Public Release Summary
on

Evaluation of the new active

TRIFLOXYSTROBIN

in the product

FLINT FUNGICIDE

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 co-operation with advisory agencies, including the Department of Health and Aged Care (Chemicals and Non-prescription Medicines Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (NOSHC) and State departments of agriculture and environment.

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

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

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

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library, Ground floor, 22 Brisbane Avenue, 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)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
d	Day
DALT	Days after last treatment
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
Fo	original parent generation
h	Hour
HPLC	high pressure liquid chromatography *or* high performance liquid chromatography
id	Intradermal
ip	Intraperitoneal
im	Intramuscular
iv	Intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	Kilogram
K_{oc}	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
mg	Milligram
mL	Millilitre
MRL	maximum residue limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	no observable effect concentration/level
OECD	Organisation for Economic Co-operation and Development
Pa	Pascals
pK_a	Dissociation constant
po	Oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
s	Second
sc	Subcutaneous
SC	suspension concentrate
STMR	Supervised Trial Median Residue
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
TRR	Total residues recovered
WG	water dispersible granule
WHP	withholding period

SUMMARY

Trifloxystrobin is a new broad spectrum fungicide. It is a synthetic derivative of the naturally occurring strobilurins found in several genera of wood decaying fungi. The mode of action of trifloxystrobin involves inhibition of mitochondrial respiration by blocking electron transfer in the electron transfer chain. The fungicidal properties of trifloxystrobin are derived from the parent ester; the acid form (the main metabolite) is inactive.

Novartis Crop Protection Australasia Pty Ltd have applied for registration of the product *Flint Fungicide*, a water dispersible granule formulation containing 500g/kg trifloxystrobin. The product will initially be marketed for the control of black spot on apples and pears, powdery mildew on apples and the control of powdery mildew and suppression of downy mildew on grapes (table, wine and dried).

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *Flint Fungicide*. Responses to this public release summary will be taken into consideration by the NRA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

Written comments are invited and should be submitted to the NRA at the address shown in the Introduction. Comments should be submitted by **30 September 2000.**

Public health aspects

Trifloxystrobin has low acute oral, dermal and inhalation toxicity. It is not a skin irritant, but can cause eye irritation if it is not rinsed out. In some skin sensitisation studies trifloxystrobin caused some sensitisation. The product *Flint Fungicide*, containing 500 g/kg trifloxystrobin, is of low acute oral and dermal toxicity. It is not an eye irritant, but is a slight skin irritant. The product also caused skin sensitisation in some studies.

Studies in rats showed that following oral administration, trifloxystrobin is poorly absorbed. That which is absorbed is extensively metabolised and excreted in urine and faeces. Consistent with its poor absorption administration of high doses resulted in significant amounts being excreted unchanged in the faeces. In short-term studies, trifloxystrobin produced mild effects on body weight gain. Vomiting and diarrhoea was seen in dogs. Liver weight increases were seen in mice, rats and dogs, although there were minimal changes observed on examining the liver under the microscope. In longer term studies there were similar findings. There was no evidence that trifloxystrobin caused any genetic damage or carcinogenic effects. Trifloxystrobin also did not have any significant effects on reproduction or foetal development.

Based on an assessment of the toxicology of trifloxystrobin and the formulated product, it was considered that there should be no adverse effects on human health when *Flint Fungicide* used in accordance with label directions.

Occupational Health and Safety aspects

Trifloxystrobin is not currently on the NOHSC *List of Designated Hazardous Substances* but is an eye irritant and a skin sensitiser. Based on this information trifloxystrobin is considered hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances*. However, *Flint Fungicide* possesses low acute oral and dermal toxicity in rats and is not an eye irritant. It is a slight skin irritant in rabbits. As a result *Flint Fungicide* cannot be classified as hazardous.

Flint Fungicide will be formulated overseas and imported into Australia fully packaged and ready for sale in a 1 kg sealed carton box. It is intended to be used for the control of foliar fungal diseases, such as black spot on apples and pears, powdery mildew on apples, and the control of powdery mildew and suppression of downy mildew on grapes. The proposed rate is 150-200 g/ha in a minimum of 100L water/ha for low volume application, or a minimum of 1000 L water/ha for high volume application at 10-14 day intervals. Application will be by either dilute or concentrate boom spray equipment at a maximum of 3 times per season.

Worker exposure data were not available for trifloxystrobin or *Flint Fungicide*. The occupational health and safety risk assessment was based on estimates obtained from an exposure model.

Based on the risk assessment, cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves are recommended for users of *Flint Fungicide*. A re-entry restriction is also recommended for this product.

Residues aspects

Comprehensive residue data were presented for trials conducted on apples, pears and grapes. Both overseas and Australian data were provided enabling the following MRLs to be established: 0.5 mg/kg grapes and 0.3mg/kg pome fruit, with a 35 day WHP for both grapes and pome fruit. Residues in grape pomace, a potential animal feed were also addressed and a Processed Commodity MRL for Grape Pomace (dry) of 3 mg/kg has been recommended. Apple pomace is also a potential animal feed however as no adequate processing data was provided apple pomace that has been treated with *Flint Fungicide* is not to be used as an animal feed. No Processed Commodity MRL has been set for apple pomace. Animal transfer studies in lactating dairy cows showed that finite residues are not expected in tissues or milk following consumption of treated produce when the product is used as directed.

There are significant concerns with the potential impact on trade. The use of *Flint Fungicide* on grapes and pome fruit may present a risk to Australian trade as finite residues are expected in grapes, dried fruit and pome fruit. The major importing countries of these commodities do not have tolerances and therefore any residue detection would constitute a violation. There are no CODEX MRLs for trifloxystrobin. Relevant industry bodies are expected to respond to this publication with comments on this issue.

Finite residues may appear in wine grapes however processing studies have demonstrated that these residues are removed during the wine making process. Therefore the use of *Flint Fungicide* is not expected to present a risk to Australia's wine trade. Finite residues are not expected to be present in animal tissues and milk from the use of treated materials in stock feeds. Therefore the use of *Flint Fungicide* is not expected to present a risk to Australia's animal commodity trade.

Environment aspects

Trifloxystrobin is expected to have widespread use in viticulture and pome fruit orchards around Australia. Based on the tested environmental effects of this chemical, and its proposed use pattern, the environmental risk is estimated to be unacceptable to aquatic organisms in the case of aerial application. This method has been forbidden on the label. A potential hazard was shown to exist with ground based application also. However, this hazard is mitigated through the chemicals short field and aquatic half lives, and on the basis of microcosm testing showing no treatment related impacts on aquatic communities at levels higher than expected through ground application drift or runoff.

Trifloxystrobin becomes more hydrolytically unstable as aqueous conditions tend towards basic. In aqueous systems, breakdown through photolysis was rapid (less than 2 days half life). Breakdown is also rapid in soil systems but this breakdown is not attributed to photolytic processes because the results were the same in irradiated and non-irradiated samples. Trifloxystrobin is rapidly degraded in viable soils (laboratory half life less than 3 days), primarily to the acid metabolite which has a significantly longer laboratory half life of around 100 days, although isomers of the parent and acid were also formed under most conditions. The relatively high logPow and low water solubility suggests that the chemical moves quickly from water to sediments. This is supported by laboratory and field studies, although the rapid formation of the more soluble acid metabolite results in movement back to the water column as the acid is produced. Both batch and column studies indicate leaching is not expected to be a concern with the parent compound, although the main metabolite is identified as a leacher, regardless of soil type.

Field dissipation studies largely confirmed laboratory experimental results with trifloxystrobin dissipating rapidly in all soils tested, with a field half life less than 5 days. A wide range of soils were tested with similar results in all.

Accumulation is unlikely, and although the chemical can be classed as concentrating and lipophilic, bioaccumulation is not expected to occur as testing showed rapid elimination during the depuration period.

Testing has shown trifloxystrobin to be practically non toxic to birds and mammals. With respect to the aquatic environment, the chemical is very highly toxic to all trophic levels. The main metabolites were tested showing significantly less toxicity than the parent, with the main acid metabolite being classed as practically non toxic to all trophic levels. Testing on terrestrial invertebrates provided mixed results with the chemical generally classed as harmless to beneficial organisms except for one aphid species demonstrating a high level of sensitivity and the chemical being classed as harmful to this species. Trifloxystrobin was shown to not be of concern to soil dwelling invertebrates, soil micro-organisms, or bees.

Efficacy and Crop Safety Aspects

The product claims are for control of black spot on apples and pears, powdery mildew on apples and the control of powdery mildew and suppression of downy mildew on grapes (table, wine and dried). Data from thirteen field trials was presented, each trial was completed using 3-5 application of *Flint Fungicide*, each application being 10-15g of product per 100L or with spray volumes ranging from 300-1533 L/ha. The results provided adequate confirmation that the product claims are valid. The trials demonstrated that *Flint Fungicide* is equivalent to, or better than the standard fungicide treatments.

