of two additional 14C-labelled field lysimeter studies were provided, again showing little downward movement of pymetrozine or its metabolites and indicating a biphasic degradation pattern. Half-lives estimated for these studies for days 0-14 after application were 7.9-10.7 d at a Georgian site and 15.0-20.4 d at a Californian site, while the corresponding half-lives estimated for days 14-180 were 103-114 d and 297-1269 d, respectively.

Brief reports of eight 60-150 day field dissipation/soil residue studies conducted in Europe were provided, with the substance applied as the 250 WP (250 g ai/kg) formulation to bare soil at cumulative rates of 300-900 g ai/ha. These indicated DT50s of 10.6-60 days, with variable data and non-first order decay patterns indicating much longer DT90s in most cases (a DT50 value could not be estimated in one study). Maximum concentrations of pymetrozine in soil at 0-10 cm depth were 0.23-0.70 mg/kg and little movement was detected below this depth (maximum concentration 0.02 mg/kg). Two outdoor confined accumulation on rotational crops studies were provided where the 250 WP formulation was applied to bare soil at 460-500 g ai/ha, with crops planted at 63-307 days after application. Estimated pymetrozine DT50/DT90 values pooling the available soil data were 110/370 days in one study (calculated by Environment Australia and not robust - measured initial soil concentrations were not available in this case), and 13.2/146 days in the other study (company estimate, log concentration/square root of time model).

Accumulation potential in soils

The proposed low rate and frequency of application of this substance mean it is unlikely to accumulate significantly in soil, despite the slowing in degradation rate of the substance evident in field and laboratory studies. Calculations by *Environment Australia* assuming repeated annual application at 200 g ai/ha and a worst case situation of 20% carryover from year to year indicate peak pymetrozine concentrations in the top 15 cm of soil reaching 0.11 mg ai/kg in the third year, compared to a peak concentration of 0.09 mg/kg in the absence of accumulation. Furthermore, it is likely that the decline in degradation rate with time is due to reduced bioavailability, minimising any potential environmental effects of aged residues of the parent substance.

Bioaccumulation in aquatic organisms

The applicant argues that bioconcentration of pymetrozine is not likely to occur because the substance has a log P_{OW} well below 3, because the proposed uses of the product involve application at worst four times per year (twice in each of two separate crops), and because

pymetrozine dissipates from the water phase very rapidly (DT50 <7 days, because of partitioning to the sediment rather than degradation) and the residual concentrations are very low. Based on the adsorption/desorption studies and the solubility data in octanol, it is likely that pymetrozine has a higher affinity to the octanol phase than the log P_{OW} would indicate, but this would be mitigated by pymetrozine's labile nature in the environment and its metabolic instability in animals. *Environment Australia* further notes that the low application rates and infrequent use proposed under the current submission mean that pymetrozine is unlikely to be present to a sufficient extent for bioaccumulation in fish to occur.

Environmental Toxicity

Birds

An acute avian oral toxicity test with mallard ducks (*Anas platyrhynchos*) found no mortalities at doses of 31.3-2000 mg ai/kg, but a reliable LD50 value could not be established as emesis was observed at doses above 31.3 mg ai/kg. A similar test with Bobwhite quail (*Colinus virginianus*) indicated an LD50 >2000 mg ai/kg bw, with a NOEL of <500 mg ai/kg bw due to temporary effects on behaviour. Limit tests with a single dose of 2000 mg ai/kg to mallard ducks and Japanese quail (*Coturnix coturnix japonica*) found no mortalities at that dose. Subacute dietary toxicity tests with pymetrozine TGAC and mallard ducks or Bobwhite quail indicated that the subacute dietary LC50 of pymetrozine to both species was >5200 ppm in the diet, but with significantly lower food consumption and weight gain at some doses (NOEL = 325 and 2600 ppm, respectively, for mallard ducklings and Bobwhite quail chicks). An avian reproductive toxicity test with 20 weeks dietary exposure of Bobwhite quail to pymetrozine TGAC found no statistically significant treatment-related effects on adult birds or reproductive indices at up to 300 ppm. These studies indicate that according to US EPA classifications, pymetrozine is practically non-toxic to birds by both acute oral exposure (LD50 > 2000 mg ai/kg bw) and subacute dietary exposure (LC50 > 5000 ppm in diet).

