Public Release Summary
on

Evaluation of the new active
THIAMETHOXAM

in the product

CRUISER 350 FS INSECTICIDE SEED TREATMENT

National Registration Authority
for Agricultural and Veterinary Chemicals

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FOREWORD

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

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

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

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

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

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

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

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	acceptable daily intake (for humans)
ai	active ingredient
d	Day
DT_{50}	Time for 50% loss, half life
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
h	Hour
HPLC	high pressure liquid chromatography *or* high performance liquid chromatography
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
IOBC	International Organisation for Biological Control
kg	Kilogram
Koc	Adsorption coefficients based on organic carbon content
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOEC	lowest observed effect concentration
mg	Milligram
mL	Millilitre
MRL	maximum residue limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
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
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 considering an application to register the product Cruiser 350FS Insecticide Seed Treatment (Cruiser 350). This product contains the new active thiamethoxam. This product claims to control eastern false wireworm and southern false wireworm in sorghum, cotton, maize and sweet corn crops, striate or large false wireworm in maize and sweet corn, cotton seedling thrips, tomato thrips and cotton aphid on cotton, protection of sorghum, cotton, maize and sweet corn from damage by sugarcane (true) wireworm and protection of sorghum from damage by black field earwig.

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of thiamethoxam. Before deciding whether to approve this product for use in Australia, the NRA invites public comment. Comments should be submitted by 30 January 2000, to the NRA at the address indicated on page 1.

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

Public Health Aspects

Toxicology

Thiamethoxam, an insecticide intended for the control of insect pests that attack cotton, sorghum, maize and sweetcorn during early crop establishment, is excreted mainly in an unchanged form when fed to rats in their diet. Thiamethoxam has low acute oral, dermal and inhalational toxicity. It is not a skin or eye irritant and is not allergic to skin. Formulations containing thiamethoxam such as Cruiser 350 FS Insecticide Seed Treatment also have low oral, dermal and inhalation toxicity. Cruiser 350 FS Insecticide Seed Treatment is a slight skin irritant and skin sensitiser but is not an eye irritant.

In repeat-dose feeding studies in mice, rats and dogs bodyweight gains were generally lower and the target organs associated with toxicity were the liver and kidney. Changes in the liver included an increased weight and size due to the presence of masses and nodules, some pigmentation, death of some individual liver cells and the presence of scavaging cells to remove the dead cells. In the kidneys there was damage to the process involved in urine production. In dogs there was also an indication of changes within the reproductive organs.

Special studies gave no indication that thiomethoxam causes any damage to genetic material and life-time exposure studies in mice and rats revealed that there was a slight elevation in the incidence of liver cancer in mice but this only occurred at high concentrations which also caused marked toxicity. Thiomethoxam did not have any effect on the reproductive performance of rats in a two-generation study and effects on fetal development were only seen at doses that caused toxicity to the maternal animals. In studies intended to determine changes in behaviour, effects were seen only at high doses which caused toxicity.

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 Chemistry and Residues Evaluation Section of the NRA has undertaken a residues assessment of a formulated product based on the new active constituent thiamethoxam. Cruiser 350 FS Insecticide Seed Treatment is a suspension concentrate containing thiamethoxam as the active ingredient. Data concerning thiamethoxam residues in cotton, maize and sweetcorn and sorghum, metabolism in crops and animals, environmental fate and chemistry were considered as part of the residue evaluation of the application.

The following new Maximum Residue Limits are proposed for thiamethoxam:

TABLE 1

Thiamethoxam

SO 0691	Cotton seed	*0.02
VO 0447	Sweetcorn	*0.02
GC 0645	Maize	*0.02
GC 0651	Sorghum	*0.02

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

Based on this assessment, risk on these aspects is considered low and acceptable.

Occupational health and safety aspects

NOHSC has conducted a risk assessment on Cruiser 350 FS Insecticide Seed Treatment (Cruiser 350) containing thiamethoxam at 350 g/L. Cruiser 350 can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Cruiser 350 will be imported fully formulated and packaged in plastic containers.

Cruiser 350 is a suspension concentrate formulation. The product has a low acute oral and low dermal toxicity. The product is not an eye irritant but a slight skin irritant. Cruiser 350 is a weak skin sensitiser.

The product will be used as a seed treatment in the control of insect pests that attack cotton, sorghum, maize and sweet corn during early crop establishment. It is expected that Cruiser 350 will be used by commercial seed treaters and small operators such as farmers.

Worker exposure data were not available for thiamethoxam or Cruiser 350.

Instructions and Safety Directions are provided on the product label to minimise exposure to the product. Based on the risk assessment, elbow length PVC gloves and cotton overalls are

recommended for users of Cruiser 350. A re-handling statement is not recommended for treated seed.

Environmental aspects

Thiamethoxam is to be used to treat sorghum, cotton, maize and sweetcorn seeds before sowing to control early season sucking and chewing pests. Residues are expected to be associated mainly with the treated seeds and surrounding soil. Contamination of water bodies via spray drift is not expected. Hydrolysis is a possible degradation route in alkaline media (pH 9) and thiamethoxam is expected to be readily to fairly readily degraded by aqueous photolysis although turbidity often present in Australian waters is likely to slow down this degradation route. Photolysis of soil adsorbed thiamethoxam is not expected to be a significant route of degradation. Measured DT_{50} values of thiamethoxam in aerobic soils in the laboratory were in the order of 300 days. However, under field conditions, the half-lives were ca. 7 to 109 days with evidence of steady degradation of thiamethoxam taking place. While thiamethoxam has high potential soil mobility, it did not show any significant leaching in soil. Additionally there were no mobile degradation products seen in any significant quantity in a lysimeter study. In soil/water systems, thiamethoxam moves readily to the sediment phase where degradation continues. Overall, accumulation in soils and water is not expected to be a major concern. Thiamethoxam is not expected to bioaccumulate on the grounds of its ready water solubility, ready movement from the water to sediment phase and its subsequent degradation and eventual mineralisation.

Thiamethoxam is slightly toxic to birds by acute oral exposure and practically non-toxic to birds by sub-acute dietary studies. Acute exposure of fish to thiamethoxam and as formulated product and also to the metabolite CGA 322704 was at worst slightly toxic with no mortalities recorded. The principal aquatic sediment metabolite, NOA 407475, was practically non-toxic to fish. Chronic exposure of fish to thiamethoxam over a 28 day period was very slightly toxic to the fish. No mortalities were seen over the test period. Chronic exposure of Rainbow trout embryos to thiamethoxam for a 28 day hatch period and a 60 day post-hatch period was slightly toxic to the embryos and fry.

Acute exposure of *Daphnia magna* to thiamethoxam, formulated products containing thiamethoxam and the metabolite CGA 322704 was at worst slightly toxic to the exposed organisms while chronic exposure to thiamethoxam was slightly toxic. Acute exposure to the metabolite NOA 407475 was of slight toxicity to the daphnia while exposure of sediment dwelling *Chironomus riparius* to the same metabolite was at worst slightly toxic. While exposure of oysters to thiamethoxam was at worst practically non-toxic with respect to survival and shell growth under acute conditions, the exposure was moderately toxic to the mysid shrimp. Acute exposure of the green alga, *Selenastrum capricornutum* to thiamethoxam or formulated product or as the metabolite CGA 322704 was, at worst, slightly toxic to the alga as was exposure of *Scenedesmus subspicatus* to the metabolite NOA 407475. Thiamethoxam was at worst slightly toxic to duckweed (*Lemna gibba*).

Laboratory and field studies indicate that thiamethoxam is highly-toxic to honey bees (*Apis mellifera*) by either contact or ingestion. Semi-field studies where bees were exposed to plants grown from thiamethoxam treated seeds showed no effect on parameters such as mortality, foraging activity, flight intensities or behaviour. While some decline in hive quality was observed, it was not possible to say this had been caused by the exposure to crops grown from the treated seeds.

Similarly, predatory bugs and parasitic wasps were harmed by exposure to thiamethoxam applied as a spray. Ground dwelling beetles exposed to treated seeds were adversely affected.

Laboratory earthworm tests with *Eisenia foetida* indicated that thiamethoxam was practically non-toxic over a 14 day exposure period at a concentration of 1000 $mg.kg^{-1}$ dry soil although there were significant differences in burrowing times and weight losses in the exposed worms. Exposure of worms to thiamethoxam containing formulations gave no indications of toxicity or adverse effects. A study of the effect of thiamethoxam on soil microflora indicates that it should not have long term effects on the microbial respiration or nitrogen metabolism.

Environmental hazard

The hazard assessment conducted by Environment Australia indicates that thiamethoxam will not result in unacceptable adverse effects of birds and mammals provided the treated seed is effectively planted and covered and that spills are immediately cleaned up. Consequently, it is unlikely that the proposed use of the Cruiser formulations is a hazard to birds or mammals. A 10% runoff produces levels of contamination indicated as without adverse effect on aquatic organisms.

Thiamethoxam is highly toxic to honeybees by oral or contact exposure but there was no apparent effect on bees gathering pollen and nectar from plants grown from seeds dressed with thiamethoxam with an observed decline in hive quality not conclusively linked with the seed treatment. Thiamethoxam is hazardous to predatory bugs and parasitic wasps when exposure occurs by spray application. Ground dwelling beneficials which come in contact with treated seeds or soil containing thiamethoxam can be expected to suffer some mortality but numbers will be limited in areas sown. Significant effects on earthworms exposed to thiamethoxam in the soil are not expected.

Thiamethoxam is a “probable leacher” or "tentative leacher" with very high mobility based on laboratory adsorption/desorption studies. However, a lysimeter study and soil dissipation studies show that there is little likelihood of significant movement of thiamethoxam through the soil. Consequently, there is also low likelihood of any significant transfer to aquatic environments from the proposed use as a seed dressing.

Efficacy and crop safety aspects

Thiamethoxam is a new nitromethylene derived compound with contact, stomach and systemic activity and acts on the nervous system of the insect. The compound mimics acetylcholine and binds to the acetylcholine receptor site, which damages the target insect’s nervous system causing death. Other nitromethylene class compounds are used for soil insect control, however, this compound falls into a different subclass.

The data presented supported the claim for control of eastern false wireworm and southern false wireworm in sorghum, cotton, maize and sweet corn crops, striate or large false wireworm in maize and sweet corn, and cotton seedling thrips, tomato thrips and cotton aphid on cotton. A claim of protection of sorghum, cotton, maize and sweet corn from damage by sugarcane (true) wireworm and protection of sorghum from damage by black field earwig was also supported. The design,

analysis and conduct of the efficacy trials were adequate. Crop safety aspects were evaluated and are considered acceptable.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical thiamethoxam (Cruiser 350FS Insecticide Seed Treatment) as a seed treatment to control eastern false wireworm and southern false wireworm in sorghum, cotton, maize and sweet corn crops, striate or large false wireworm in maize and sweet corn, cotton seedling thrips, tomato thrips and cotton aphid on cotton, and for the protection of sorghum, cotton, maize and sweet corn from damage by sugarcane (true) wireworm and protection of sorghum from damage by black field earwig.