It is acknowledged that this product is likely to become a useful addition to the range of fungicides available for control of black spot and powdery mildew, and for the suppression of downy mildew. As a new Group K fungicide, it is considered likely that this product will be effective in managing diseases and will assist in reducing the development of resistance.

The safety to crops of grapes, apples and pears is assured by label restraints. The data supports *Flint Fungicide* as being safe when applied alone to grapes and pome fruit. Some overseas trials on pome fruit resulted in russeting when *Flint Fungicide* was used in conjunction with a surfactant, however a label restraint precluding the use of surfactants is proposed. No other phytotoxic effects were observed on any treated plants.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *Flint Fungicide*, containing the new active constituent trifloxystrobin.

Responses to this public release summary 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. They will also be taken into account in determining appropriate conditions of registration and product labelling.

Written comments are invited and should be submitted by 30 September 2000, addressed to:

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Applicant:

Novartis Crop Protection Australasia Ltd

Product Details:

Flint Fungicide is a water dispersible granule formulation containing 500 g/kg trifloxystrobin. Trifloxystrobin belongs to the new strobilurin fungicide group (Group K). Trifloxystrobin is a broad spectrum fungicide with activity that results from the inhibition of mitochondrial respiration of the fungi.

The active constituent is manufactured in Switzerland by Novartis Crop Protection Munchwilen AG. The end use product will be formulated by the same company at a different site in Switzerland.

Registration of *Flint Fungicide* for the purpose of controlling black spot on apples and pears, powdery mildew on apples and grapes and suppression of downy mildew on grapes, is proposed.

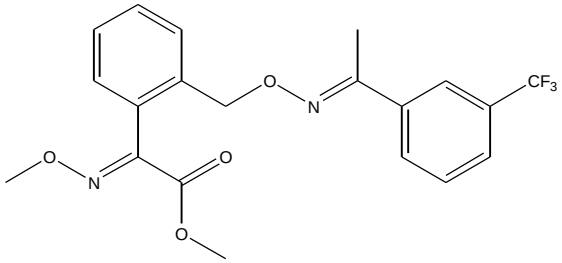
Novartis Crop Protection Australasia Ltd have provided confirmation that products containing trifloxystrobin are currently registered for use on bananas, grapes, cereals and pome fruits in the following countries: Croatia, Israel, Moldovia, New Zealand, Poland, Romania, Russian Federation, Slovenia, South Africa, Turkey, Yemen and Yugoslavia. There are provisional approvals for products containing trifloxystrobin in Belgium, United Kingdom, Macedonia, Switzerland, and USA.

CHEMISTRY AND MANUFACTURE

The product proposed for registration is a water dispersible granule formulation under the trade name *Flint Fungicide*. The formulation storage stability and the physical and chemical properties of the formulated product and active constituent have been evaluated by the NRA and are considered acceptable.

Active constituent

The source of the Technical Grade Active Constituent (TGAC) to be used in the product has been approved by the NRA (Approval No. 44479). The active constituent trifloxystrobin is manufactured by Novartis Crop Protection Munchwilen AG, Switzerland and has the following properties:

Common name:	Trifloxystrobin (ISO/SA approved)
Synonyms and code number:	CGA 279202
Chemical name:	(E,E)-Methoxyimino-{2-[1-(3-trifluoromethyl-phenyl)-ethylideneaminooxymethyl]-phenyl}-acetic acid methyl ester (IUPAC) (E,E)-α-(methoxyimino)2-[[[[1-[3(trifluoromethyl) phenyl]ethylidene]amino]oxy]methyl]-benzeneacetic acid methyl ester (CAS)
CAS Number:	139485-98-9
Molecular formula:	$C_{20}H_{19}F_3N_2O_4$
Molecular weight:	408.37
Chemical structure:	
Physical state:	Fine powder
Colour:	White
Odour:	Odourless

Melting point:	72.9 °C
Boiling point:	Approx. 312 °C (thermal decomposition starts at about 285 °C)
Solubility in water	610 µg/L at 25 °C (not effected by pH 4-10)
Density/specific gravity:	1.36 g/cm^3
Solubility in organic solvents (at 20 °C)	Acetone >500 g/L Dichloromethane >500 g/L Ethyl acetate >500 g/L Hexane 11 g/L Methanol 76 g/L Octanol 18 g/L Toluene 500 g/L
pK_a values:	Does not have a dissociation constant within the range 2 to 12
Octanol/water partition coefficient:	P_{ow} = 32000 ± 680 at 25 °C (log P_{ow} = 4.5)
Vapour pressure:	3.4 x 10^{-6} Pa at 25 °C (extrapolated)
Flash point:	Not determined.
Melting point:	> 40 °C
Flammability:	Not highly flammable
Explosive properties:	Not explosive
Oxidising properties:	Not an oxidising substance
Storage stability:	Trifloxystrobin is stable to hydrolysis and is demonstrated to be thermally stable for 2 years
Chemical family:	Fungicide
Chemical type:	Strobilurin
Mode of Action:	Involves the inhibition of mitochondrial respiration by blocking electron transfer in the electron transfer chain.

Formulated product

Distinguishing name:	*Flint Fungicide*
Formulation type:	WG – Water dispersible granule
Active constituent concentration:	500 g/kg trifloxystrobin

Physical and Chemical Properties of the Product

Physical state:	Solid granule
Colour:	Grey to beige
Odour:	Weak, non-specific
Density or specific gravity:	0.597 g/cm^3 after 50 taps
Acidity, alkalinity or pH value:	9.7 (1 % dispersion in deionised water)
Flammability/autoignition:	Not highly flammable, not a self-heating substance
Explodability:	Not explosive
Oxidising properties:	Not an oxidising substance
Storage stability:	Stability data provided by the applicant supports a shelf life of 2 years when the product is stored below 30 °C in sealed paper/polyethylene laminate bags with PVDC barrier (1 kg)

TOXICOLOGICAL ASSESSMENT

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

Toxicokinetics and Metabolism

In rats, trifloxystrobin was poorly absorbed from the gastrointestinal tract and the half life in plasma was relatively long. Trifloxystrobin is extensively metabolised, and little of the absorbed dose remained in tissues after 7 days. Most of the administered dose was excreted via bile in the faeces, although some was also excreted in the urine. Percutaneous absorption of trifloxystrobin was very poor.

Acute Studies

Trifloxystrobin has low acute oral toxicity in rats and mice (LD50>2000 mg/kg bw), low acute dermal toxicity in rats and rabbits (LD50>2000 mg/kg bw), low acute inhalational toxicity in rats and is not a skin irritant in rabbits. It is a moderate eye irritant in unwashed rabbit eyes but is not an irritant in washed eyes and was a skin sensitiser in one test using guinea pigs, but not in a second.

The product *Flint Fungicide*, containing 500 g/kg trifloxystrobin, has low acute oral and dermal toxicity and is not an eye irritant but is a slight skin irritant in rabbits. The product showed similar properties for skin sensitisation to the active ingredient.

Short-Term Studies

In a three month study, trifloxystrobin was fed to mice at 0, 500, 2000 or 7000 ppm in the diet. There were no abnormal clinical signs observed. Males at 7000 ppm showed a decreased body weight gain. Food consumption was slightly increased in males at all doses and in females only at 7000 ppm. Water intake was increased in females at 7000 ppm, but not in males. Liver and spleen weights were increased from 2000 ppm with microscopic abnormalities were also being seen.

In a 28 day dietary study in rats trifloxystrobin was fed at 200, 1000, 4000 or 12000 ppm and no deaths occurred at any dose. Diarrhoea was seen in a few animals, and decreased food consumption and body weight gain were seen in males from 1000 ppm in males and females at 12000 ppm. Changes in enzymes, including increased blood glucose and cholesterol levels were seen at 4000 ppm. Relative liver weights were increased from 4000 ppm, but there were no abnormalities on postmortem examination. In a three month oral study in rats, trifloxystrobin was fed at 0, 100, 500 or 2000 ppm to both sexes and 8000 ppm to females only. Several deaths occurred among females at 8000 ppm. Body weight gain and food consumption were decreased in males from 500 ppm and in females from 2000 ppm. Water consumption was reduced in females at 8000 ppm. There were minor changes in serum enzymes and blood parameters, however these were reversed during a recovery period. Increased liver weights were seen in males from 500 ppm and in females from 2000 ppm which was associated with microscopic changes. No treatment related abnormalities were found on a gross and microscopic examination of tissues in the central nervous system. The NOEL was 6.4 mg/kg bw/day for males and 32.8 mg/kg bw/day for females.

In a 28 day dermal study in rats, trifloxystrobin was applied at 0, 10, 100, or 1000 mg/kg bw, 5 days/week for 28 days. No deaths or abnormal clinical signs were seen, and there was no sign of local irritation of the skin. No effects on body weight, food consumption or haematology (blood effects) or serum enzymes were seen. Liver and kidney weights were increased in males, but no abnormalities were found on post mortem examination.