Aquatic toxicity

Fish

A total of 7 fish studies with pymetrozine TGAC indicate that the substance is practically non-toxic (LC50 > 100 mg ai/L) with acute (96 h) exposure to the freshwater fish test species rainbow trout (*Oncorhynchus mykiss*), bluegill sunfish (*Lepomis macrochirus*), carp (*Cyprinus carpio*) and catfish (*Ictalurus punctatus*) and the saltwater fish species sheepshead minnow (*Cyprinodon variegatus*). Very slight toxicity to rainbow trout was also found in a 21 day prolonged exposure toxicity study with the TGAC (21 d LC50 > 120 mg/L, NOEC = 35.2 mg ai/L due to effects on growth at the highest test concentration), and in a 90 day early life-stage study (NOEC = 11.7 mg ai/L, the highest test concentration). Two acute (96 h exposure) toxicity studies with the Chess 250 WP Insecticide formulation suggest that it has greater toxicity than the TGAC to rainbow trout (LC50 in the range 21-46 mg test substance/L in one study and 12.5-25.0 mg test substance/L in the other), presumably because of a non-active ingredient/s. Acute (96 h exposure) toxicity studies with the pymetrozine metabolites CGA 359009, CGA 215525 and CGA 249257 indicated LC50 values > 90-105 mg test substance/L, while a similar study with the metabolite CGA 300407 (supplied as a 20.1% solution in water) found the 96 h LC50 was in the range 25.0-32.3 mg test substance/L, or

5.0-6.5 mg CGA 300407/L, correcting to the substance itself. Thus the first mentioned metabolites were at most slightly toxic (LC50 in the range 10-100 mg/L), while CGA 300407 was moderately toxic (LC50 in the range 1-10 mg/L).

Aquatic invertebrates

Two acute (48 h exposure) toxicity studies with the daphnid *Daphnia magna* indicated that pymetrozine TGAC was at most slightly toxic to this species [EC50 values = 87.0 (95% confidence limits 68-130) mg ai/L in one study and >99.1 mg ai/L in the other], but in both cases all test concentrations caused non-lethal effects on activity or swimming behaviour in all daphnids surviving at 48 h except those in the control (NOEC <19.2 and <5.0 mg ai/L, respectively). Toxicity increased rapidly with increasing duration of exposure, the 21 d NOEC being 94 µg/L (21 d EC50 > 415 µg/L) in one study and 25.1 µg/L (21 d EC50 = 73.5 µg/L) in the other. In the latter case, *Environment Australia* notes that mortality commenced between days 1-3 of exposure at concentrations ≥ 10 µg ai/L and that the EC50 (calculated by *Environment Australia*) fell from >462 µg/L after 2 days' exposure to 215 µg/L after 4 days, and continued to decline thereafter to reach the 21 day value. An acute (48 h exposure) study with the Chess 250 WP Insecticide formulation produced an EC50 value of 629 mg nominal test substance/L (concentration uncertain - precipitate present), indicating that it is practically non-toxic to daphnids. Acute (48 h) exposure studies with the pymetrozine metabolites CGA 359009, CGA 215525, CGA 249257 and CGA 300407 gave EC50 values >88-102 mg test substance/L (>20 mg/L for CGA 300407 itself), indicating these substances are at most slightly toxic to *Daphnia magna*.

An acute (96 h exposure) toxicity study with the TGAC and mysid shrimp (*Mysidopsis bahia*) gave an LC50 value of 61.7 (52.4-73.1) mg ai/L, indicating slight toxicity to this species. At most moderate toxicity (EC50 in the range 1-10 mg ai/L) was also indicated in a 96 h exposure test with eastern oyster (*Crassostrea virginica*), where the EC50 for shell growth was in the range 2.02-3.23 mg ai/L.

Algae and aquatic plants

Toxicity studies (72 or 120 h exposure) with the freshwater green alga species *Selenastrum capricornutum* and *Scenedesmus subspicatus* and the duckweed *Lemna gibba* found pymetrozine TGAC was at most slightly toxic to these species (EC50 in the range 10-100 mg ai/L or higher). The Chess 250 WP Insecticide and the pymetrozine metabolites CGA 359009, CGA 215525 and CGA 249257 were also at most slightly toxic to *Selenastrum capricornutum*. A similar study with the metabolite CGA 300407 and *Scenedesmus subspicatus* indicated that this substance too was at most slightly toxic to this species of algae.