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 thiamethoxam, 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 30 January 2001. They should be addressed to :

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Product Evaluator
Agricultural Chemicals Evaluation Section
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Applicant

Novartis Crop Protection Australasia Limited

Product details

Thiamethoxam will be marketed under the trade name Cruiser (containing 350g/L thiamethoxam) as a suspension concentrate formulation.

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

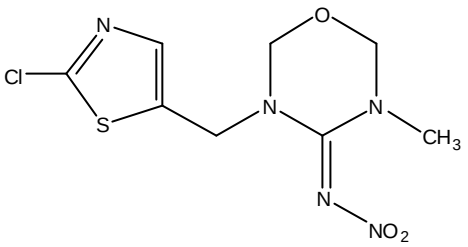
Novartis Crop Protection Australasia Limited intend to market Cruiser in all States and Territories.

CHEMISTRY AND MANUFACTURE

The active constituent thiamethoxam is manufactured in the USA by Novartis Crop Protection Inc at St Gabriel Plant, 3905 Highway 75, Louisiana 70776-0011.

Chemical Characteristics of the Active Constituent

Common name (ISO): thiamethoxam
Synonyms and code number: CGA 293343
Chemical name: (IUPAC): 3-(2-chloro-thiazol-5-ylmethyl)-5-methyl-[1,3,5]oxadiazinan-4-ylidene-N-nitroamine
(CA): 3-[(2-chloro-5-thiazolyl)methyl]tetrahydro-5-methyl-N-nitro-4H-1,3,5-oxadiazin-4-imine
Chemical Abstracts Service (CAS) Registry Number: 153719-23-4
Molecular formula: $C_8H_{10}ClN_5O_3S$
Molecular weight: 291.7
Chemical structure:



Physical and Chemical Properties of Pure Active Constituent

Physical state: fine crystalline powder
Colour: slightly cream
Odour: odourless
Melting point: 139.1 °C
Density at 20 °C: 1.57 g/cm^3
Solubility in water: 4.1 g/L at 25 °C
Solubility in various organic solvents at 25 °C:

acetone	48 g/L
dichloromethane	110 g/L
ethyl acetate	7 g/L
hexane	<1 mg/L
methanol	13 g/L
octanol	620 mg/L
toluene	680 mg/L

Vapour pressure: 2.7×10^{-9} Pa at 20°C, 6.6×10^{-9} Pa at 25°C
Dissociation constant: no dissociation within the range pH 2 to pH 12
Octanol/water Partition Coefficient: P_{ow} = 0.73±0.0029 at 25°C, log P_{ow} = -0.13±0.017 at 25 °C
pH of 1% aqueous solution of technical grade material: 4.8 at 25 °C
Storage stability: stable for at least 12 months storage at 30°C

Corrosion characteristics: non-corrosive toward galvanised sheet metal, stainless steel DIN 1.4541 and polyethylene. Slightly corrosive toward iron steel ST 37 and tin plate.
Pesticide type: insecticide
Chemical family: nitroguanidine

PRODUCT
Distinguishing name or trade name: Cruiser 350 FS Insecticide Seed Treatment
Formulation type: suspension concentrate for seed treatment
Active constituent concentration: 350 g/L
Mode of Action: Thiamethoxam acts on the nicotinic acetylcholine receptor of insects where it mimics the messenger chemical acetylcholine and binds to the receptor site, irreparably damaging the insects nervous system and eventually leading to insect death.

Physical and Chemical Properties of the product

Physical state: liquid
Colour: red
Odour: like chalk, weakly sweetish
Specific gravity: 1.15-1.19 g/cm^3 at 20 °C
pH value for a 1% in deionised water: 6.8
Viscosity:

Shear rate (s^{-1})	Viscosity at 20°C (mPa.s)	Viscosity at 40°C (mPa.s)
5	525	452
250	51.9	38.3

Surface tension:
Supernatants of 1.0 g/L suspension 44.0-44.6 mN/m (time independent)
Supernatants of 150 g/L suspension 37.5-38.0 mN/m (time independent)
Supernatants of 750 g/L suspension 29.0-35.3 mN/m (after 20 min)
Storage Stability: The applicant provided data to show that the formulation is stable on storage at 30°C for at least 18 weeks and at 54 °C for at least 2 weeks.
Flash point: negative to 100 °C
Flammability: auto-ignition at 410 °C
Explodability: not explosive
Corrosion Characteristics: not corrosive to stainless steel DIN 1.4541, tin plate or polyethylene, slightly corrosive to galvanised sheet metal, corrosive to iron steel ST 37 (weight loss 0.05 g/m^2.h)

The active constituent to be used in the product has been approved by the NRA (Approval number: 51873).

Review of the product chemistry data has been completed. The available data supports the registration of Cruiser 350 FS Insecticide Seed Treatment for the proposed use.

TOXICOLOGICAL ASSESSMENT

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

Metabolism and Toxicokinetics

Orally administered thiamethoxam was well absorbed and rapidly excreted in the urine in rats and mice. It was widely distributed and there was no evidence of bioaccumulation. Absorption after dermal exposure was low in rats (<3% in 48 h). Toxicokinetics and metabolism studies revealed species differences in the metabolism and excretion of thiamethoxam although the major metabolic pathways (demethylation and cleavage of the oxadiazine ring) were essentially the same. Whereas about 30-60% of orally administered thiamethoxam was excreted metabolised in mouse excreta it was only between 20-30% in rats. About 19% of the total administered radioactivity was found in mouse faeces but only 5% of the dose was recovered in the faeces of rats.

Acute Studies

Thiamethoxam was of low acute oral toxicity in rats (LD_{50} = 1563 mg/kg bw) and mice (LD_{50} = 783 mg/kg bw in males and 964 mg/kg bw in females). It was of low dermal (LD_{50} >2000 mg/kg bw) and inhalational (LC_{50} >3720 mg/m^3) toxicity in rats. The compound was not a skin or eye irritant and was not allergic to skin.

Cruiser 350 FS Insecticide Seed Treatment (containing 350 g/L thiamethoxam) showed low acute oral (LD_{50} >3000 mg/kg bw) and dermal (LD_{50} >4000 mg/kg bw) toxicity in rats. It was a slight skin irritant in rabbits and was slightly allergic to skin in guinea pigs but was not an eye irritant in rabbits.

Short-Term Studies

In 28-day feeding studies in rats and dogs, toxic signs were seen at concentrations of 43 mg/kg bw/day and above. The effects included lower body weights and food consumption; and changes in the liver and thyroid (increased size of the cells: hypertrophy); fatty changes in adrenal cortex (rats); and higher weights of testes (dogs).

In 3-month dietary toxicity studies in mice, rats and dogs, the animals were treated with thiamethoxam at 0, 10, 100, 1250, 3500 or 7000 parts per million (ppm) in mice; 0, 25, 250, 1250, 2500 or 5000 ppm in rats and 0, 50, 250, 1000 or 2500/2000 ppm in dogs. Lower weight gains (with or without lower food consumption) were seen at concentrations at or above 1250 ppm. Higher liver weights and lower ovary weights in mice at or above 3500 ppm, and reduced testis and ovary weights (with histopathology indicative of delayed maturation) in dogs at 1000 ppm. Mice were found to be anaemic at 7000 ppm. In mice and rats, histological changes were seen in the liver which included increased cell size (hypertrophy); lymphocyte infiltration; liver cell death (necrosis) or pigmentation at or above 100 ppm in male mice, at or above 2500 ppm in female mice and in rats. In male rats at 250 ppm and above, hyaline change (glassy appearance) of kidney cells (renal tubular epithelium) was associated with acute or chronic tubular lesions. Atrophy of ovaries in mice, changes in spleen (haemosiderosis: accumulation of haemosiderin, an iron containing protein) and adrenal gland (fatty change) in rats were seen at or above 1250 ppm. The NOELs were 10 ppm in mice, 25 ppm in rats and 250 ppm in dogs. Based on the food consumed these concentrations of thiamethoxam were equal to doses of 1.4, 1.7 and 8.2 mg/kg bw/day in mice, rats and dogs respectively.

Chronic Studies

In long-term studies mice (18 months), rats (24 months) and dogs (12 months) were treated daily with thiamethoxam in the feed at 0, 5, 20, 500, 1250 or 2500 ppm in mice; 0, 10, 30, 500 or 1500 ppm in rats and 0, 25, 150, 750 or 1500 ppm in dogs. In these animals, body weight gains were lower at or above 1500 ppm. Water consumption was higher in male rats at 1500 ppm. In mice, increased liver weights in females at or above 500 ppm and in males at 1250 and 2500 ppm were seen. Lower kidney weights in males and spleen weights in females were seen at or above 1250 ppm in mice. In dogs, heart weights were higher and testes weights were lower at 1500 ppm. In mice, the incidence of liver tumours (adenoma and adenocarcinoma) were increased at 500 ppm and above. However, in rats and dogs, thiamethoxam did not induce cancer. In mice, histological changes in liver such as hypertrophy of liver cells, inflammatory cell infiltration and single cell necrosis; pigment deposition; and increased cell division (mitotic activity); changes in stomach epithelium (hyperplasia: increased number of cells) and extracellular haematopoiesis (formation of blood cells) in spleen were seen at or above 500 ppm. In rats, histological changes were seen in kidneys (lymphocytic infiltration; lesions or damage of kidney cells viz. chronic nephropathy and chronic tubular lesions) at or above 1500 ppm. Incidence of hydrocephalus of brain (accumulation of fluid) was higher in male rats at 1500 ppm. In dogs, atrophy of testes and cellular debris in the epididymides were seen at 750 and 1500 ppm. The NOELs were 20 ppm in mice (2.6 mg/kg bw/day); 500 ppm in rats (21 mg/kg bw/day) and 150 ppm in dogs (4.1 mg/kg bw/day).

Reproduction Studies

To investigate possible changes in reproductive performance attributable to thiamethoxam, a two-generation reproduction study in rats was perfomed. Although rats were fed thiamethoxam at 0, 10, 30, 1000 or 2500 ppm in their diet, bodyweight gains were only lower in F0 generation males at 2500 ppm. In the dams of the first generation (F1), food consumption was higher at 2500 ppm during pregnancy. In the treated adult male groups (F0 and F1 generations), sperm motility was lower though no dose-related effect was apparent. Body weight gains were lower at 2500 ppm in the pups of the two generations at or above 1000 ppm. In the adult males (F0 and F1 generations), histological changes in kidneys (hyaline changes or renal tubular cast) were seen at 1000 and/or 2500 ppm. Based on reduced bodyweight gain observed in weaned pups at 1000 ppm, the NOEL for the study was 30 ppm (2 mg/kg bw/day).