In a 28 day oral study in dogs, trifloxystrobin was given at 0, 20, 50, 150 to 500 mg/kg bw/day. No deaths occurred. Vomiting was seen at 150 to 500 mg/kg bw/day. Slight bodyweight loss was noted in a few males at 50 mg/kg bw/day, but not among females. No abnormalities were found in the eyes or in tests of the blood or urine. Liver weight was increased at 150 to 500 mg/kg bw/day but no abnormalities were found on post mortem examination. In a 3 month oral toxicity study in dogs, trifloxystrobin was given by capsule at 0, 5, 30, 150 or 500 mg/kg bw/day. Vomiting, diarrhoea and body weight loss was seen at doses in excess of 30 mg/kg bw/day. Food consumption was decreased at 500 mg/kg bw/day throughout the study. Changes in haematology and clinical chemistry were seen at 500 mg/kg bw/day. Liver weight was increased from 150 mg/kg bw/day, with minimal changes observed on post mortem examination. The NOEL was 30 mg/kg bw/day.

Long-Term Studies

Mice were fed trifloxystrobin in the diet at 0, 30, 300, 1000 or 2000 ppm for 18 months. No treatment related mortality or abnormal clinical signs were seen at any dose. Body weight gain was seen in males at 2000 ppm and in females at concentrations in excess of 30 ppm. Liver weights were increased from 1000 ppm, which was associated with microscopic changes in the liver (hepatocellular hypertrophy and focal liver necrosis). The NOEL was 300 ppm (131 mg/kg bw/day) in males and 30 ppm (39.4 mg/kg bw/day) in females.

Rats were fed trifloxystrobin in the diet at 0, 50, 250, 750 or 1500 ppm for 24 months. Diarrhoea was seen in males at 1500 ppm. Reduced body weight gain was seen from 750 ppm, and food consumption was decreased at 1500 ppm. The incidence of cancer was decreased from 750 ppm; this is likely to be related to the lower body weight, rather than a direct effect of trifloxystrobin. The NOEL was 250 ppm, equal to 9.8 mg/kg bw/day in males and 11.4 mg/kg bw/day in females.

Dogs were given trifloxystrobin in gelatine capsules at 0, 2, 5, 50 or 200 mg/kg bw/day for 52 weeks. There were no deaths during the study. Diarrhoea and vomiting was seen at 200 mg/kg bw/day. Mean body weight gain was slightly decreased in females from 50 mg/kg bw/day. Food consumption was slightly decreased from 50 mg/kg bw/day. Minor changes in haematological and clinical chemistry parameters were seen from 50 mg/kg bw/day. Liver weights were increased in males and females from 50 mg/kg bw/day which was associated with microscopic change (hepatocellular hypertrophy) in the tissue. The NOEL was 5 mg/kg bw/day.

Reproduction and Developmental Studies

Rats were fed trifloxystrobin in the diet at 0, 50, 750 or 1500 ppm for 2 generations. No deaths or abnormal clinical signs were seen. Food consumption was decreased at 1500 ppm in both generations, which was associated with decreased body weight gain. Gestation, parturition, viability and lactation indices were unaffected by treatment. Body weight gain was lower in pups during lactation at concentrations in excess of 50 ppm. At post mortem examination, minor liver, kidney and spleen abnormalities were seen at similar doses. The NOEL was 50 ppm in the diet.

Trifloxystrobin was given to pregnant rats at 0, 10, 100 or 1000 mg/kg bw/day from days 6 to 15 of gestation. Body weights and body weight gain were decreased at 1000 mg/kg bw/day, and were associated with decreased food consumption. No effects on the number of live foetuses/litter or foetal weight were seen. There were no external or skeletal abnormalities on examination of the foetuses. Post-mortem examination of the dams revealed enlarged thymus at 1000 mg/kg bw/day. The NOEL for maternal toxicity was 10 mg/kg bw/day, and the NOEL for embryotoxicity was 100 mg/kg bw/day.

Trifloxystrobin was orally administered to pregnant rabbits at 0, 10, 50, 250 or 500 mg/kg bw/day from days 7 to 19 of gestation. Weight loss, associated with decreased food consumption, was seen at doses in excess of 50 mg/kg bw/day. No effects on the number of implantation sites or postimplantation losses were observed. The number of live foetuses and foetal weights were not affected by treatment. External and visceral examination of foetuses showed no treatment related abnormalities. Skeletal examinations showed an increase in the incidence of fused and asymmetrically shaped sternebrae from 250 mg/kg bw/day. This was considered to be a marginal effect, with no impact on the development of the animals. The NOEL for maternal toxicity was 50 mg/kg bw/day, and the NOEL for embryotoxicity was 250 mg/kg bw/day.

Genotoxicity

Trifloxystrobin was negative in the Ames test both with and without metabolic activation at concentrations up to 5000 µg/plate. It was negative in non-activated Chinese hamster V79 lung fibroblasts *in vitro*, but results were equivocal with activated fibroblasts. No chromosomal aberrations were produced in Chinese hamster cells either with or without metabolic activation, and no unscheduled DNA damage was produced in rat hepatocytes *in vitro*. Trifloxystrobin was negative in a test on mouse bone marrow. Overall, trifloxystrobin was not considered to be genotoxic.

Neurotoxicity

In an acute oral neurotoxicity study in rats given trifloxystrobin at 2000 mg/kg bw, there was no evidence (in a functional observation battery of testing) for any neurologic or behavioural effect.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

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

On the basis of its toxicity, the NDPSC has recommended that that trifloxystrobin be listed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The lowest NOEL observed for trifloxystrobin was 5 mg/kg bw/day in a 1-year dog study. This NOEL was based on reduced bodyweight gain and an increased liver weight due to hepatocellular hypertrophy at the next higher tested dose of 50 mg/kg bw/day. In order to calculate an Acceptable Daily Intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor has been selected to account for uncertainties in extrapolation from animal data to humans, variation within the human population, the quality of the experimental data, and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.05 mg/kg bw/day was established for trifloxystrobin.

METABOLISM AND TOXICOKINETICS ASSESSMENT

Plant Metabolism

Metabolism studies have been conducted in apples, cucumbers and wheat using two ^{14}C-ring-radiolabelled compounds, [glyoxylphenyl-U-^{14}C]-trifloxystrobin and [trifluoromethylphenyl-U-^{14}C]-trifloxystrobin. Penetration studies in apples showed that the rate of trifloxystrobin penetration into fruit tissues was relatively low, with ~82% of the applied radioactivity being located on the surface of the apple 14 days after last treatment (DALT). Similar studies with wheat showed that trifloxystrobin penetration of the wheat plant was quite rapid. Characterisation of the surface radioactivity revealed that trifloxystrobin is relatively stable (photolytically), with the parent compound comprising about 86 % of the surface total residues recovered (TRRs) after 14 days.

In contrast to the surface radioactivity, the penetrated radioactivity appears to undergo quite rapid breakdown. Up to 35 metabolite fractions were found in wheat, most of which constituted less than 1% of the TRRs. Interestingly, the number of metabolite fractions in apples and cucumbers was significantly lower than that for wheat. Irrespective of the observed differences in the number of metabolite fractions obtained with different plant species, the metabolic pathways for each crop are comparable. The primary residue component is the parent compound: trifloxystrobin and its isomers (CGA 331409, CGA 357262 and CGA 357261) made up ~92 % of the residues in apples (14 DALT), while in cucumbers (leaves and fruit), the residue was comprised mainly of trifloxystrobin (80 to 93 %), isomers of trifloxystrobin (2.3 to 3.8 %), and the demethylated derivative of trifloxystrobin, CGA 321113 (0.9 to 4.2 %).

Based on the metabolic studies conducted with wheat, apples and cucumbers, the metabolism of trifloxystrobin occurs primarily via:

- isomerisation to CGA 331409 (EZ-isomer), CGA 357262 (ZZ-isomer) and CGA 357261 (ZE-isomer);
- cleavage of the methyl ester group to form CGA 321113;
- hydroxylation of the trifluoromethylphenyl group to form NOA 414412 and NOA 417076;
- oxidation of the 2-ethylideneaminooxymethyl group to the corresponding carboxylic acids to form the isomeric metabolites NOA413161 and NOA 413163; and
- sugar conjugation of hydroxylated metabolites, to give their water-soluble derivatives.

Animal Metabolism

The metabolism of trifloxystrobin was investigated in rats, goats and poultry, and the metabolic pathways were found to be comparable in all three species. The principal route of elimination in all three species is via the faeces (60 to 80 % of the administered dose) and urine (10 to 35 % of dose), with ~85 % of the dose being eliminated in the first 48 to 78 hours. Characterisation of the radioactivity in rat excreta showed that the parent trifloxystrobin was the principal component of the faecal residue. In contrast, the metabolic profile of urine was complex, with about 27 metabolite fractions being isolated: no parent trifloxystrobin was present in urine, and individual fractions comprised less than 7% of the administered dose.