Non-target terrestrial invertebrates

Insect pollinators

The acute contact and oral toxicity of pymetrozine TGAC and Chess 250 WP Insecticide to honey bees (*Apis mellifera* – Hymenoptera:Apidae) was examined in laboratory tests to standard guidelines. Although temporary behavioural problems were observed in some cases, recorded problems did not include food refusal or vomiting. and in all cases, the oral or

contact 48 h LD50 values exceeded 100 µg TGAC or formulation per bee. Hence pymetrozine as TGAC or in the Chess 250 WP Insecticide is virtually non-toxic to bees (LD50 > 100 µg per bee).

High (90%) mortality of bumble bees (*Bombus terrestris*) was found in a semi-field test with this species, where sugar solution containing 0.02% ai was placed in hives placed in the field. Subsequent laboratory and field (glasshouse, plant tunnel) tests found no mortality was caused by pymetrozine (as Chess WP 250 Insecticide) through various means of exposure, but similar behavioural problems in bumble bees exposed to contaminated food were observed to those seen in some of the honey bee toxicity tests. It was hypothesised that repeated dietary exposure in the hive was the reason for mortality in the semi-field test, affected bumble bees being unable to find the exit from the hive. No harmful effect on pollination activity was observed in glasshouse or plant tunnel tests. *Environment Australia* notes that similar toxic effects to that found in the semi-field study might also be possible with honey bees, but that such continuous dietary exposure is unlikely to arise in practice.

Predators & parasites

Laboratory studies with pymetrozine formulated as A-8811B/Chess 250 WP Insecticide applied at a rate equivalent to 0.6 or 1 kg ai/ha in the field (compared to a maximum cumulative rate of 0.2 kg ai/ha per crop in Australia) indicated that according to the IOBC toxicity scale for mortality or mortality together with fecundity, pymetrozine was "harmless" to the ground beetle *Poecilus cupreus*, rove beetle *Aleochara bilineata* and predatory mite *Typhlodromus pyri*; "slightly harmful" to the lacewing *Chrysoperla carnea* and predatory bug *Orius insidiosis*; and "moderately harmful" to the parasitic wasp *Aphidus colemani*. Summaries of similar studies with the test substance at rates of ~0.2 kg ai/ha (full reports not provided) again found the substance was "harmless" to *Typhlodromus pyri* and at this lower rate also found it was "harmless" to *Chrysoperla carnea* and *Orius insidiosus*, and to other ground beetle species (*Bembidion* spp.), the predatory bug *Orius majusculus*, the ladybird beetle *Coccinella septempunctata* and the capsid bug *Macrolophus caliginosus*. However, two laboratory studies with the parasitic wasp *Encarsia formosa* at a similar application rate found strong effects on adult mortality and parasitisation, rating pymetrozine as "slightly harmful" to adults of this species in one study and "harmful" in the other, though when the latter study was repeated with pupae the test substance was found to be "harmless" to this life stage.

In contrast to the above laboratory results, 8 glasshouse studies with A-8811B/Chess 250 WP Insecticide at ~0.1-0.3 kg ai/ha found no indications of harmful effects on *Encarsia formosa*, but 2 other glasshouse studies found populations of the capsid bug *Macrolophus caliginosus* were reduced after spraying. Glasshouse studies also found no harmful effect of the substance on the parasitic wasp *Aphidus matricariae*, the predatory mite *Phytoseiulus persimilis* or the parasitic fungus *Verticillium lecanii*, but that a decline in population of the predatory gall midge *Aphidoletes aphidomyza* occurred following spraying. A decline in availability of prey was suggested as a likely reason where a fall in predator population occurred, but it was also suggested that *Macrolophus* bugs may have been affected directly, as they may suck the foliage in addition to predating (but corrected nymph mortality was only 10.6% in a laboratory study). A total of eight field studies with carrot, okra, cotton, apples, citrus and wheat generally found no signs of harmful effects on a wide range of spiders and other

predator and parasitoid species. The exception was ladybird beetles (*Coccinella septempunctata*), where a reduction in larvae and/or eggs, pupae and adults recorded in two studies was found at the same time as aphid numbers fell heavily, suggesting the decline in predator populations was due to lack of prey.

Thus laboratory studies indicate that harmful effects due to direct mortality and/or effects on reproduction may occur with some predator and parasite species if they are exposed to high rates of pymetrozine, but that significant direct toxicity is unlikely to arise with most species tested at field rates similar to those proposed in Australia, the exception being the parasitic wasp *Encarsia formosa*. Glasshouse and field studies confirm that predators (including *Encarsia formosa*) and parasite populations are generally not affected by use at field rates, with some exceptions which may be due to low prey density, rather than direct toxicity.