In a separate study to assess effects on sperm, thiamethoxam was administered to male rats in the diet at 0, 10, 30, 1000 or 2500 ppm (ie. 0.6, 2.0, 65 and 165 mg/kg bw/day) for 10 weeks. Although bodyweight gain was significantly lower at 2500 ppm, there were no dose-dependent effect on the number of spermatids, sperm motility or morphology.

Developmental Studies

Studies designed to determine the effects of orally administered thiamethoxam on fetal organ development were performed in mated rats and rabbits. The animals were treated during the period of organ development (pregnancy days 6-15 in rats and 7-19 in rabbits) at doses of 0, 5, 30, 200 and 750 mg/kg bw/day in rats and 0, 5, 15, 50 and 150 mg/kg bw/day in rabbits. In the 750 mg/kg bw/day group in rats, one dam was killed on day 9 due to marked weight loss. A dose dependent reduction in body weight as a consequence of reduced food consumption occurred in the 200 mg/kg bw/day group rats. In rabbits at 150 mg/kg bw/day maternal toxicity was severe, resulting in a bloody discharge in the perineal area or from the vagina (15/24 dams). Three of these dams were found dead or killed in moribund condition. At necropsy, haemorrhagic contents were noticed in the uteri of these three dams. A slight reduction in body weight gain occurred in the 50 mg/kg bw/day group. Food consumption was dose-dependently reduced during treatment in the 50 and 150 mg/kg bw/day groups. Fetal weights were lower in the 750 mg/kg/day group rats and 150 mg/kg bw/day group rabbits. Post-implantation losses resulted from total resorptions in 3 rabbits given 150 mg/kg bw/day. An increased incidence of skeletal anomalies was seen in the 750 mg/kg bw/day group rats but were considered to represent a treatment-related delay of fetal development resulting from, or secondary to, significant maternal toxicity. The NOEL in rats was 30 mg/kg bw/day for dams and 200 mg/kg bw/day for fetuses. In the rabbits, the NOELs were 15 mg/kg bw/day of for dams and 50 mg/kg bw/day for fetuses.

Genotoxicity Studies

Genotoxicity was not evident in a range of assays. The test systems included strains of *Salmonella typhimurium* and *Escherichia coli*; cultured Chinese hamster cells (V79); *in vitro* chromosome aberration assay in Chinese hamster ovary cells and mouse bone marrow; and DNA repair activity in rat liver cells.

Other studies

Thiamethoxam increased the activities of several liver enzymes in a 14-day oral study in mice at or above 74 mg/kg bw/day. Liver cell proliferation was higher in mice at 2500 ppm (386/463 mg/kg bw/day; 3-59 days) but not in rats (711 mg/kg bw/day). In cultured mouse and rat liver cells, thiamethoxam or a structurally-related chemical, imidacloprid did not produce any morphological changes or release of lactate dehydrogenase, suggesting the absence of a cytotoxic effect. In acute and repeat-dose neurotoxicity studies in rats, neurobehavioural effects were seen only at doses in excess of 500 mg/kg bw in the acute study. In acute oral toxicity studies in rats, the metabolites of thiamethoxam had low toxicity.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the products and its active ingredient and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning. The NDPSC recommended that thiamethoxam be listed in Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). Preparations containing 60% or less of thiamethoxam are listed in Schedule 5. Cruiser 350 FS Insecticide Seed treatment is therefore in Schedule 5. There are provisions for appropriate first-aid instructions and safety directions on the product label.

NOEL/ADI

The acceptable daily intake (ADI) for thiamethoxam is 0.02 mg/kg bw/day based on a NOEL of 2 mg/kg bw/day in a two-generation reproduction study in rats and a safety factor of 100. The safety factor was selected based on the presence of an adequate toxicology database.

RESIDUES ASSESSMENT

The Chemistry and Residues Evaluation Section of the NRA has undertaken a residues assessment of a formulated product based on the new active constituent thiamethoxam. Cruiser 350 FS Insecticide Seed Treatment is a suspension concentrate containing 350 g/L thiamethoxam as the active ingredient. Data concerning thiamethoxam residues in cotton, maize and sweetcorn and sorghum, metabolism in crops and animals, environmental fate and chemistry were considered as part of the residue evaluation of the application.

Metabolism

The metabolism and distribution of thiamethoxam was studied in corn and rice from seed treatment and in the rotational crops lettuce, radish and wheat following bareground application. When applied as a seed treatment to corn and rice, radioactive residues declined with plant growth and minimal residues were detected in mature plants or seeds. The major residue components in the crops were parent thiamethoxam, and several metabolites produced from removal of the nitro group and opening of the oxadiazine ring. Prior to plant maturity, parent compound is the major residue component, with most of the radioactive residues located in the foliage. The majority of radioactive residues in grain were non-extractable, and comprised plant components including starch, proteins and other carbohydrates. Similar metabolite patterns were observed when thiamethoxam was applied to rotational crops as a bareground application.

The animal metabolism of thiamethoxam was studied in rats, goats and laying hens. Goats and hens were administered orally ^{14}C-thiamethoxam at the nominal dose rate of 100 ppm in the feed. Urine and faeces, and milk or eggs were collected throughout the trial, and tissues were collected at sacrifice. Samples were extracted then analysed for radioactive residues using HPLC. In rats greater than 80% of orally administered radioactivity was eliminated in urine, with about 5% eliminated in faeces, within 24 hours.

Excretion of radioactivity following oral administration of thiamethoxam was less in goats than in rats. Approximately 9% of the dose was eliminated in faeces and 45% in urine within 78 hours of dosing. Less than 1.3% of the dose was eliminated in milk up to 78 hours after dosing. Between 80-90% of the administered radioactivity was recovered. Highest residues were found in liver and kidney. Parent compound was the major residue in fat, milk and kidney, while the major residues in liver were metabolites derived from cleavage of the N-NO_2 bond and opening of the oxadiazine ring.

In hens, tissues contained a lower proportion of parent compound residues than in the goat and rat studies, and the metabolite I15, derived from oxadiazine ring opening, was the major residue. Transfer of the dose into eggs was minimal even at the highest dose level.

Analytical methods

A validated analytical method was provided for the determination of thiamethoxam and metabolite CGA 322704 in plant and soil material. The method involves extraction of residues with a mixture of methanol and water. The extract is filtered and diluted with water, then cleaned up on a phenyl solid phase cartridge and a ENVI-Carb graphiticised non-porous carbon cartridge (plant material only). The organic solvent part is evaporated, the remaining solution is diluted with water and analytes determined on a two column reverse phase HPLC system with UV detection at 255 nm for parent thiamethoxam and 270 nm for metabolite CGA 322704. The limit of quantitation for both parent and metabolite is 0.02 mg/kg for edible and 0.05 mg/kg for non-edible plant material.

Storage stability

Storage stability data for thiamethoxam residues in rice and corn were presented in the application. Residues were found to be stable in rice samples for up to 5 months, and for up to 9 months in corn samples, when stored below –18°C.

Residue definition

Parent compound is a major residue component in both plant and animal commodities. The analytical method provided is capable of determining thiamethoxam and the metabolite CGA 322704 [N-(2-chloro-thiazol-5-ylmethyl)-N'-methyl-N"-nitroguanidine] in plant commodities. It is therefore appropriate to set the definition of the thiamethoxam residue as parent compound.

Residue trials

Australian and overseas residue trials were provided for cotton, sweetcorn and maize and sorghum. The trials used various application rates, and residues in sweetcorn, maize and sorghum grain and cottonseed were determined. In addition, residues in the animal feed commodities were determined for cotton trash and hulls, sweetcorn and maize forage and fodder, and sorghum straw and fodder.

Cotton:

Australian and overseas residue trials were presented. In the Australian trial, thiamethoxam was applied to cottonseeds at a rate of 0.63, 1.25 and 2.5x the maximum Australian rate (280 g ai/100 kg seed). Crops were harvested at maturity, and plants were separated into seed and trash, after ginning. Residues were reported as <0.02 mg/kg in cottonseed and <0.3 mg/kg in trash (dry weight) at all application rates. In overseas trials, residues in cottonseed treated at 1.1x the maximum label rate were reported at <0.02 mg/kg in de-hulled seed and <0.05 mg/kg in hulls. In a Spanish trial, cottonseed was treated with thiamethoxam at 1.1x the label rate, then 4 months after seeding the plants were sprayed with three foliar applications of thiamethoxam at about 50 g ai/ha. Plants were harvested 28 days after the last application. De-hulled cottonseed contained residues <0.02 mg/kg, while the hulls contained residues <0.05 mg/kg at harvest.

Taken as a whole, the residue data support the applicant's proposed MRL of *0.02 mg/kg for thiamethoxam in cottonseed. An MRL of 0.5 mg/kg for thiamethoxam residues in cotton, hulls and trash (dry) is also recommended. No harvest WHP is considered necessary when the products are used as directed.

Sweetcorn and maize:

Australian and overseas residue trials were presented. In the Australian trial, corn and maize seeds were treated with thiamethoxam at 1.5 and 3x the Australian label rate (ca. 0.5 g ai/1000 seeds). Plants were sampled at 4, 6, 8 and 9 weeks after planting and at maturity, and the foliage (forage), straw and seeds were analysed for parent residues. Thiamethoxam residues were reported at 0.60 and 1.40 mg/kg in foliage 4 weeks after planting in the 1.5x and 3x treatment groups, respectively, in one location. Residues in forage sampled 6, 8 and 9 weeks after planting were reported as below the limit of quantitation in all trials and at all application rates. On a dry weight basis, residues in forage were <0.44 mg/kg at 6, 8 and 9 weeks after planting. Residues in grain and straw (dry weight) at harvest were reported as <0.02 and <0.21 mg/kg, respectively.

In overseas trials, thiamethoxam residues in whole plants taken 28 days after seed application were up to 0.08 mg/kg when treated at up to 2x the Australian label rate. No residues of the metabolite I16 were detected in any samples. No thiamethoxam residues were detected in forage, cobs or grain sampled more than 28 days after planting, except for one apparently anomalous maize grain sample, which contained residues at 0.04 mg/kg. The applicant has proposed a 6 week grazing restraint for the use of Cruiser Insecticide. Residues are not expected to be present in treated produce 6 weeks after application of Cruiser Insecticide.