Characterisation of the radioactive tissue residues revealed that the parent trifloxystrobin was the principal residue component in the muscle, fat and skin, and egg yolk of laying hens. In contrast, the carboxylic acid derivative of trifloxystrobin (CGA 321113) was the major residue component in egg white and chicken liver. Analysis of the tissue residue composition of lactating goats revealed the presence of three main metabolite fractions – the parent compound and CGA 321113 (similar to poultry), along with amino acid conjugates (taurine and glycine) of CGA 321113. Amino acid conjugates of CGA 321113 were the principal residue component in goat liver and kidney. The CGA 321113 metabolite was the main residue component of muscle, and the parent trifloxystrobin was the principal residue component in milk and fat.

Overall, the metabolism of trifloxystrobin in animals is similar to that of plants, and occurs primarily via cleavage of the methyl ester group to form CGA 321113. In plants, the principal residue component is the parent trifloxystrobin, and the CGA 321113 metabolite does not comprise a significant portion of the residue. In contrast, CGA 321113 is the principal residue component in a number of animal tissues, with trifloxystrobin comprising a lesser (but still significant) proportion of the residue.

RESIDUES ASSESSMENT

Residue definition

It is concluded that the residue definition for trifloxystrobin should consist of the parent compound plus the metabolite CGA 321113 the demethylated derivative of trifloxystrobin, to cover the occurrence of all trifloxystrobin residues in both plant and animal commodities.

Analytical methods

Trifloxystrobin and the metabolite CGA321113 are quantified in plant material using an HPLC method. Briefly, the method involves extraction of residues from macerated solid samples (grapes and apples) with acetonitrile/water, and analysis by reverse phase HPLC with UV detection at 250 nm. Liquid commodities (juice and wine) are not treated in any way prior to analysis. The Limits of Quantitation for trifloxystrobin and CGA321113 are both 0.02 mg/kg.

Trifloxystrobin and CGA321113 are extracted from animal tissues with acetonitrile and water, then partitioned into hexane followed by solid phase extraction cleanup. Residues are quantified using GC with nitrogen-phosphorous detection. The LOQ for both analytes was 0.02 mg/kg in all samples except milk, where the LOQ was 0.01 mg/kg.

Residue trials in food commodities

Novartis Crop Protection Australasia Pty Ltd provided residue reports for numerous trials, conducted in both Australia and overseas, where apples, pears and grapes were treated with *Flint Fungicide*. The results obtained from the trials provided were summarised and the data corrected in order to reflect the maximum proposed use-pattern (application rate).

Pome fruit

The residue data reveal that trifloxystrobin residues in pome fruit range from <0.03 to 0.26 mg/kg (1x application rate, 35 day WHP). It is noted that the maximum value of 0.26 mg/kg was observed in one of the French trials, and appears to be an anomalous data point. In the absence of this data point, the trifloxystrobin residues ranged from <0.03 mg/kg to <0.16 mg/kg (STMR = <0.07 mg/kg; n=33). Therefore, an MRL of 0.3 mg/kg is recommended for trifloxystrobin residues in pome fruit, with a 35 day WHP.

Some of the data with re-treatment suggest that it makes little difference whether a 10 or 14 day interval is used between applications. The proposed re-treatment interval of 14 days is therefore considered acceptable.

Grapes

When *Flint Fungicide* was applied to grapes at the maximum proposed use-pattern (1x application rate with a 35 day WHP), the trifloxystrobin residues (the sum of trifloxystrobin and CGA 321113, expressed as trifloxystrobin equivalents) in grape berries ranged from <0.02 to 0.48 mg/kg. The STMR was 0.11 mg/kg (n=33). It is noted that the three highest

residue values (0.38, 0.44 and 0.48 mg/kg) were from German trials conducted during 1995-1996. In Australian trials, the trifloxystrobin residues in grapes ranged from <0.02 to 0.18 mg/kg (STMR = 0.10 mg/kg; n=18). On the basis of the available data, it is recommended that a trifloxystrobin MRL of 0.5 mg/kg be established for grapes (berries), with a 35 day WHP.

Processing

No reliable concentration factors could be determined from the apple residue trials since no quantifiable residues were present in raw or processed apple commodities. In the absence of adequate data, no MRL can be set for apple pomace. Apple pomace from treated apples must not be used as an animal feed commodity. There was no appreciable concentration of residues in washed, pureed or dried pears.

In grapes, trifloxystrobin and acid metabolite (CGA321113) residues were found to concentrate 2.3× in grape marc/wet pomace and 1.4× in raisins. No concentration of residues occurred in grape juice or wine. No MRL is necessary for dried grapes, as the MRL for grapes is adequate to cover residues in the dried fruit, allowing for the loss of moisture in the drying process. An MRL of 3 mg/kg is recommended for grape pomace (dry) [MRL for grapes 0.5 × concentration factor 2.3 × drying factor 90/40 = 2.6, rounded to 3].

Animal commodities

Animal transfer studies and MRLs

From the residue trials and processing studies, maximum residues likely to be present in grape pomace (dry) were determined to be approximately 3 mg/kg. No MRL was recommended for apple pomace (dry) because of inadequate data from the processing studies. Grape pomace (dry) may comprise up to 20% of the diet of beef cattle, giving an estimated maximum intake of trifloxystrobin residues of 0.6 ppm in the feed.

The animal feeding study in dairy cattle showed residues at or about the analytical Limit of Quantitation of 0.02 mg/kg in tissues and milk following oral dosing at 2 and 6 ppm in the diet (1× and 3× dose rates). Since intake of trifloxystrobin residues from consumption of treated produce is estimated at around 0.6 ppm, lower than the lowest dose level in the animal transfer study, finite residues are not expected in tissues or milk when the product is used as directed. Animal commodity MRLs are therefore set at or about the limit of quantitation of 0.02 mg/kg.

Estimates dietary intakes

The risk to human health from the use of trifloxystrobin is considered to be low. The chronic dietary risk is estimated by the National Estimate of Dietary Intake (NEDI) calculation, which is based on the Acceptable Daily Intake (ADI) for trifloxystrobin of 0.05 mg/kg body weight (bw) and the mean consumption of the relevant commodities for consumers aged 2 years and above. The ADI is set based on a NOEL of 5 mg/kg bw. The NEDI for trifloxystrobin was calculated to be 2.0% of the ADI. As it is widely recognised that this calculation is a gross overestimate of actual dietary intake, it is concluded that the chronic dietary exposure to trifloxystrobin is low and the risk is acceptable.

The chronic dietary risk was also estimated using ANZFA's Diamond modelling application, which show that intake of trifloxystrobin from the proposed use represents approximately 2.2% of the ADI, consistent with the NEDI calculation.

Bioaccumulation potential

The log P_{ow} value for trifloxystrobin was determined to be approximately 4.5. This log P_{ow} value suggests that trifloxystrobin has the potential to bioaccumulate in fat and tissues. However, animal transfer studies conducted in dairy cows showed that no finite residues were detected in animal tissues or milk when fed trifloxystrobin at 2 ppm in the feed for 28 consecutive days. It is concluded that trifloxystrobin and the acid metabolite (CGA321113) residues do not accumulate in animal tissues or fat. This is consistent with Environment Australia's conclusions relating to bioaccumulation.

MRL Standard

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

Table 1

Compound	Food			MRL (mg/kg)
Delete:				
CGA 279202				
	FI	0327	Bananas	T0.1
	FB	0269	Grapes	T3
	FP	0009	Pome fruit	T0.5
Add:				
Trifloxystrobin				
	FI	0327	Bananas	T0.1
	MO	0105	Edible offal (mammalian)	*0.05
	FB	0269	Grapes	0.5
	MM	0095	Meat (mammalian)	*0.05
	ML	0106	Milks	*0.02
	FP	0009	Pome fruit	0.3

Table 3

Compound	Residue
Delete:	
CGA 279202	(E,E)-methoxyimino-{2-[1-(3-trifluoromethyl-phenyl)ethylideneaminoxymethyl]-phenyl}acetic acid methyl ester (Temporary entry)
Add:	
Trifloxystrobin	Sum of trifloxystrobin and its acid metabolite

((E,E)-methoxyimino-[2-[1-(3-trifluoromethyl-phenyl)ethylideneaminooxymethyl]phenyl]acetic acid), expressed as trifloxystrobin equivalents.

Table 4

Compound	Food			MRL (mg/kg)
Add: Trifloxystrobin	AB	0269	Grape Pomace (dry)	3

The following withholding period is recommended in relation to the above MRLs.