Earthworms

Laboratory tests where earthworms (*Eisenia foetida foetida*) were exposed to pymetrozine TGAC or in the formulation A-8811B (Chess 250 WP Insecticide) indicated 14 day LC50 values of >1000 mg ai/kg dry soil and >1000 mg product/kg dry soil, respectively, indicating that the active ingredient and formulation have very slight toxicity to this earthworm species. While no harmful effects were evident at the highest test concentration with the formulation, mortality was observed at all test concentrations with the TGAC (NOEC < 12.3 mg ai/kg), increasing with concentration and suggesting a very shallow toxicity curve (*Environment Australia* notes moisture levels at the highest test concentrations in the TGAC study deviated from guideline levels).

Phytotoxicity

No laboratory tests have been performed on Australian native plant species, but a herbicide screening test (not seen by *Environment Australia*) with CHESS 250 WP Insecticide and 33 different crop and weed species with pre- or post-emergence application showed no herbicidal or morphological effects on any of the species tested. No adverse effects on native flora have been reported from any trial site in Australia and practical and research experience since 1990 has not revealed adverse effects on succeeding crops, adjacent crops or treated plant products to be used for propagation. Thus the substance is generally not likely to be phytotoxic to terrestrial plants at rates used in practice for insect pest control.

Micro-organisms

A soil respiration and ammonification/nitrification study with pymetrozine applied at a rate of 0.6 and 3.0 mg/kg soil (4.5 and 22.5 X the proposed Australian rate per application, in 5 cm soil) indicated negligible effects on glucose-enriched short term respiration and at most minor and transient effects on ammonification and nitrification in soil amended with lucerne meal. A similar incubation study with Chess 250 WP Insecticide at 2.67 or 26.7 mg/kg soil (5 and 50 X the proposed Australian rate per application, in 5 cm soil) again showed at most minor and transient effects on soil microflora, as indicated by nitrogen turnover and dehydrogenase activity. Activated sludge respiration inhibition tests with the parent substance and the metabolites CGA 215525, CGA 249257 and CGA 300407 (the latter only 20.1% purity in

water) indicated that substances were all non-toxic to bacteria (EC50>100 mg test substance/L).

Environmental Hazard

It is proposed that Chess 250 WP Insecticide will be sprayed on crops via ground-based boomspray equipment in at most two non-consecutive applications per crop, at a maximum total rate of 800 g product/ha (200 g ai/ha), the worst case situation being that this might occur on two crops per year. Residues would be expected in the crop area on plant and soil surfaces and spray drift and run-off are potential means of contamination of adjacent areas and surface water. Laboratory and field data indicate that pymetrozine is unlikely to leach significantly, but movement in run-off may occur via chemical adsorbed to soil particles.

Hazard to birds and mammals

Estimated residues on feed at the maximum proposed rate are likely to be well below the acute oral LD50s and 5 day dietary exposure NOECs for bobwhite and Japanese quail and mallard duck, hence pymetrozine used in accordance with label recommendations is not likely to present a hazard to birds ingesting these residues. Acute or chronic toxicity in mammals is also highly unlikely.

Aquatic hazard

The hazard presented by direct overspray of a shallow (15 cm deep), lentic waterbody with 1 or 2 X the proposed single application rate (ie a single application at 100 or 200 g ai.ha^{-1}, the latter representing an extreme worst case situation with repeated spraying) was evaluated for representative aquatic species from those for which toxicity data were available (above). The only species for which a hazard was indicated with direct overspray was the aquatic invertebrate *Daphnia magna*, at either application rate. Spray drift or run-off reaching a similar waterbody at 10% of this rate was found unlikely to cause a hazard even to *Daphnia magna*, at either rate. The aquatic hazard from this substance is relatively low, but a suitable label warning has been included to indicate the potential hazard to some aquatic invertebrates and the need to minimise spray drift and avoid contamination of water bodies.