Overall, when treated at 1-1.5x the maximum label rate, residues in sweetcorn were <0.02 mg/kg and <0.04 mg/kg in maize grain (STMR <0.02 mg/kg) at maturity. Residues were present at <0.44 mg/kg in corn and maize forage (dry weight) harvested 6 weeks after treatment, and <0.20 mg/kg in corn and maize straw (dry) at harvest. The data support an MRL of *0.02 mg/kg for thiamethoxam in sweetcorn and maize grain, and an MRL of 0.5 mg/kg for maize fodder (dry) and maize forage (dry). A harvest WHP of 6 weeks applies to the use of Cruiser on sweetcorn and maize.

Sorghum:

One Australian trial was provided for sorghum. Sorghum grain was treated with thiamethoxam at 1x and 2x the label rate. Foliage was sampled at 4, 6 and 8 weeks after planting, and straw and grain were sampled at harvest at plant maturity. Residues were detected in foliage sampled 4 and 6 weeks after planting in one trial location. Six weeks after planting, residues were present at up to 0.31 mg/kg on a dry weight basis. Residues in straw (dry) were <0.06 mg/kg, and <0.02 mg/kg in grain at harvest. The applicant has proposed an 8 week grazing restraint for the use of Cruiser on sorghum. No residues above 0.20 mg/kg were found in forage harvested more than 8 weeks after planting. Overall, the data support an MRL of *0.02 mg/kg for thiamethoxam in sorghum grain, and 0.5 mg/kg for sorghum straw and fodder (dry).

It should be noted that the MRLs set for animal feed commodities from the above residue trials were determined from fresh weight samples. Results from these samples were corrected for moisture content and expressed on a dry weight basis, then rounded up. Residues in the animal feed commodities were below the limit of quantitation in almost all samples and therefore do not represent finite residues in the treated produce.

Animal transfer studies and MRLs

No animal transfer studies were provided for thiamethoxam. Metabolism studies in animals demonstrated that parent thiamethoxam was a major residue in all tissues, with the exception of liver. A dose level of 100 ppm in the feed was used in these studies. For animal feed commodities, an MRL of 0.5 mg/kg is recommended for dry straw, forage, fodder and trash of maize, sweetcorn, sorghum and cotton. If we assume that treated produce contains residues at the MRL of 0.5 mg/kg and comprises 100% of the animal diet, then scaling the residue results from the metabolism study (goats) gives an estimate of the likely residues in tissues from normal feeding of treated produce.

By these calculations, no individual residue in muscle, fat, liver, kidney or milk will be higher than 0.008 mg/kg. Parent compound is estimated in muscle, fat, kidney and milk at 0.0006, 0.0014, 0.008 and 0.002 mg/kg, respectively. These values are considered to be an overestimate of residues in tissues from consumption of treated produce. Residue trials provided for various crops demonstrated that thiamethoxam residues will be present below the analytical limit of quantitation in crop parts after the appropriate grazing / stock food restraints of 6 and 8 weeks for maize/corn and sorghum, respectively. The estimates of residues in tissue and milk are therefore considered to be conservative and much higher than would be expected from normal consumption of treated produce.

No residue analytical method was provided for routine determination of thiamethoxam residues in animal commodities. Since non-detectable residues are expected in animal commodities, and no analytical method was provided, no animal commodity MRLs will be set in this instance. By omission of MRLs, residues in animal commodities must be non-detectable.

Processing

No data were provided for processed commodities. Since no residues were found in cottonseed, and thiamethoxam has a low fat solubility (log Pow = -0.13), thiamethoxam is not expected to concentrate in cottonseed oil. In the absence of data, no MRL for cottonseed oil will be set in this instance, and residues in cottonseed oil will refer to the whole un-processed commodity.

Sweetcorn may be processed by canning the kernels or snap freezing the kernels or cobs, and no concentration of residues in expected from these operations. Other animal feed commodities are not processed prior to consumption.

Estimated dietary intakes

The risk to human health from the use of thiamethoxam is considered to be low. The chronic dietary risk is estimated at 0.01% of the Acceptable Daily Intake (ADI) for thiamethoxam using the National Estimate of Dietary Intake (NEDI) calculation. The mean consumption of the relevant commodities for consumers aged 2 years and above, taken from the 1995 ANZFA National Nutrition Survey, were used in the calculation. As it is widely recognised that this calculation is a gross estimate of actual dietary intake, it is concluded that the chronic dietary exposure to thiamethoxam is small and the risk is acceptable.

Bioaccumulation potential

The log Pow value for thiamethoxam of –0.13 indicates that thiamethoxam is not fat soluble and residues will not accumulate in fat or tissues.

Recommendations

1. There are no objections, from a residues perspective, to the registration of Cruiser 350 FS Insecticide Seed Treatment containing the new active thiamethoxam for use on cotton, maize and sweetcorn and sorghum.
2. The following amendments to the *MRL Standard* are recommended:

Table 1

Compound	Food		MRL (mg/kg)
DELETE:			
3-(2-chloro-thiazol-5-ylmethyl)-5-methyl-[1,3,5]oxadiazin-4-ylidene-N-nitroamine			
	SO 0691	Cotton seed	T0.05
	OC 0691	Cotton seed oil	T0.05
	GC 0645	Maize	T0.05
	GC 0651	Sorghum	T0.05
	VO 0447	Sweetcorn	T0.05
ADD:			
Thiamethoxam			
	SO 0691	Cotton seed	*0.02
	VO 0447	Sweetcorn	*0.02
	GC 0645	Maize	*0.02
	GC 0651	Sorghum	*0.02

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

Table 3

Compound	Residue
DELETE:	
3-(2-chloro-thiazol-5-ylmethyl)-5-methyl-[1,3,5]oxadiazin-4-ylidene-N-nitroamine	3-(2-chloro-thiazol-5-ylmethyl)-5-methyl-[1,3,5]oxadiazin-4-ylidene-N-nitroamine
ADD:	
Thiamethoxam	Thiamethoxam

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
DELETE:			
3-(2-chloro-thiazol-5-ylmethyl)-5-methyl-[1,3,5]oxadiazin-4-ylidene-N-nitroamine			
	AM 0691	Cotton fodder, dry	T0.05
		Cotton seed meal, hulls and trash	T0.05
	AS 0645	Maize fodder	T0.05
	AF 0645	Maize forage	T0.05
	AF 0651	Sorghum forage	T0.05
	AS 0651	Sorghum straw and fodder, dry	T0.05
ADD:			
Thiamethoxam			
	AF 0645	Maize forage	0.5
	AS 0645	Maize fodder	0.5
	AS 0651	Sorghum straw and fodder, dry	0.1
	AF 0651	Sorghum forage (green)	0.5
		Cotton, hulls and trash (dry)	0.5

The following WHPs are recommended in relation to the above MRLs for Cruiser Insecticide:
Cotton
(Harvest) – NOT REQUIRED WHEN USED AS DIRECTED.
(Grazing) – DO NOT GRAZE OR FEED COTTON TRASH TO STOCK.
Sorghum
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 8 WEEKS AFTER PLANTING
Maize, Sweetcorn
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER PLANTING

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Trade Implications

Commodities Exported

Export statistics for 1997/8 were obtained from 1999 Australian Commodity Statistics (ABARE). These figures are tabulated below:

Commodity	Total Australian Production (tonnes)	Total Export (tonnes)
Sweetcorn	64,786	1,495
Sorghum	1,081,000	251,000
Cottonseed	941,300	296,060
Maize	271,000	19,000

Countries Where Exported

Major export markets for Australian sweetcorn crops are Japan and New Zealand. For cottonseed and coarse grains such as sorghum and maize the major export markets are countries such as Japan and Chinese Taipei.

Overseas Registrations and Use Patterns and International MRLs.

The applicant has stated that products containing thiamethoxam are registered for use in several countries including Argentina, Bolivia, Brazil, New Zealand and Paraguay, Croatia, El Salvador, Guatemala, Honduras, Indonesia, Romania and South Korea, however no MRLs have been established.

CODEX Alimentarius Commission MRL

CODEX has not established an MRL or residue definition for thiamethoxam.

Australian MRLs

The MRLs recommended for inclusion in the Australian *MRL Standard* are detailed in the Residues assessment above.

Potential Risk to Trade

In assessing the risk to Australian export trade the destination, volume and value of cottonseed, sweetcorn, maize and sorghum was considered.
Cotton: The value of Australia's export of cottonseed in 1998 was $91m. Residue trials indicate that residues in cottonseed are below the analytical limit of quantitation for all samples treated at up to 5x the maximum label rate. Most samples of cottonseed are expected to contain residues below the limit of detection and therefore it is considered unlikely that residues will be detected by importers of

treated produce. The risk to Australia's trade in cottonseed from use of Cruiser Insecticide is therefore considered to be low.

Sweetcorn and maize: Australia's total production of sweetcorn in 1997/98 was about 64,000 tonnes, valued at about $26m. Exports of Australian sweetcorn were 1495 tonnes, with the majority exported to Japan (1359 tonnes), with an estimated value of about $600,000. Residue trials indicate that residues in sweetcorn and maize are below the analytical limit of quantitation for all samples treated at label rates. Since most grain samples are expected to contain residues below the limit of detection, it is unlikely that importers of treated produce will detect thiamethoxam residues. The risk to Australia's trade in sweetcorn and maize from use of Cruiser Insecticide is therefore low.

Sorghum: In 1998 Australia exported about 266 kt of grain sorghum, with an estimated value of $47m. The major importer of Australian sorghum is Japan, who imported 221 kt in 1998. Residue trials indicate that sorghum grain will not contain residues above the LOQ and detection of residues in treated produce by importing countries is unlikely. The risk to Australian trade in sorghum grain is therefore low.

Given the very low levels of thiamethoxam residues expected in treated produce, animals consuming treated produce are not expected to give finite residues in animal tissues, milk or eggs. On this basis the risk to Australian trade in plant and animal commodities from use of Cruiser Insecticide containing thiamethoxam is considered to be low and the risk is acceptable.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

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

Thiamethoxam is in the form of a slightly cream colour, fine crystalline powder. It has low acute oral, dermal and inhalation toxicity in rats. The compound is not a skin or eye irritant and is not allergic to skin.

Cruiser 350 FS Insecticide Seed Treatment (Cruiser 350) is classified as non-hazardous according to NOHSC criteria based on the information supplied to NOHSC.

Cruiser 350 is a suspension concentrate formulation. The product has a low acute oral toxicity and low dermal toxicity in rats. In rabbits, the product is not an eye irritant but a slight skin irritant. It is slightly allergic to skin in guinea pigs. This effect is unlikely to occur during normal use of the product. The product will be supplied in 1, 10, 20, 100, and 200L plastic containers.

End use

The proposed application rate varies with different crops. Under the General Directions section, the draft label advises users to mix the product(s) with water to a total volume of 5-10 ml per kg of seed for small lots. For large seed lots, volumes not less than 500 ml and no more than 1 L of water per 100kg of seed are recommended. The maximum application rate of 800 ml/100kg seed corresponds to a concentration of 28% thiamethoxam.