Apples, pears and grapes
DO NOT HARVEST FOR 35 DAYS AFTER THE LAST APPLICATION

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Overseas registration status

Products containing trifloxystrobin are registered for use in several countries, on crops including pome fruit, cereals, grapes and bananas. The countries in which products are registered for use on grapes or pome fruit are shown in the table below.

Country	Approval type	Crop
Belgium	Provisional	Apples
Croatia	Definitive	Grapes, Pome fruit
UK	Provisional	Pome fruit
Israel	Definitive	Grapes, pome fruit
Macedonia	Provisional	Grapes
Moldavia	Definitive	Apples
New Zealand	Definitive	Pome fruit
Poland	Definitive	Pome fruit
Romania	Definitive	Pome fruit
Russian Federation	Definitive	Pome fruit
Slovenia	Definitive	Grapes, apples
South Africa	Definitive	Grapes, apples
Switzerland	Provisional	Grapes, pome fruit
Turkey	Definitive	Pome fruit
USA	Provisional	Grapes, pome fruit
Yemen	Definitive	Apples, grapes
Yugoslavia	Definitive	Pome fruit

Codex Alimentarius Commission MRLs

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

Potential risk to Australian export trade

In assessing the risk to Australian export trade, the destination, volume and value of treated commodities was considered:

Grapes

Table grape production in 1997 was approximately 63,000 tonnes, with a total grape production (including fresh, dried and wine processing) of about 940,000 tonnes. The estimated farmgate value of table grapes in 1996/7 was $106 m, while the total value of wine grape production was $532 m for the same period. The major destinations and export values of table grapes are shown in the table below.φ

Major destinations and export values of Australian table grapes in 1996/7

Importing country	Tonnes	Value ($ m)
Hong Kong	5,373	14.4
Singapore	4,897	12.4
Malaysia	4,973	12.0
New Zealand	2,070	4.0
Indonesia	5,197	12.9
Thailand	1,699	5.5

Sultana production was the major commodity for dried grapes, with approximately 25,000 tonnes produced in Australia in 1997. The estimated farmgate value of dried vine fruit in 1997 was $45 m, which comprised $35 m for sultanas, $5.6 m for raisins and $4.2 m for currants. The major importers of Australian dried vine fruits in 1997/8 were Germany ($5.6 m), Canada ($7.5 m), UK ($6.9 m), New Zealand ($4.3) and Japan ($1.3 m). It is noted that the value of exports to Germany and Canada in 1997/8 fell by approximately 60% from the previous year.

The major importers of Australian wines include the UK (102 ML), US (37 ML), New Zealand (21 ML) and Canada (9 ML). The value of wine exports in 1998/9 was approximately $990 m.ϕ

ϕ ABARE Commodity Statistics, 1999.

φ Data taken from Australian Horticultural Statistics Handbook 1999-2000.

Pome fruit

Major destinations and export value of Australian apples and pears in 1997/8

Importing country	Apples		Pears	
	Tonnes	Value ($ m)	Tonnes	Value ($ m)
Malaysia	12,976	11.2	4,928	5.5
Singapore	8,839	8.7	8,069	8.9
UK	2,906	7.3		
Sri Lanka	2,729	2.2		
Indonesia	1,748	1.7	2,090	2.3
Hong Kong	1,326	1.5	3,242	3.6
Taiwan	1,228	1.8		
Papua New Guinea	924	1.0	104	0.12
Canada			699	0.78
New Zealand			306	0.33

Table Grapes

Residues in grapes in the residue trials presented ranged from <0.02 – 0.18 mg/kg (excluding three anomalous German trials), with a median residue (STMR) of 0.10 mg/kg. It is noted that only 3 countries have MRLs for grapes, and these range from 0.5 mg/kg for South Africa to 3 mg/kg for Switzerland. Residues in grapes from the use of *Flint Fungicide* are expected to be well below these values.

The major importers of Australian grapes (Hong Kong, Singapore, Malaysia and Indonesia) do not have import tolerances for grapes. Any residue detection would therefore constitute a violation and the use of *Flint Fungicide* on grapes may therefore present a risk to Australia's trade in table grapes.

Wine

Processing studies on grapes for wine shows that trifloxystrobin (or acid metabolite CGA321113) residues do not concentrate in wine. Residues in wine were at or about the Limit of Quantitation of 0.02 mg/kg in the trials presented and therefore the likelihood of the presence of detectable residues in wine is low.

The major importers of Australian wine (US, UK, Canada and New Zealand) do not have import tolerances for trifloxystrobin in wine. Only Switzerland is known to have an MRL for wine, of 0.3 mg/kg. Any residue detection would therefore constitute a violation. Since detectable trifloxystrobin residues are not expected in wine, the use of *Flint Fungicide* on grapes is likely to present a low risk to Australia's trade in wine.

Dried grapes

Processing studies showed that while residues appeared to concentrate in the dried fruit, it was noted that residues did not concentrate when the loss of moisture was taken into account. The use of *Flint Fungicide* on grapes may result in finite residues in dried grapes.

It is not known whether any of the importing countries of Australian dried grapes have import tolerances. Any residue detection may therefore constitute a violation and the use of *Flint Fungicide* on grapes may therefore present a risk to Australia's trade in dried grapes.

Pome fruit

The recommended Australian MRL of 0.3 mg/kg for pome fruit is the same as or lower than that in overseas countries, with the exception of South Africa, which has an MRL for pome fruit of 0.1 mg/kg. Residues in pome fruit from the trials presented ranged from <0.02 mg/kg to <0.16 mg/kg (except one apparently anomalous result of 0.26 mg/kg), with a median residue of <0.07 mg/kg. Since residues in pome fruit are expected to be low, detection by importing countries is unlikely.

However, as finite residues in pome fruit may occur, the use of *Flint Fungicide* on pome fruit may present a risk to Australian trade. Although several countries have MRLs for trifloxystrobin on apples or pome fruit, of the major importers of Australian pome fruit, only the UK has an established MRL (1 mg/kg). Any detection of trifloxystrobin residues in Australian pome fruit in importing countries other than the UK would therefore constitute a violation.

Overall, the use of *Flint Fungicide* on grapes and pome fruit may present a risk to Australian trade as finite residues are expected in grapes, dried grapes and pome fruit. Major importing countries of treated produce do not have tolerances and therefore any residue detection would constitute a violation. There are no Codex MRLs for trifloxystrobin. The relevant industry bodies are expected to provide comment on this issue.

Finite residues are not expected to be present in animal tissues or milk from the use of treated produce in animal feeds. The use of *Flint Fungicide* is not expected to present a risk to Australia's trade in animal commodities.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Although trifloxystrobin is not currently on the NOHSC *List of Designated Hazardous Substances*, it has been determined that trifloxystrobin is a hazardous substance. This is based on evidence that trifloxystrobin is moderately irritating to the unwashed eyes of rabbits and has caused skin sensitization to guinea pigs in acute toxicity studies. The following risk phrases are allocated to trifloxystrobin:

R36	Irritating to eyes
R43	May cause sensitization by skin contact

The following safety phrases are allocated to trifloxystrobin:

S24	Avoid contact with skin
S25	Avoid contact with eyes

Trifloxystrobin is in the form of a fine white, odourless powder. It has low acute oral, dermal and inhalation toxicity in rats. It is not an eye irritant but is a slight skin irritant in rabbits. It is a skin sensitising agent in guinea pigs.

Flint Fungicide is a water dispersible granule formulation. It possesses low acute oral and inhalation toxicity in rats and low acute dermal toxicity in rabbits. The product is a slight skin irritant. Based on this information *Flint Fungicide* cannot be classified as hazardous.

Formulation, transport, storage and retailing

Flint Fungicide will be formulated overseas and imported into Australia in 1 kg sealed cartons. Transport workers, storepersons and retailers will handle the packaged product and could only become contaminated if the packaging were breached.

End use

Flint Fungicide is proposed for the control of powdery mildew and suppression of downy mildew of grapes and control of black spot (scab) of apples and pears, and powdery mildew of apples. It will be applied as a high volume (dilute) or a low volume (concentrate) spray, using airblast equipment. The proposed rate is 150-200 g/ha in a minimum 100L water/ha for low volume application or a minimum of 1000 L water/ha for high volume application at 10-14 day intervals. The label recommends not to apply *Flint Fungicide* more than 3 times per season.

The primary route of occupational exposure is dermal and ocular. Workers can be exposed to *Flint Fungicide* while mixing/loading, spraying and cleaning up spills and equipment. In addition, workers re-entering treated crops, for tending crops or for other agricultural practices, and those harvesting crops manually can be exposed to product residues.

In the absence of worker exposure data on trifloxystrobin and the product, NOHSC used the UK Predictive Exposure Model (POEM) and margin of exposure (MOE) to determine worker exposure. The MOE estimates are acceptable for high volume ground application of *Flint*

Fungicide when gloves are worn during mixing/loading. For low volume ground application of *Flint Fungicide*, the MOE from POEM estimates show that workers would require personal protective equipment when mixing/loading and during application. Cotton overalls, washable hat and elbow length PVC gloves should be worn during preparation and application of *Flint Fungicide*.