Hazard to terrestrial invertebrates and soil micro-organisms

Pymetrozine TGAC and the EUP Chess 250 WP Insecticide have been found virtually non-toxic to honey bees (*Apis mellifera*) and the product is used at most twice per crop. Hence use of pymetrozine as proposed in brassica vegetables and potatoes is unlikely to present a hazard to honey bees. A large number of laboratory, glasshouse and field studies were provided with pymetrozine formulated as A-8811B/Chess 250 WP Insecticide and covering a wide range of insect and mite predators and parasitoids. From these tests, it appears that significant direct toxicity is unlikely to arise to most non-target species, though there may be indirect effects in some cases due to suppression of prey. The product is also unlikely to present a hazard to earthworms: even in the extreme worst case of repeated spraying over 4-5 years, peak soil concentrations would remain well below the LOEC in the TGAC toxicity study. Similarly, pymetrozine would not be expected to affect carbon turnover or cause long term detrimental effects on the turnover of nitrogen in soils.

Desirable terrestrial vegetation

As there is no indication of crop phytotoxicity from use in a range of crops at specified application rates nor in a herbicide screening test, it appears unlikely that phytotoxicity should arise from direct overspray of pymetrozine or spray drift onto native plants, despite it being chemically related to triazine herbicides.

Conclusions

Environmental fate studies indicate that while initial degradation of pymetrozine occurs at a moderate to rapid rate in soil and sediment/water systems, degradation may then slow and some residues may persist, possibly due to reduced bioavailability of residues adsorbed to soil or sediment. Laboratory and field data generally indicate that pymetrozine is likely to have little movement through the soil profile, and field studies also show limited movement of metabolites, though laboratory adsorption/desorption studies had shown some metabolites to be potentially very mobile. Environmental toxicity data indicate that pymetrozine is not toxic or is only slightly toxic to a wide range of species, with a relatively specific toxicity profile to aphids and other plant sucking insects, but that it is highly toxic to the aquatic invertebrate *Daphnia magna* on prolonged exposure. However, pymetrozine is a low application rate and low frequency insecticide, and the only hazard emerging from assessments by Environment Australia was to daphnids in the event of direct overspray. 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 SAFETY ASSESSMENT

Justification for use

Chess 250 WP Insecticide contains 250g/kg of the new insecticide, pymetrozine.

Pymetrozine has low impact on benificial insects compared with some insecticides used for aphid control. Its use will be appropriate in IPM programs and will also be beneficial for use in resisitance management as it will redice selection pressure on the currently registered products.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Chess 250 WP Insecticide is proposed to be used to control cabbage aphid and green peach aphid on brassica vegetables(cauliflowers, cabbages, broccoli and Brussels sprouts) and the control of green peach aphid on potatoes. This use is proposed for all States and Territories, as specified in the directions for use on the product label (see pp 25-29).

I t is proposed the product will be available in 1kg (5x200g water soluble sachets) pack size. The application rate for the product is 400g/ha.

A 14 day withholding period for brassica vegetables has been recommended. No withholding period is recommended for potatoes when used as directed.

Evaluation of efficacy

The data presented supported the claims of control of cabbage aphid and green peach aphid on brassica vegetables (cauliflower, broccoli, Brussels sprouts, cabbage) and the control of green peach aphid on potatoes. The trial data were generally well presented in consistent format. Treatments were replicated adequately in randomised complete block designs with appropriate controls. The data analysis and interpretation was satisfactory.

Phytotoxicity

Chess 250 WP Insecticide produced no phytotoxic effects on brasssicas or potatoes in the trials reported.

Resistance management

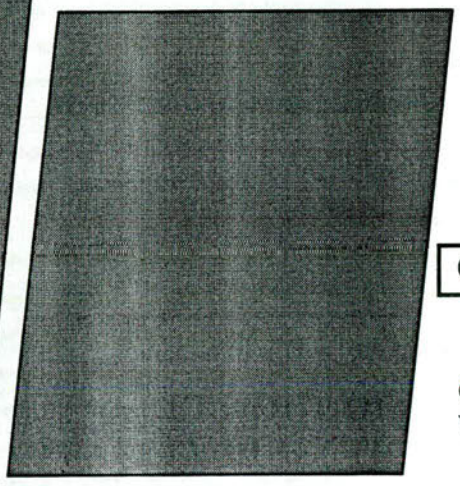
The label includes a resistance note (see pp 26) and in addition a maximum of 2 applications is recommended. There is a potential for development of resistance to pymetrozine if its use is not properly managed.

CAUTION

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

CHESS® 250 WP

INSECTICIDE



Active Constituent:
250 g/kg PYMETROZINE

GROUP 9 A INSECTICIDE

Controls Aphids in Brassica Vegetables and Potatoes

1 kg NET

Contains 5 x 200g water soluble measure packs which it is illegal to sell separately.