The product will be used as a seed treatment in the control of insect pests that attack cotton, sorghum, maize and sweet corn during early crop establishment. It is expected that Cruiser 350 will be used by commercial seed treaters and small operators such as farmers.

Worker exposure data were not available for thiamethoxam or Cruiser 350.

<u>Recommendations for safe use</u>

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 label. Based on the toxicity of the active ingredient and the products, elbow-length PVC gloves and cotton overalls are recommended for users of Cruiser 350.

The PPE recommended should meet the relevant *Standards-Australia* specified below:

AS 2161-1978	***Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)***
AS 3765-1990	***Clothing for protection against hazardous chemicals***

Active constituent label

Thiamethoxam should be labelled in accordance with NOHSC National Code of Practice for the Labelling of Workplace Substances.

Conclusions

Cruiser 350 can be used safely if handled in accordance with the instructions on the product label.

Environmental Assessment

Novartis Crop Protection Australasia Pty Ltd has made an application for registration of the new technical grade active constituent, thiamethoxam, a new nitromethylene derived chemical with a broad spectrum of activity against sucking and chewing pests. The application also seeks registration of Cruiser® 350 FS Insecticide Seed Treatment which contains thiamethoxam as the active ingredient at a concentration of 350 $g.L^{-1}$. The formulation is a suspension concentrate for seed treatment. The use situations are control of False wireworm (*Pterohelaeus* spp. and *Gonocephalum* spp), Sugarcane (True) wireworm (*Agrypnus variabilis*) and Black field earwig (*Nala lividipes*) in sorghum, Thrips, Cotton aphid (*Aphis gossypii*), False wireworm and Sugarcane (True) wireworm in cotton; and False wireworm and Sugarcane (True) wireworm in maize and sweetcorn. These insects are early season sucking and chewing pests.

Environmental Fate

Thiamethoxam has very slight volatility and is readily water soluble. The log n-octanol/water coefficient value confirms the high water solubility and indicates low potential for bioaccumulation, soil sorption, and toxicity.

- **Hydrolysis/Photolysis**

While stable at pHs 1 and 5 at 25°C, thiamethoxam is slowly hydrolysed at pH 7 with reported half-lives of 572 and 644 days in two studies, while at pH 9 the hydrolysis is rapid, with 4.2 and 8.4 day half-lives reported. Significant degradates were CGA 355190, CGA 309335 and NOA 404617. Hydrolysis is a possible degradation route in alkaline media.

Solution photolysis of thiamethoxam at pH 5 and 25°C for thirty days with the equivalent of natural sunlight showed that thiamethoxam degraded readily with a half-life of 2.3 days following first order kinetics. A total of at least 22 degradates were reported with only a multicomponent fraction and material remaining at the origin present in more than 10% of the total dose. CGA 322704 and CGA 355190 were identified photolysis products, each present at about 3% of the applied radioactivity. Under non-irradiated or hydrolytic conditions, there was no significant degradation.

Based on quantum yield studies, the half-life of thiamethoxam exposed to natural sunlight at 40°N and near the surface of a water body were estimated from 0.76 days [Summer] to 3.3 days [Winter]. At 50°N, the estimated half-lives were from 0.84 days [Summer] to 7.8 days [Winter]. Based on these results, thiamethoxam is expected to be readily to fairly readily degraded by aqueous photolysis. However, turbidity often present in Australian channel and dam water is likely to slow aqueous photodegradation.

In soil exposed to filtered xenon arc lamp light for up to 30 days for 12 hours per day, the half-life of thiamethoxam was 54 days (first order kinetics) while in non-irradiated soils, the half-life was 124 days. The soil was viable over the period of the study with thiamethoxam the major component identified at the study's conclusion with no other major degradates found. While photolysis appears to increase the rate of degradation on soil, it did not result in any new degradation products being isolated and photolysis of soil adsorbed thiamethoxam may not be a major route of dissipation.

- **Soil metabolism**
  - **aerobic soils**

When a US sandy loam was treated with ^{14}C-thiamethoxam labelled in either the guanidine or thiazole ring under aerobic conditions for 12 months, DT_{50} values were 294 and 353 days in viable soil at the lower dose rate with degradation following a two compartment model in which the primary and secondary half-lives were 7 or 4.7 and 521 or 471 days. In sterile soil and in viable and sterile soils treated at the 5 ppm rate, overall half-lives were 241 to 318 days. Thiamethoxam was the major extractable material over the study period, making up 35-51% of the applied soil radioactivity. Volatile radioactivity at the studies' finishing times was 3.6-15% of the applied radioactivity with the radioactivity confirmed as $^{14}CO_2$. Four minor degradation products were detected, all less than 8% of the applied radioactivity. The study showed there was a slow mineralisation of thiamethoxam occurred once the parent was modified. Thiamethoxam is "readily degradable" [DT_{50} <20 days] for the primary degradation but only "very slightly degradable" [DT_{50} >180 days] for the secondary degradation with the average half-lives also in the latter category. As the first phase only involves a few percent of the degradation, on soil under aerobic conditions, thiamethoxam is expected only to be of very slight degradability.

The fate of ^{14}C-thiamethoxam applied to a silty loam soil under aerobic conditions using various temperature and soil moisture levels was investigated over periods of up to a year. At the end of the study, extractable radioactivity had decreased to 18-32% of the added radioactivity (66% in soil stored at 10°C) while bound residues made up 16-20% of the added radioactivity (8.4% for the soil kept at 10°C) with volatiles (essentially all $^{14}CO_2$) making up with 24-44% (17% at 10°C) of the added radioactivity. DT_{50} values for the soils kept at 20°C were 34-143 days and 233 days for the soil kept at 10°C. At the study's completion, thiamethoxam made up 1-18% of the applied radioactivity (34% in soil kept at 10°C) with the metabolite CGA 322704 the only other major component present (11-14% [29% for the soil at 10°C]). Thiamethoxam was classified as slightly to fairly degradable depending on the concentration applied to the soil while CGA 322704 is slightly degradable in the tested soil. In a second laboratory study conducted under aerobic conditions, loamy sand, sand and sandy loam soils treated with ^{14}C-thiamethoxam for up to about 180 days gave results similar to the previous study. Radioactivity distributions (as percentages of the applied radioactivity) at the study's end were of 56-70% extractable radioactivity, 7.6-17% bound radioactivity and ca. 8-21% volatile [$^{14}CO_2$] radioactivity. DT_{50} values were 80-219 days using a single compartment model. At the study's end, thiamethoxam was present in all the soils at 36-61% of the applied radioactivity along with CGA 322704 at 4.6-19%. Thiamethoxam was classified as very slightly to slightly degradable in the tested soils.

  - **aerobic soil/water**

When ^{14}C labelled thiamethoxam was added to river and pond water/sediment systems at ca. 0.1 $mg.kg^{-1}$ water, radioactivity steadily transferred from the aqueous to the sediment phase such that after 100 days, there was only 6 to 12% of the thiamethoxam remaining in the water . At that time, there was 52-59% of the applied radioactivity in the sediments. After 100 days, the major identifiable component was the metabolite, NOA 407475, which was found in the sediment at 35-45% of the added radioactivity. Volatiles, characterised as $^{14}CO_2$, accounted for 6-9% of the applied radioactivity after 100 days. Observed DT_{50} times for thiamethoxam in the water phases were 5.8-ca. 13 days (DT_{90} times 70-132 days) while for the sediment the DT_{50} times were ca. 10-ca. 16 days and the DT_{90}s, 42->100 days. DT_{50} values for the entire water/sediment systems were

ca. 26-36 days and DT_{90}s were 131-615 days. Thiamethoxam is aquatic systems is expected to move to the sediment and breakdown there.

In simulated paddy water/soil studies, thiamethoxam added to the system at ca. 0.5 ppm with respect to the dry soil content) rapidly moved from the aerobic water phase to the anaerobic sediment such that after three days approximately 50% of the added radioactivity remained in the water phase. After a 363 day period, carbon dioxide made up about 2-4% of the radioactivity present. Thiamethoxam reached maximum values of 65-75% of the applied dose in the sediments after sixteen days and then declined to about 2-5% of the applied dose after 363 days. The major sediment metabolite was NOA 407475 which was present at 27-31% of the applied dose after 363 days. This metabolite was not seen in the soil degradation of thiamethoxam. Thiamethoxam DT_{50} values in the water phase were very short, 3-4 days with these values confirming the rapid movement to the soil phase. DT_{50} values in the soil phase were 39-47 days and for the whole system 52 days.

- **anaerobic soil/water**

When ^{14}C labelled thiamethoxam was added to anaerobic water/sediment systems at ca. 0.1 or ca. 5 $mg.kg^{-1}$ water, radioactivity steadily transferred from the aqueous to the sediment such that, while the bulk of the radioactivity was initially in the water phase (ca. 78%), over time this migrated into the sediment phase leaving four or less percent in the water phase after 365 days. At that time, there was 67-74% of the applied radioactivity in the sediments. Volatiles, characterised as $^{14}CO_2$, accounted for ca. 1-6.5% of the applied radioactivity after 365 days. After 365 days, the major identifiable component was the metabolite, NOA 407475, which was found in the sediment at 54-56% of the added radioactivity. Observed DT_{50} times for thiamethoxam were 15-24 days in these systems.

- **Mobility**

Thiamethoxam has only very slight volatility and its Henry's law constant indicates very slight volatility from water. There were no unexplained volatility losses in laboratory studies indicating little loss through volatility may be expected.

- **adsorption/desorption**

Batch equilibrium studies of adsorption of thiamethoxam in one study of two near neutral soils and one acid soil using 24 hours for equilibration, found organic carbon adsorption constants (K_{OC}) of 32 to 35 for thiamethoxam, rating it as having very high mobility in soil (K_{OC} = 0-50). Calculations of the Gustafson Ubiquity Score (GUS) using the available data indicate that thiamethoxam is a “probable” leacher (GUS >2.8), or perhaps a "transition" leacher (1.8<GUS<2.8). i.e. there is the possibility of thiamethoxam reaching groundwater before degrading. CGA 322704, a major soil degradation product, was also identified as having Koc values of 57-80, indicative of high soil mobility (Koc = 50-150).

An adsorption/desorption study with ^{14}C-NOA 407475, a major metabolite associated with sediment in water/sediment systems, applied to a variety of soils using the batch equilibrium method with 24 hours for equilibration, found organic carbon adsorption constants (K_{OC}) of 430 to 1600 for the metabolite, rating it as having low (K_{OC} = 500-2000) to medium (K_{OC} = 150-500) mobility in the tested soils.