Entry into treated areas or handling treated crops

The main route of exposure upon re-entering sprayed areas is via dermal contact. No data are available on dislodgeable foliar residues of trifloxystrobin. However, there is a possibility of workers entering orchards to check the fruits or vineyards to check the grapevines. Considering the toxicity of the product (including skin sensitization) and its use pattern, a re-entry statement as follows, is recommended on the draft label:

"Do not allow entry into treated areas until the spray has dried. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist and a washable hat and chemical resistant gloves. Clothing must be laundered after each days use".

Recommendations for safe use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of clothing and elbow-length PVC gloves are recommended for mixers/loaders and applicators of *Flint Fungicide*.

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

Material Safety Data Sheet

Novartis Crop Protection Australasia Limited has produced MSDS for trifloxystrobin and *Flint Fungicide*. These should contain information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that their employees have ready access to it.

Flint Fungicide can be used safely if handled in accordance with the instructions on the product label. Additional information is available on the MSDS for *Flint Fungicide*.

ENVIRONMENTAL ASSESSMENT

Trifloxystrobin is proposed to be used in Australia in orchard and vineyard situations on apples, pears and grapes. The proposed use pattern is for three sprays spaced 14 days apart, applied as a foliar spray.

Environmental Fate

Hydrolysis

Two hydrolysis studies were provided with labels in alternate rings. Both showed the chemical to become more hydrolytically unstable as conditions became more basic. In the environmentally relevant pH range, the hydrolysis half life can be measured in terms of years (5-9) at pH 5, weeks (10-12) at pH 7, and hours (around 24-27) at pH 9 and at 20^{o}C. The main product detected is the parent acid metabolite CGA 321113, which is expected to be hydrolytically stable in the environmental pH range.

Photolysis

Atmospheric: Atmospheric degradation, modelled on the chemicals reaction with hydroxy radicals, indicated a short atmospheric half life between 18 and 24 hours under midday summertime conditions. This estimate should be treated with caution as so far, no measured rate values have been determined for this type of compound.

*Aqueous***:** Two tests showed that photolysis of the parent compound is rapid with a half life under 2 days. Isomerisation was the main result of photolysis initially, with all three possible isomers formed. Further degradation of these tended to form the main parent acid metabolite. Where the product was labelled in the trifluoromethyl-(u)-phenyl ring, further degradation led to a cleavage of the molecules between the two ring systems resulting in a large formation of the acetophenone metabolite CGA 107170.

Two tests investigating aqueous photolysis of the main metabolite, with radiolabelling in alternate rings were provided. This metabolite showed a rapid photolysis half life of less than 2 days under mid summertime conditions (less than 4 days under springtime conditions). Half lives considering all isomers and the parent acid were significantly longer, between 20 and 40 days.

*Soil***:** Two soil photolysis studies with radiolabelling in alternate rings were provided. Trifloxystrobin was rapidly metabolised in the soil surface to its acid derivative, regardless of irradiation indicating photolysis was not the factor controlling degradation. Half lives in irradiated and non-irradiated samples were all under 1 day in both tests. However, photolysis did seem to be a controlling factor with respect to degradation of the acid derivative although half lives were not determined in the tests.

Degradation in Soil and Water

Soils: Five tests with radiolabelling in the glyoxy-phenyl ring and one test with labelling in the CF_3-phenyl ring were provided covering a total of 7 different soil types. All showed that under aerobic conditions, trifloxystrobin was readily degraded with a half life under 2 days. The major metabolite was the parent acid CGA 321113 which had a much longer half life of from around 100 up to 493 days. However, where the soil was sterile, degradation was significantly retarded with a half life of trifloxystrobin in excess of 100 days. Degradation rates appeared to

be affected by temperature (slower dissipation with lower temperature) and soil moisture content (slower dissipation with lower moisture content). This held for both the parent and main acid metabolite. Under normal field conditions for temperature (20^oC) and moisture content (60%), mineralisation can be expected to be high, in the order of 50% or more. The observed rapid degradation appeared to be independent of soil type. However, where microbial activity was less in soils, the degradation rate was significantly slower. A detailed residue leaching study included a metabolism component and supported these results. Based on analysis of soil extracts, the parent compound was rapidly degraded to its hydrolysis product CGA 321113 with approximate half lives ranging from 0.5 day (sandy loam, silt loam, both sands) to 1 day (loamy sand, loam, and clay loam). CGA 321113 in turn slowly degraded, was incorporated into soil constituents (humic/fulvic acids and humin, ranging from 6.8 to 14.9% in loam, silt loam and clay loam), and was then slowly converted to $^{14}CO_2$, representing mineralisation of the radiolabelled portion of the molecule.

***Water*:** Two experiments were submitted with trifloxystrobin labelled in alternate rings. Systems consisted of river and pond water on a sediment layer. The parent compound disappeared rapidly from water bodies (half life around 1 day) with rapid formation of the acid metatolite CGA-321113 resulting. Some movement to sediment was observed to be almost immediate, and the level of non extractable activity in sediments increased gradually. Incomplete mineralisation was observed.

Under anaerobic conditions in the sediments, the parent compound degraded rapidly with a half life of 2-3 days. In sediments, the main metabolite was the acid CGA 321113.
Considering the water/sediment system as a whole, trifloxystrobin was rapidly degraded with a half life less than 3 days. The half life for the main metabolite was significantly lower, in excess of 300 days. As the parent degrades to the acid metabolite in sediments, movement of radioactivity back to the water column was observed, due to the higher solubility of the acid metabolite.

Ready biodegradability: Trifloxystrobin cannot be considered ready biodegradable based on a test following OECD guidelines. After 29 days, 0% biodegradation was observed.

Mobility
***Volatility*:** In a study designed to determine volatilisation of trifloxystrobin from leaf surfaces, results indicated up to 15% of the applied amount may volatilise from the leaf surface, with most of this occurring rapidly, ie within the first hour after application.

***Adsorption/desorption*:** One experiment in 5 soils was provided for both the parent and main metabolite. Trifloxystrobin showed Koc values ranging from over 1500 to almost 4000, and may be regarded as a strongly adsorbing compound. However, desorption coefficients were also high, ranging from over 2100 to almost 4000. The main acid metabolite exhibited far less tendency to adsorb in the same 5 soils with Koc values ranging from 84-197. As with the parent compound, desorption coefficients were of a similar order ranging from 51 to 383. For both these substances, the increase of the binding constants comparing the adsorption and desorption processes points to a partial irreversibility of the adsorption of trifloxystrobin to soil or to very slow desorption processes.

Leaching studies
Column Leaching Study: One column leaching study showed trifloxystrobin to be classified as immobile to slightly mobile. In five soils, the compound was retained almost entirely within

the top 2 cm with the exception of one sandy soil where it leached to a distance of 8 cm. The parent was metabolised to its acid derivative, especially in biologically active soils, and this compound was classified as slightly to moderately mobile.

Aged Residue Column Leaching: Three aged residue column leaching studies were provided where residues aged to approximate half life of the parent (1-2 days), and residues aged up to 46 days were used. The leaching behaviour of parent isomers CGA 357261 and CGA 331409 can be classified as 'immobile' to 'slightly mobile'. The mobility of aged residues (acid isomers and polar metabolites) of trifloxystrobin can be classified as 'slightly mobile' to 'moderately mobile', equivalent to the mobility of CGA 321113. These compounds were detected at the same leaching distances, independent of soil types. One of the more detailed studies concluded that residual trifloxystrobin was not significantly mobile in any of the soil types since it was found in the uppermost portions of the soil columns (0 to 12 cm). In contrast, CGA 321113, the major metabolite, was found to be mobile in all sandy soils having very low carbon contents (loamy sand, pure sand) and a little mobile in loamy soils (sandy loam, loam, silt loam and clay loam).

***Lysimeter/Field Leaching Study*:** One lysimeter study was provided. The study was conducted in soil characterised as a sand, over a test period of 90 days. Results revealed the vast majority of recovered radioactivity (> 90% at day 90) to be found in the first 30 cm. Radioactivity was detected periodically in the leachate and in the overflow. The study showed rapid degradation of the parent compound over the first 30 days of the study with the main acid metabolite being the predominant formation. A CO_2 evolution test was conducted to determine if the loss of radioactive mass balance was due to degradation of the test substance. Mineralisation was shown to be a major removal process.