Novartis Crop Protection Australasia Pty. Ltd.
140-150 Bungaree Road, Pendle Hill NSW 2145
In a transport emergency dial 000, police or fire brigade.
For specialist advice in an emergency only, call 1800 033 111 (24 hours)

N1
UN No. Free

NRA approval No.: 50598/....

NOVARTIS

Batch No.	
Date of Manufacture	

DIRECTIONS FOR USE:

Restraints: DO NOT apply more than 2 applications per crop.
DO NOT apply consecutive applications
Refer to the AVCARE Resistance Management Guidelines

Crop	Pest	Rate g/ha	Critical comments
Brassica Vegetables (Broccoli, Brussel sprouts, Cabbage, Cauliflowers,	Green Peach aphid, Cabbage aphid,	400	Add a suitable wetting agent at recommended rates. Minimum retreatment interval 14 days
Potatoes	Green Peach aphid	400	Minimum retreatment interval 14 days

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

WITHHOLDING PERIOD:
***Brassica Vegetables*: DO NOT HARVEST FOR 14 DAYS AFTER APPLICATION.**

Potatoes: **NOT REQUIRED WHEN USED AS DIRECTED**

GENERAL INSTRUCTIONS

Mixing: Add the required amount of CHESS 250 WP to clean water in half filled spray tank with the agitator or by-pass in operation. Maintain agitation while filling tank with remainder of water. Agitation must also be maintained throughout the spray operation.

Application: To be effective CHESS 250 WP requires thorough spray coverage. Ensure that equipment is properly calibrated to give an even distribution at the correct volume.

Boomspray application in brassicas and potatoes: Apply as a spray in a minimum of 100 - 800 L of water/ha. The use of hollow cone nozzles and droppers are recommended.

Insecticide Resistance Warning **GROUP 9 A INSECTICIDE**

For insecticide resistance management CHESS 250 WP Insecticide is a Group 9A insecticide.

Some naturally occurring insect biotypes resistant to CHESS 250 WP Insecticide and other Group 9A insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if CHESS 250 WP Insecticide and other Group 9A insecticides are used repeatedly. The effectiveness of CHESS 250 WP Insecticide on resistant individuals could be significantly reduced. Since occurrence

of resistant individuals is difficult to detect prior to use, Novartis Crop Protection accepts no liability for any losses that may result from failure of CHESS 250 WP Insecticide to control resistant insects.

CHESS 250 WP Insecticide may be subject to specific resistance management strategies. For further information contact your supplier, Novartis Crop Protection representative or local agricultural department agronomist.

PRECAUTIONS

Re-entry Period: DO NOT enter treated area without protective clothing until spray has dried.

PROTECTION OF LIVESTOCK

Low hazard to bees.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

May be hazardous to aquatic invertebrates. DO NOT contaminate streams, rivers or waterways with the chemical or used container. DO NOT apply under meteorological conditions or from spraying equipment which could be expected to cause spray to drift onto adjacent areas, particularly wetlands, waterbodies or watercourses. DO NOT spray across open bodies of water.

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight. Shake empty container into spray tank. DO NOT dispose of undiluted chemicals on site. Puncture or shred and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS

Will irritate the eyes. Avoid contact with eyes and skin. When using the prepared spray wear:

- **cotton overalls buttoned to the neck and wrist (or equivalent clothing)**
- **a washable hat**
- **elbow length PVC gloves. Wash hands after use.**

After each day's use, wash gloves and contaminated clothing.

FIRST AID

If poisoning occurs contact a doctor or Poisons Information Centre. Phone 13 11 26

MATERIAL SAFETY DATA SHEET

If additional hazard information is required refer to the Material Safety Data Sheet. For a copy telephone 1800 025 931.

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY

Novartis has no control over storage, handling and manner of use of this product. Where this material is not stored, handled or used correctly and in accordance with directions, no express or implied representations or warranties concerning this product (other than non-excludable statutory warranties) will apply. Novartis accepts no liability for any loss or damage arising from incorrect storage, handling or use.

CAUTION

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

CHESS® 250 WP
INSECTICIDE

ACTIVE CONSTITUENT: 250 g/kg PYMETROZINE

NOT TO BE SOLD SEPARATELY

Before Use read all directions on the outer pack.

Water soluble packaging

Keep dry

NRA approval number: 50598/

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.