- **leachability**

When ^{14}C-thiamethoxam was applied to 30 cm columns of four soils (classified as a loamy sand, a sand, a loam and a silt loam) and leached with 0.01 M $CaCl_2$ [equivalent to 200 mm of rain], levels of thiamethoxam in the leachate (as percentages of the applied thiamethoxam) were respectively 1.6, 23, 0.6% and not measurable in the leachate from the silt loam. On the columns there were respectively 97, 30, 89 and 96% of the applied thiamethoxam retained on the column at various depths with radioactivity being measurable at all depths (up to 30 cm) of the columns. No thiamethoxam degradation was recorded and, compared to the mobile monuron, thiamethoxam was classified as moderately mobile with a relative mobility factor of 1.29.

After aerobically aging a silty loam and a loamy sand treated with ^{14}C-thiamethoxam labelled in either the guanidine or thiazole rings for 56 days at 18-22^{o}C maintained in the dark, the aged soil was leached with distilled water through 30 cm columns containing the same soils. Approximately 2-3% of the applied radioactivity was found in the leachates. The majority of the applied radioactivity (40-51%) was found in the 10-26 cm layers. Thiamethoxam was the major identified column component at 56--68%% of the soil radioactivity. CGA 322704 was also present on the columns (mainly in the 0-18 cm layer) at approximately 20-25% of the soil radioactivity. Although aged residues of thiamethoxam showed movement through the soil columns, little material actually entering the leachate. Degradation to thiamethoxam during aging and while on the column was of significance with the metabolite moving to a lesser degree through the soil columns.

- **Field dissipation**

In a field dissipation study using two lysimeters, four applications of thiamethoxam as a 25 WP formulation were made to a German loamy sand planted initially with potatoes at intervals of 18, 19 and 17 days at an application rate of 200 g thiamethoxam.ha^{-1} with the treatment repeated in the following year for one of the lysimeters and the study completed in the third year. Total leachate radioactivity was ca. 3% of the applied radioactivity with approximately 66% of the applied radioactivity not recovered and attributed to mineralisation in the soil over the study period. Average thiamethoxam concentrations in the leachate over the three years were 0.002-0.1 µg.L^{-1} with the most significant residue being the metabolite, CGA 322704 which was present at average concentrations of 0.01-0.27 µg.L^{-1}. In the soil after three years, residues of thiamethoxam were negligible (<5 µg.kg^{-1}) except for one lysimeter where it was present at 5.3 µg.kg^{-1} in the 10-20 cm layer. CGA 322704 was the only other identified soil metabolite (ca. 1.4-5.3 µg.kg^{-1}). The results presented show that thiamethoxam is not expected to be found in leachates under field conditions nor for long periods in treated soils.

Further evidence for the lack of movement of thiamethoxam through soil came from a series of residue trials where thiamethoxam applied to bare soils showed no significant movement past the 0-10 cm soil layers (concentrations at deeper levels were generally ≤0.01 mg.kg^{-1} soil with initial calculated concentrations of ca. 0.14-0.16 mg.kg-1 soil declining to <0.01 mg.kg^{-1} after a year with a 51 day DT50 value calculated for thiamethoxam. In a series of residue studies with thiamethoxam, field dissipation data were generated which showed no significant movement of residues to soil layers greater than 10 cm and a diminishment of concentrations to ≤0.02 mg.kg^{-1} soil (dry weight) after approximately a year with DT_{50} values of 6.8 to 109 days. DT_{50} values of 20 to 86 days were reported in a further series of soil field studies, confirming the expectation that thiamethoxam will not persist for lengthy periods in the soil. Although the presence of thiamethoxam in soil leachates is not

expected, a study in which rape seeds were treated with formulated thiamethoxam, showed that dissipation of the thiamethoxam into the surrounding soil occurred homogeneously after 17 days.

- **Accumulation/Bioaccumulation**

Although thiamethoxam has some limited persistence in soils, it does undergo degradation and mineralisation and soil accumulation is not expected to any significant extent, as confirmed by modelling. Thiamethoxam in water/soil systems is expected to move rapidly to the soil phases with subsequent degradation to NOA 497475 and eventual mineralisation. No study was provided but bioaccumulation is not expected to occur due to thiamethoxam's high water solubility.

Environmental Toxicity

- **Birds**

Mallard ducks and Bobwhite quail were used in both acute and sub-acute oral dietary studies. The acute oral LD_{50}s determined were 576 mg thiamethoxam.kg^{-1} bodyweight for Mallard ducks and 1552 mg thiamethoxam.kg^{-1} bodyweight for the Bobwhite quail. The LC_{50}s for the 5 d sub-acute dietary studies were >5200 mg.kg^{-1} for both species. These studies indicate that thiamethoxam is slightly toxic to Mallard ducks and Bobwhite quail by acute oral exposure (LD_{50} 501-2000 mg ai.kg^{-1} bw) and practically non-toxic to these birds by subacute dietary exposure (LC_{50} > 5000 ppm in diet). Palatability and dietary toxicity of pigeons exposed to thiamethoxam treated maize (315 g.100 kg^{-1} seed) and wheat (ca. 53 g.100 kg^{-1}) seeds were inconclusive with respect to feeding behaviour and effect of treatment related changes in body weight. When pheasants were exposed to the similar feeding regimes there was again no clear evidence of a treatment related effect on body weights. Both pigeons and pheasants remained in good health during these studies and there were no mortalities recorded. The conclusion is that birds may eat uncovered thiamethoxam treated seed if no other seed is available.

- **Aquatic species**

The acute aquatic toxicity of thiamethoxam to Rainbow trout (*Oncorhynchus mykiss*), Bluegill (*Lepomis macrochirus*), Sheepshead minnow (*Cyprinodon variegatus*), and as 70 WS and 25 WG formulations to Rainbow trout and of the metabolite, CGA 322704 to Rainbow trout were assessed as was the chronic toxicity of thiamethoxam to Rainbow trout. Similarly the acute toxicity of thiamethoxam to various aquatic invertebrates (including *Daphnia magna*) and of 70 WS and 25 WG formulations and the metabolite CGA 322704 to *Daphnia magna* were assessed in separate studies. Studies on the effect of thiamethoxam and as formulated products and of the metabolite CGA 322704 to the green alga, *Selenastrum capricornutum* were also presented. A study of the effect of thiamethoxam on *Lemna gibba* G3 was presented. Toxicity of the metabolite NOA 407475 to Rainbow trout, *Daphnia magna*, the sediment dwelling *Chironomus riparius* and the alga *Scenedesmus subspicatus* was also assessed.

- **Fish**

In the acute studies with fish, the measured LC_{50}s were all greater than 100 mg thiamethoxam.L^{-1} under flow-through conditions while the LC_{50}s for a WS 70 formulation (flow-through conditions) and for a WG 25 formulation (static system) were also both greater than 100 mg of the relative formulated product.L^{-1} (respectively equivalent to ca. 70 and 25 mg thiamethoxam.L^{-1}). Thiamethoxam is shown by these studies to be practically non-toxic to fish (LC_{50} >100 mg.L^{-1}). LC_{50}s for the formulated products and the metabolite, CGA 322704, were all greater than 100 mg of the relative formulated product or metabolite.L^{-1} and also classified as "practically non-toxic", or, if based on the thiamethoxam concentration, as worst "slightly toxic".

A chronic 28 day exposure study with Rainbow trout and thiamethoxam had an NOEC of 100 $mg.L^{-1}$ which indicates thiamethoxam is "very slightly toxic" [NOEC > 1 $mg.L^{-1}$]. Rainbow trout embryos exposed to concentrations of thiamethoxam of up to 20 $mg.L^{-1}$ for a 28 days hatching period followed by a 60 day post-hatch exposure gave indications of the exposure being "very slightly toxic" with a NOEC of 20 $mg.L^{-1}$ reported. NOA 407475, a significant aquatic metabolite of thiamethoxam, was reported as having a 96 h LC_{50} of >100 $mg.L^{-1}$ for rainbow trout, a value that suggests NOA 407475 is "practically non-toxic" to rainbow trout.

- **Aquatic invertebrates**

Daphnid acute toxicity studies (48 h) with thiamethoxam or as WS 70 and WG 25 formulations and as the metabolite CGA 322704 were carried out under static conditions. EC_{50} values for thiamethoxam, the WG 25 formulation and CGA 322704 were all >100 mg thiamethoxam.L^{-1}, a result indicative of "practically non-toxic" effects [EC_{50} >100 ppm]. For the WS 70 formulation the 48 h EC_{50} was 39 $mg.L^{-1}$, rating a classification of "slightly toxic" [10 ppm <EC_{50} ≤ 100 ppm]. When based on the their thiamethoxam concentrations, the formulations are at worst "slightly toxic". Eastern oysters exposed to thiamethoxam for 96 hours in a shell deposition study produced an LC_{50} value of >119 $mg.L^{-1}$, again indicative of "practically non-toxic" effects. In contrast, there were mortalities in mysid shrimp exposed to thiamethoxam for 96 hours with the LC_{50} being reported as 6.9 $mg.L^{-1}$, identifying thiamethoxam as "moderately toxic" to these marine organisms [10 ppm <LC50 ≤ 10 ppm]. The metabolite NOA 407475 had 48 hour EC_{50}s of 83 and 92 $mg.L^{-1}$, indicative of a slight toxicity to *Daphnia magna* (EC_{50} 10 to ≤100 $mg.L^{-1}$).

Under chronic exposure conditions and based on a reproduction NOEC of 100 $mg.L^{-1}$ (and an EC_{50} of greater than 100 $mg.L^{-1}$), thiamethoxam is "very slightly toxic" to *D. magna* Straus [NOEC > 1 $mg.L^{-1}$]. The metabolite NOA 407475 had a NOEC for emergence rate and development rate of 1 $mg.kg^{-1}$ sediment (dry weight) after a 28 day exposure period. Under these conditions, NOA 407475 is rated as at worst slightly toxic to sediment dwelling *Chironomus riparius* larvae (NOEC 0.1-1.0,

- **Algae and aquatic plants**

Acute exposure of the green alga, *Selenastrum capricornutum*, to thiamethoxam, WS 70 and a WG 25 formulations and as the metabolite CGA 322704 (all up to nominal 100 $mg.L^{-1}$ concentrations of the relevant material) resulted in EC_{50} values of >82 $mg.L^{-1}$ and >100 $mg.L^{-1}$ for thiamethoxam, and >100 $mg.L^{-1}$ for the formulations and the metabolite. Thiamethoxam is classified as "slightly toxic" (10 < EC_{50} ≤ 100 ppm) or "practically non-toxic" (EC_{50} > 100 ppm) and the formulations and the metabolite as "practically non-toxic" with the formulations classified as at worst "slightly toxic" if based on their thiamethoxam concentrations. With a 72 h E_bC_{50} (biomass) of 14 $mg.L^{-1}$ and a 72 h E_rC_{50} (growth rate) of 34 $mg.L^{-1}$, the metabolite NOA 407475 is "slightly toxic" (EC_{50} of 10 to ≤100 ppm) to *Scenedesmus subspicatus*.