Field Dissipation

Soils: Following bare ground application to eight different soil types at high rates, trifloxystrobin degraded rapidly and was not detected in soil layers below 10 cm. The ZE and ZZ parent isomers were observed up to day 28 in the 0-10 cm soil layer indicating their formation by photochemical processes on the soil surface, although their detections were generally only minor. The acid metabolite CGA 321113 (EE) was the major compound formed accounting for 30-55% at its peak in all soils. It was detectable, often in significant quantities during the first sampling period (Day 0). This metabolite showed some tendency to leach. Based on these results, kinetic evaluations were undertaken, and the general behaviour of trifloxystrobin in the field was explained as follows:

- In a first step, photolytic isomerisation of trifloxystrobin gives its ZE and ZZ parent isomers. Because of the short half lives of these, the ZE acid was formed rapidly. Consequently, higher amounts of ZE-acid were always found as compared to ZE and ZZ isomers.
- Parallel to the photolytic isomerisation, trifloxystrobin degrades in a fast and in a slower competitive step to form the EE parent acid. This is a major step with this being the major metabolite formed (30-50% at its peak).
- Degradation of this acid was the slowest of all observed processes in the field with half lives ranging from 39 to 104 days (typically, 72 days).

Water: An outdoor microcosm study examining the chemical fate of repeated applications of trifloxystrobin to aquatic ecosystems was provided. Sampling was conducted at all time points for 1.31, 4.10 and 12.3 µg/L dosing levels, and these data were used to calculate the half life of trifloxystrobin in microcosms treated after the 5th, 7th and 8th applications. These concentrations and application dates were selected to determine representative half life values over a range of dosing concentrations. Based on the data a representative half life for trifloxystrobin in the microcosm water was determined to be 0.28 days. The range of half lives was from 0.18-0.63 days indicating rapid degradation. The parent acid CGA 321113 was the major metabolite formed (higher than 80% of residual activity). Trifloxystrobin levels found in the sediments were erratic with no clear accumulation or decline trends able to be discerned.

Plants: No studies were provided.

Accumulation/Bioaccumulation

Neither trifloxystrobin or its major metabolite CGA 321113 are expected to accumulate in soils under the expected use pattern. The longer half life of the major metabolite indicates accumulation may be greater than the parent, but levels are expected to plataeu around 0.03 mg/kg with the parent expected to be undetectable in soil at the start of each new season.

Trifloxystrobin may be regarded as a lipophilic compound and a bioaccumulation study was provided to address potential accumulation in aquatic biota, using bluegill sunfish as the test organism. The bioconcentration factors of trifloxystrobin indicated a potential for limited bioconcentration in fish. However, trifloxystrobin was shown to be rapidly eliminated in the depuration phase of the study. Bioconcentration of the main acid metabolite, CGA 32113, from the water following the degradation of CGA 279202 is unlikely as this compound has a much lower octanol/water partition coefficient.

Environmental Toxicity

***Avian*:** Trifloxystrobin, administered as a single dose (acute oral) or for five days mixed in the diet, was shown to be non-toxic to bobwhite quail and mallard duck. Even after prolonged dietary exposure up to a dose level of 320 mg/kg feed (bobwhite quail) and 500 mg/kg feed (mallard duck) under laboratory conditions, the compound did not affect the birds or their reproduction.

***Aquatic*:** For fish, two freshwater and one saltwater species were tested under flowthrough conditions. Three invertebrate species and two algal species were also tested under flowthrough conditions. Trifloxystrobin is highly toxic to all trophic levels of the aquatic compartment under acute exposure. 96 hour LC_{50}'s for fish ranged from 15-78 ppb with rainbow trout being the most sensitive. For invertebrates, EC_{50}'s ranged from 9-34 ppb with mysid shrimp being the most sensitive. The green algae *Scenedesmus subspicatus* showed the highest intolerance to the chemical with an EC_{50} for growth rate of 5.3 ppb. Trifloxystrobin did not exhibit high toxicity to the aquatic macrophyte *Lemna gibba*, with an EC_{50} unable to be determined due to a lack of effects at concentrations over 1 ppm.

Four major metabolites detected during degradation studies were all tested for acute effects on fish, aquatic invertebrates and algae, and all showed significantly lower toxicity than the parent compound. The most toxic metabolite tested was the parent isomer with an LC50 of 900 ppb to fish, 1400 ppb to invertebrates and 1400 ppb to algae. Other metabolites exhibited LC_{50}/EC_{50} values ranging from 13.6 ppm to >200 ppm.

Chronic testing on fish and invertebrates also showed trifloxystrobin to be classed as highly toxic with NOEC's of 7.7 ppb and 2.76 ppb for fish and invertebrates respectively. However, chronic exposure is not expected to be of concern due to the chemicals rapid degradation under normal environmental conditions. Low acute to chronic ratios for both these trophic levels were determined.

A microcosm study failed to show treatment related effects of trifloxystrobin on complex ecosystems at repeated applications up to 12.3 ppb. The study involved six applications of trifloxystrobin with 1 week between applications and may be used as a worst case scenario for real world application. Levels of trifloxystrobin were observed to degrade rapidly and the chemical had largely been eliminated from the water column prior to the next application. As expected with an experiment of this type, great variability in plant and animal populations were observed. However, these were not statistically significant. No adverse or treatment related effects on the ecosystems were observed.

Non-target Invertebrates: Testing was performed on predators (ground beetle, mite, aphid and lady beetle); parasites (parasitic wasp); honeybees, earthworms and soil micro-organisms. Trifloxystrobin was classified as harmless to predator species except aphids where it was classified as harmful in this laboratory experiment. Some effect on the beneficial capability of lady beetles may be expected although its nature is difficult to determine as at the lower application rate, the chemical was classified as slightly harmful while it was classified as harmless at the higher application rate. Only a minimal impact may be expected on beneficial parasites based on the study provided, and negligible impacts can be expected for honeybees, earthworms or soil microorganisms.

Plants: No studies were provided.

PREDICTION OF ENVIRONMENTAL HAZARD

Trifloxystrobin has low water solubility and low vapour pressure. When present, it would be expected to associate with sediments. However, the chemical has been shown to be relatively unstable in the environment, rapidly isomerising and degrading to its principal acid metabolite. This main metabolite is relatively soluble in environmental terms, far more persistent and expected to be somewhat mobile in the environment. Studies were provided addressing four of the main metabolites behaviour and toxicity, and they are considered in this hazard assessment. Application of trifloxystrobin will occur in orchard situations to apples and pears, and in vineyards. Application will primarily be by ground rig, although the label does not preclude aerial application. As such, aerial calculations will be conducted when considering the aquatic hazard to determine if this method is environmentally acceptable.

Terrestrial organisms

Trifloxystrobin is practically non-toxic to birds and the environmental hazard to bird has been determined to be low.

Testing on terrestrial invertebrates such as beneficial predators and parasites was performed at a maximum of 5 times the highest application level proposed for Australia. Generally, the chemical was considered harmless to terrestrial invertebrates. However, the potential for adverse impacts exists with a predator aphid species proving sensitive to the chemical, and a classification of harmful being assigned in this case. Any adverse impacts occurring in the

field are expected to be shortlived. The half life of trifloxystrobin in the field is short, and recolonisation would be expected to occur rapidly from surrounding areas.

Honeybees were tested via contact and oral routes and no adverse impacts were observed in either case at 200 µg/bee indicating that trifloxystrobin may only be considered very slightly toxic to bees.

Soil dwelling invertebrates were tested using earthworms, and these organisms showed no sensitivity to trifloxystrobin at 1000 mg/kg soil suggesting a low environmental hazard to soil invertebrates. However, based on testing on terrestrial invertebrates, it may be expected that some impact may occur on some soil dwelling insects, although exposure through the soil is unlikely to be high, and any effects should be short-lived.
Testing showed no impact on soil microorganisms.

Aquatic organisms

Aerial Application:
Calculations showed the potential hazard to aquatic systems through either direct overspray or drift (using the AgDRIFT model) to be unacceptably high for most scenarios, and mitigation (eg through increasing buffer zones) could not alleviate this risk. As such, aerial application should not be conducted, and a label statement forbidding it has been included.

Ground Application
Using Ganzelmeier tables, it was shown clearly that amounts of spray drift likely to exist up to 30 m from the orchard scenarios result in Q-values in water indicating there was still likely to be an acute hazard to algae. Where orchards are directly juxtaposed with natural watercourses, that is trees within 20-50 m of water, these aquatic toxicities are likely to cause concern.

Tier 1 calculations from the AgDRIFT model suggest a potential concern from exposure to trifloxystrobin with Q values over 0.1, although this concern was less than those derived using Ganzelmeier tables. However, this model is suspected to understate drift, and Ganzelmeier calculations are considered more robust.

Mitigating Factors
Trifloxystrobin has shown itself to be unstable in aquatic situations in both laboratory and field studies with an aquatic half life well under one day. In a microcosm study, aquatic systems were repeatedly dosed with concentrations up to 12.3 µg/L. 80% of the application was in solution with 20% bound to soil. The aqueous component of the dose gave an expected concentration in water above the predicted EEC from calculations. No treatment related impacts were found on microcosm communities which included fish, invertebrates and aquatic flora at this level, and this test may be considered a “real world” scenario. Additionally, the water depth in permanent streams/rivers is expected to be greater than 15 cm and in the range 30-40 cm, therefore the hazard identified above is considered to be too high for a realistic Australian situation.