After a seven day study of the effect of thiamethoxam on duckweed (*Lemna gibba* G3), the reported EC_{50} (for either growth rate or biomass) was >90 $mg.L^{-1}$. Such a value suggests thiamethoxam is at worst "slightly toxic" (EC_{50} of 10 to ≤100 ppm) to *Lemna gibba* G3.

Conclusions for non-target invertebrates

- **Honey bees**

In bees exposed to oral doses of 0.002 to 0.02 µg thiamethoxam.bee^{-1}, mortalities were recorded at all concentrations above 0.002 µg thiamethoxam.bee^{-1} with the 24 and 48 hour oral LD_{50} values both calculated as 0.005 µg thiamethoxam.bee^{-1}. This value identifies thiamethoxam as "highly toxic" to bees . When bees were exposed by contact to thiamethoxam at doses of 0.005 to 0.05 µg.bee^{-1},

fifty per cent mortality occurred between 0.02 and 0.03 µg.bee^{-1}, leading to a contact LD_{50} of 0.027 (24 hours) and 0.024 (48 hours) µg.bee^{-1}. On this basis, thiamethoxam is "highly toxic" to bees via contact exposure. Exposure to bees to the metabolite CGA 322407 at doses of 0.0016 to 0.0625 µg CGA 322407.bee^{-1}, by either the oral or contact routes, gave calculated 48 hour LD_{50} values of 0.017 (oral) and 0.028 (contact) µg.bee^{-1} which identify CGA 322704 as also being "highly toxic" to bees via oral and contact exposure.

A semi-field study of the effect of thiamethoxam as a 25 WG formulation on bees showed that treatments at 0.2 and 0.8 kg formulation.ha^{-1} caused irritation, aggression, reduced foraging activity and increased mortality compared to untreated hives. Thiamethoxam exposure is expected to be harmful to foraging bees. Two further semi-field studies using rape and sunflower grown from seeds dressed with thiamethoxam formulations showed no difference in parameters such as mean mortalities, flight intensities, duration of flower visits, foraging activity, behaviour. Both studies noted declines in the colonies after the exposure but noted this could have been related to the test conditions rather that a specific effect of the seed treatments.

- **Beetles**

In two laboratory studies, Rove beetles (*Aleochara bilineata*) and the ground beetle, *Poecilus cupreus*, were exposed to cotton seeds treated with a 70 WS formulation (ca. 71% thiamethoxam) at a rate of 300 g formulation.100 kg^{-1} seed. After five days exposure, the corrected Rove beetle mortality was 90% and no eggs had been laid by the beetles exposed to the treated seeds. Based on the corrected mortality value, the 70 WS formulation was "moderately harmful" (IOBC rating, 80% ≤ corrected mortality ≤ 99%). There was a 67% mean cumulative mortality seen in the exposed *Poecilus cupreus* after 14 days exposure with behavioural changes seen within two hours of exposure to the treated seeds. Based on the mean cumulative mortality value, the 70 WS formulation was "slightly harmful" (IOBC rating, 30% = Mortality <80%). In a semi-field study, *Poecilus cupreus* were exposed to soil treated twice with a 25 WG formulation at rates of 12.5 or 100 g thiamethoxam.ha^{-1} with a 13 day interval between applications. Of the beetles exposed to the two applications, 50% were dead by 27 days after the initial treatment. Behavioural abnormalities were recorded shortly after the two applications but had ceased 13 days later. At the higher rate, there was a 68% mortality 27 days after the initial treatment with similar behavioural abnormalities reported and being more extended after the first exposure. Food consumption had declined in treated beetles (22 and 46% reduction for the 12.5 and 100 g.ha^{-1} rates compared to untreated controls). Corrected mortalities for the lower treatment rate were -9% and 39% and 24 and 93% for the higher treatment rate. Based on IOBC ratings for corrected mortalities, the formulation was "harmless" (corrected mortality <25%), "slightly harmful" (25%≤ corrected mortality ≤ 50%) or "harmful" (corrected mortality > 75%), depending on the number of applications and the concentration applied. These results show that some mortality among beetles exposed to thiamethoxam from seed treatment can be expected.

- **Predatory bug**

In a semi-field study, the predatory bug, *Orius laevigatus*, was exposed to apple trees that had been treated twice with a 25 WG formulation at an estimated rate of ca. 210 g thiamethoxam.ha^{-1}. Juveniles and adults were exposed and oviposition and egg hatch monitored for periods of up to 14 days. One hundred per cent mortality was seen in both juveniles and adults. There was 94% mortality in nymphs added to the trees three days after the last treatment (a persistence study). The

study concluded that the 25 WG formula would be harmful to *Orius laevigatus* when applied at the recommended Dutch field rates.

- **Parasitic wasps**

When the parasitic wasp, *Aphidius rhopalosiphi*, was exposed to thiamethoxam treated summer wheat (via a 25 WG formulation applied twice at 12.5 or 100 g thiamethoxam.ha^{-1}) there were no recorded wasp deaths or repellency action. The toxic endpoint of the study was the effect on reproduction (via parasitization capacity of cereal aphids) with the results showing that exposure of the wasp to thiamethoxam was rated as slightly harmful to harmful for the exposures at 12.5 g.ha^{-1} [36-99% reduction] and harmful at all exposures at the 100 g.ha^{-1} level [83-100% reduction].

- **Earthworms**

In a study with thiamethoxam, the 14 day LC_{50} was >1000 mg.kg^{-1} soil (dry weight) with 7.5% mortality recorded after 14 days exposure. Thiamethoxam is rated as "very slightly toxic" to earthworms (LC_{50} > 1000 mg.kg^{-1} dry soil). Statistically significant increases in burrowing time and decreases in the weight of exposed worms indicate there were effects on the worms at the single 1000 mg thiamethoxam.kg^{-1} level tested. Consequently a NOEC could not be determined. Exposure of earthworms to a 70 WS thiamethoxam formulation at levels of 12 to 1000 mg.kg^{-1} soil (dry weight) for 14 days resulted in no mortality in the exposed worms and no flaccidity or loss of weight significantly different from the control. The LC_{50} was >1000 mg.kg^{-1} soil (dry weight), indicating the formulation was also "very slightly toxic" to earthworms and the NOEC set at 1000 mg formulation.kg^{-1}. Exposure of earthworms to applications of a 25 WG thiamethoxam formulation. at 931 or 4616 g of ha^{-1}, resulted in no mortality in the treated worms after 28 days exposure and no statistically significant difference in weight gains or numbers of offspring between the control and exposed worms. Consequently the NOECs for mortality at 28 days and for number of hatched offspring alive after 56 days were both set at 4616 g of formulated product.ha^{-1}.

- **Soil respiration and nitrogen mineralisation**

Following treatment of a loamy sand with thiamethoxam at 200 or 2000 g.ha^{-1} (1X and 10X proposed maximum European field rate) and incubations at 19-21^{o}C, short-term respiration rates in the treated soils were within ±3.5% of control values at the 200 g.ha^{-1} and 0 to -7% of the control values at 2000 g.ha^{-1}. Total nitrogen concentrations in the treated soils were between -6.4 and -1.1% of control values at the 200 g.ha^{-1} level and from -12 to -3.4% at the 2000 g.ha^{-1} rate. Based on a Malkome classification, the effect of thiamethoxam on soil respiration and nitrogen mineralisation after a 28 day exposure at the tested levels was considered "negligible".

PREDICTION OF ENVIRONMENTAL HAZARD

It is proposed that the Cruiser products be used for treating sorghum, cotton, maize or sweetcorn seeds to control various early season soil and sucking pests. The proposed label recommends treatment prior to planting at rates equivalent to 140 g thiamethoxam.100 kg^{-1} sorghum seed, 280 g thiamethoxam.100 kg^{-1} cotton seed and 0.5 g thiamethoxam.1000 maize or sweetcorn seeds^{-1}. Based on seed planting density, Environment Australia has taken the maximum amounts of thiamethoxam likely to be used as 17 g.ha^{-1} for sorghum, 72 g.ha^{-1} for cotton and 46 g.ha^{-1} for maize and sweetcorn.

Residues would be expected in the soil surrounding the treated seed leading to potential leaching and contamination of adjacent areas and surface water. Soil residues are expected to persist for sometime before eventual dissipation occurs. The main concern appears to be birds eating the seed, a problem generic to all seed treatments.

Hazard to birds and mammals

- **Birds**

Exposure to birds is expected to be low provided there is immediate covering of sown seed and by having any spillage of treated seed either during the seed treatment process or in field operations cleaned up immediately. Consumption of emerging seedlings is expected to be a minor route of exposure. Environment Australia notes that the draft labels state that wild or domestic birds are not to be fed or exposed to treated seed and that spillages of treated seed during either the seed treatment process or in the field operations are to be cleaned up immediately. Calculated seed intakes needed to reach the avian LD_{50} and NOEC values and numbers of square metres with treated seeds needed to give toxic doses indicate very large areas would need to be grazed. Consequently there is a low hazard to birds from the proposed seed treatment uses and no problems should occur provided the treated seed is buried and not allowed to remain on the surface, particularly in heaps.

- **Mammals**

Acute and chronic toxicity to mammals are considered unlikely from the proposed use as a seed treatment.

- **Aquatic hazard**

Hazard to aquatic organisms is expected to be minimal as the insecticide will be buried in soil on the treated seed. While thiamethoxam shows some movement through soil, field dissipation studies indicate that only low levels are expected in the leachate. Moreover, any thiamethoxam that entered aquatic systems is expected to move rapidly to the soil phase with subsequent degradation (via the metabolite NOA 409475) and mineralisation. Aquatic risk may attend the cleaning of application equipment. However, adherence to label Protection statements that streams, rivers and waterways are not to be contaminated by the product should ensure that aquatic ecosystems are not exposed to thiamethoxam. Entry into, and contamination, of water bodies by overspray and spray drift are not considered of relevance with the proposed seed treatment use pattern.

Adsorption/desorption studies indicate that thiamethoxam has very high mobility in soil and estimates made by Environment Australia of the Gustafson Ubiquity Score indicate thiamethoxam is a “probable” or "tentative" leacher with one study using treated rapeseeds showing a surprising mobility away from treated seeds into the surrounding soil. However, a field lysimeter study and a field dissipation studies have shown thiamethoxam is not expected to leach significantly when applied under field conditions. Calculations assuming a 10% run-off show that there would be no hazard to any aquatic organism.

- **Hazard to non-target invertebrates and micro-organisms**

The product is very highly toxic to bees, and there is no warning to this effect appearing on the label. Exposure to bees of plants grown from thiamethoxam treated seeds has not been conclusively linked

to declines in hive quality but Environment Australia will continue to monitor this issue. While spray applications of thiamethoxam is harmful to predatory bugs and parasitic wasps, the proposed seed dressing use is not expected to result in significant exposure to these and similar beneficials. Ground dwelling beneficials may have the opportunity for exposure to treated seeds, either through the seeds being unburied or through foraging activity. Laboratory studies have shown that exposure to treated seeds is expected have some hazard to ground dwelling beetles (and by extrapolation, to other ground dwelling beneficials). However, if limited to cotton, sorghum and maize paddocks, Environment Australia expects little exposure to non-target native ground dwelling beneficials. Calculations made by Environment Australia show that the theoretical soil concentration over a 10 cm soil depth after application of treated cotton seed was ca. 0.05 mg thiamethoxam.kg^{-1} soil, well below the 14 day LC_{50} level of >1000 mg.kg^{-1} to earthworms. Consequently the proposed use pattern is not expected to have adverse impact on earthworms.

- **Soil microorganisms**

As noted above, the expected maximum environmental concentration arising from the proposed Australian use pattern is ca. 0.05 mg thiamethoxan.kg^{-1}. After treatment of a loamy sand with thiamethoxam at rates equivalent to 0.27 and 2.7 mg of thiamethoxam.kg^{-1} soil there were no significant effects on either the soil's short-term respiration rate or nitrogen mineralisation. Consequently, the Australian environmental concentration remaining in the soil after use as seed treatment agents is not expected to adversely affect soil microorganisms.

- **Native vegetation**

Hazard to non-target plants appears minimal as the mode of application will not entail significant exposure of non-target plants. Additionally, company advice notes that foliar uses of thiamethoxam have not shown any adverse effects in a wide range of crops.

Conclusions

Environment Australia concludes that a low hazard to the environment may be predicted provide the Cruiser products are used according to the proposed label recommendations and good agricultural practice.

Environment Australia's assessment of this application has been completed.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Thiamethoxam is a new nitromethylene derived compound with a broad spectrum of activity against sucking and chewing insects. Thiamethoxam has contact, stomach and systemic activity and acts on the nervous system of the insect. The target site is the nicotinic acetylcholine receptor where the compound mimics the messenger chemical acetylcholine and binds to the receptor site. However, unlike acetylcholine, thiamethoxam is not rapidly broken down by the enzyme acetylcholinesterase. This irreparably damages the target insect's nervous system causing death. Other nitromethylene class compounds are used for soil insect control, however, this compound falls into a different subclass.

Cruiser 350FS Insecticide Seed Treatment is proposed for use as a seed treatment for use in cotton, sorghum, maize and sweetcorn crops to control various early season soil and sucking pests.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Cruiser 350FS is proposed to be used to control eastern false wireworm and southern false wireworm in sorghum, cotton, maize and sweet corn crops, striate or large false wireworm in maize and sweet corn, cotton seedling thrips, tomato thrips and cotton aphid on cotton,and to protect sorghum, cotton, maize and sweet corn from damage by sugarcane (true) wireworm and sorghum from damage by black field earwig. This use is proposed for all States and Territories, as specified in the directions for use on the product label (see page 30).

Cruiser 350FS contains a dye to distinguish treated seed from untreated seed and is proposed for both on-farm use and application by commercial seed treatment companies (see page 30). The maximum use pattern will be one application to seed, prior to planting, of 400 mL per 100kg of sorghum seed, 800 mL per 100 kg of cotton seed or 1.4 mL per 1000 maize or sweetcorn seeds.

It is proposed the product will be available in 1, 10, 20, 100 or 200 L pack sizes.

The following withholding periods are recommended for the product:
Cotton
(Harvest) – NOT REQUIRED WHEN USED AS DIRECTED.
(Grazing) – DO NOT GRAZE OR FEED COTTON TRASH TO STOCK.
Sorghum
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 8 WEEKS AFTER PLANTING.
Maize, Sweetcorn
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER PLANTING.

Evaluation of efficacy

Cruiser was tested in a large number of trials in NSW and Queensland and in general trial design was satisfactory with respect to the provision of controls, treatment sizes, plant varieties and number of replicates. The trials were conducted competently and analysed appropriately. The data presented supported the claims for control of eastern false wireworm and southern false wireworm in sorghum, cotton, maize and sweet corn crops, striate or large false wireworm in maize and sweet corn and cotton seedling thrips, tomato thrips and cotton aphid on cotton. Control (i.e. actual pest mortality) for certain pests was not able to be established on the available data. However, protection of sorghum, cotton, maize and sweet corn from damage by sugarcane (true) wireworm and protection of sorghum from damage by black field earwig was established on the basis of moderate/high populations of these pests being present and significantly better stand counts being achieved by application of Cruiser. Bioequivalence in stand count improvement for these trials was demonstrated by comparison of the performance of Cruiser with that of one or more currently registered industry standard seed treatment products. The trials presented showed that all rates of Cruiser proposed were efficacious for the claims on the label for the product.

Crop Safety

Cruiser was not toxic to sorghum unless applied at 2 to 4 times the recommended label rate. No problems were experienced in cotton trials at up to 2 times the label rate when tested on both conventional and INGARD varieties. No phytotoxicity problems occurred with maize and sweetcorn at up to 3 times the proposed rate.

Seed Germination

No data were provided to show that treated grain will successfully germinate after long periods of storage. However, the Directions for Use contain a statement that 'Treated seed should be used in the season applied'.

Resistance management

The draft label includes a resistance note (see page 31) and in addition includes the statement that when cotton seed has been treated with Cruiser, the first foliar insecticide spray must be from a different insecticide group (i.e. not Group 4A).

CAUTION

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

Cruiser® 350 FS

INSECTICIDE SEED TREATMENT

Active Constituent: 350 g/L THIAMETHOXAM

GROUP	4A	INSECTICIDE

For treatment of seed to control Eastern False Wireworm, Southern False Wireworm, Striate or Large False Wireworm, Cotton Seedling Thrips, Tomato Thrips and Cotton Aphid; and to protect seedlings from attack from Sugarcane (True) Wireworm and Black Field Earwigs in Cotton, Sorghum, Maize and Sweetcorn as per the Directions for Use Table.

1, 10, 20, 100 or 200 LITRES

Novartis Crop Protection Australasia Pty Limited,
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 hrs) ***UN - Free***

NOVARTIS

Directions for Use

Crop	Pest	Rate	Critical Comments
Sorghum	**Control of:** Eastern False Wireworm (*Pterohelaeus darlingensis*), Southern False Wireworm (*Gonocephalum macleayi*) **Protection from:** Sugarcane (True) Wireworm (*Agrypnus variabilis*), Black Field Earwig (*Nala lividipes*)	**400 mL** per 100 kg of seed	Apply diluted with water before sowing. Treated seed should be used in the season applied.
Cotton	**Control of:** Cotton Seedling Thrips (*Thrips tabaci*), Tomato Thrips (*Frankliniella schultzei*), Cotton Aphid (*Aphis gossypii*), Eastern False Wireworm (*Pterohelaeus darlingensis*), Southern False Wireworm (*Gonocephalum macleayi*) **Protection from:** Sugarcane (True) Wireworm (*Agrypnus variabilis*)	**800 mL** per 100 kg of seed	
Maize and Sweetcorn	**Control of:** Eastern False Wireworm (*Pterohelaeus darlingensis*), Striate or Large False Wireworm (*Pterohelaeus alternatus*), Southern False Wireworm (*Gonocephalum macleayi*) **Protection from:** Sugarcane (True) Wireworm (*Agrypnus variabilis*)	**1.4 mL** per 1000 seeds	

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

WITHHOLDING PERIODS:

***Cotton (Harvest)* - NOT REQUIRED WHEN USED AS DIRECTED.**

(*Grazing)* - DO NOT GRAZE OR FEED COTTON TRASH TO STOCK.

***Sorghum* - DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 8 WEEKS AFTER PLANTING.**

***Maize, Sweetcorn* -DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER PLANTING.**

GENERAL INSTRUCTIONS

Application:

Treatment in small lots by the farmer

May be applied by shaking with seed in a tin, enclosed drum, plastic bag or cement mixer.

1. Premix Cruiser 350 FS with water to a total volume of not less than 5 mL nor more than 10 mL per kg of seed.
2. Apply solution to seed and vigorously mix for 1 to 2 minutes.

Treatment of large seed lots by commercial seed-treatment equipment

For large-scale seed treatment the product should be applied diluted with water in specialised seed-treatment equipment. As for all such seed treatments, a good flow and metering system for the initial prepared solution is important. Depending on the type of seed treatment equipment, it may be necessary to increase the recommended amount of water slightly in order to ensure an optimal flow of the solution and an even treatment of seed.

Prepare the solution as follows:

1. Fill the solution tank with the required volume of water and mix with the appropriate volume of Cruiser 350 FS. Total volumes of not less than 500 mL nor more than 1 litre of water per 100 kg of seed are recommended.
2. Switch on the stirring system and stir.

Insecticide Resistance Warning:

GROUP		INSECTICIDE

For insecticide resistance management CRUISER 350 FS Insecticide Seed Treatment is a Group 4A insecticide.

Some naturally occurring insect biotypes resistant to CRUISER 350 FS and other Group 4 insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if CRUISER 350 FS or other Group 4 insecticides are used repeatedly. The effectiveness of CRUISER 350 FS 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 CRUISER 350 FS to control resistant insects. CRUISER 350 FS may be subject to specific resistance management strategies.

For further information contact your supplier, Novartis Crop Protection representative or local agricultural department agronomist.

Aphid Resistance Management

When cotton seed has been treated with Cruiser, the first foliar insecticide spray must be from a different insecticide group (ie, not Group 4A).

PRECAUTION

DO NOT use treated seed for animal or human consumption.

DO NOT allow treated seed to contaminate grain or other seed intended for animal or human consumption.

DO NOT feed treated seed, or otherwise expose, to wild or domestic birds.

PROTECTION OF BIRDS – Treated seed may be harmful to seed eating birds, and should be properly sown and completely covered by soil. Excess seed is not to be left in areas accessible to birds. Any spillage of treated seed which occurs either during the seed treatment process or in field operations must be cleaned up immediately, preferably by recovery and re-use.

When treated seed is stored it should be kept apart from other grain and the bags or other containers should be clearly marked to indicate the contents have been treated. Bags which have held treated seed should not be used for any other purpose.

PROTECTION OF LIVESTOCK

DO NOT feed treated seeds to animals, including poultry.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT contaminate streams, rivers or waterways with the product or used containers.

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

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre. Phone 131126.

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

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NRA Approval No. 51833/

Batch No.	
Date of Manufacture	

Bar Code

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 emamectin in the product Proclaim 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.

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Signature_____ Date _____