The rapid degradation of trifloxystrobin will expose aquatic systems to its metabolites. Using three times the maximum application rate (to reflect the use pattern of three applications and assuming 100% degradation to each metabolite with no further degradation), all major metabolites were calculated to have a low potential aquatic hazard.

Run-Off

Trifloxystrobin will be used as a foliar spray on established plants. It will be applied to runoff and therefore available to aquatic systems through both wash off from leaves, and from surrounding soil contaminated by the chemical, and a worst case calculation indicated that there is an unacceptable risk to nearby aquatic systems through runoff. However, in reality this is not expected to be the case. Trifloxystrobin has a very low water solubility and a high Koc. During any runoff, large amounts would be expected to partition to the soil, and the majority of any chemical entering the waterbody would be expected to do so adsorbed to soil and therefore not be readily bioavailable. Also, groundcover between rows would be expected to intercept significant amounts of the chemical. Additionally, trifloxystrobin has a short field half life of less than 5 days. With 10 days between applications, at least two half lives are expected before the next application and the chemical is expected to rapidly degrade after application, thereby reducing any chemical available for runoff between application and any storm event.

To further reduce concern surrounding exposure from runoff, a microcosm study was provided where the aquatic compartment was exposed through dosing at 6 consecutive applications up to 12.3 ppb. Of this, 20% was applied bound to soil to simulate runoff. This study is considered to be a real life situation and showed no treatment related impacts on microcosm communities including fish, invertebrates and aqautic flora.

Conclusions

Environment Australia has assessed data in support of *Flint Fungicide*. The application contains adequate environmental fate and toxicity data to demonstrate that the use of this product when used according to the label and good agricultural practice is unlikely to result in harmful effects on environmental organisms. The greatest environmental hazard from use of the product is to algae as a result of off target movement during application. However, aerial application has been forbidden on the label. This along with the very short half life of trifloxystrobin in the environment and with the provision of “real world” testing demonstrating no treatment related impacts on aquatic communities, supports the conclusion of a low environmental hazard based on the proposed use pattern and with ground application equipment.

EFFICACY AND SAFETY ASSESSMENT

Flint Fungicide (active ingredient trifloxystrobin) is to be registered for control and suppression of five important diseases of apple, pear and grape. It belongs to a new chemical group (strobilurin or Group K) and as such provides new options to better manage the development of resistant strains of downy mildew, powdery mildew and black spot to fungicides when used on grape, apple and pear crops.

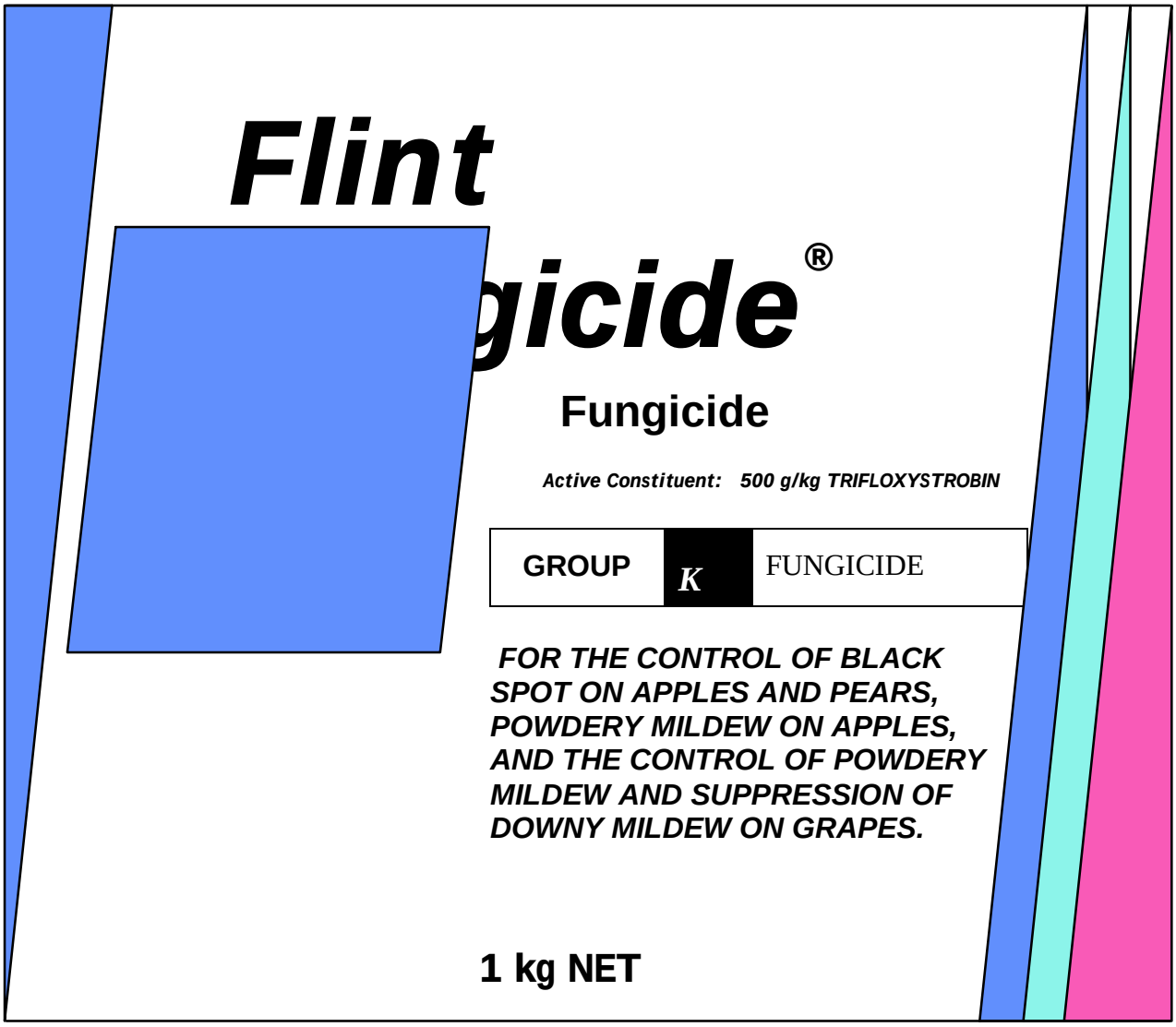
Data is presented from 13 field trials from representative grape growing districts, and 12 field trials from representative pome fruit growing districts throughout Australia. The data supports the label claims for the ability for *Flint Fungicide* to control powdery mildew and suppress downy mildew on grapes, to control black spot on apples and pears and powdery mildew on apples. Trials were conducted in a suitable manner to allow comparisons to be made between *Flint Fungicide* and standard fungicide treatments. These trials showed that in most cases this product gave control equivalent to, or better than, existing registered standards. When used as indicated on the draft label it has been shown to be safe to the crops on which it is to be registered.

LABELLING REQUIREMENTS

The following is the draft label for the product:

CAUTION

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



Novartis Crop Protection Australasia Pty Limited,
140-150 Bungaree Road, Pendle Hill, NSW,

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*

NRA Approval No.: 52035/

NOVARTIS

DIRECTIONS FOR USE

Restraint:
DO NOT add a surfactant to this product.
DO NOT apply aerially.

Crop	Disease	Rate	1.1.1.1.1 Critical Comments
Apples, pears	Protective control of **Apple scab,** *Venturia inaequalis* and **Pear scab,** *Venturia pirina;* **Powdery Mildew** *Podosphaera leucotricha* of apples	**Dilute spraying** 10 g/ 100L water Concentrate Spraying Refer to the **Application in Apple and Pear Orchards and Vineyards** section.	**This use is subject to an AVCARE anti-resistance strategy**. Follow a complete disease management program for scab by rotating with fungicides from unrelated chemical groups as per the Avcare fungicide resistance management guidelines. *FLINT FUNGICIDE* should be applied as a block of three treatments at 10 day intervals over flowering and into early fruit development. DO NOT apply more than 3 applications of *FLINT FUNGICIDE* per season (part of the Avcare anti-resistance strategy). When used over flowering, apply *FLINT FUNGICIDE* alone. Apply with a DMI (Group C) scab fungicide if intervals are longer than 10 days. Apply by dilute or concentrate spraying equipment. Apply the same amount of product to the target crop whether applying this product by dilute or concentrate spraying methods.
Grapes	**Powdery Mildew** *Uncinula necator* Suppression of **Downy Mildew** *Plasmopara viticola*	**Dilute spraying** 15 g/ 100L water Concentrate Spraying Refer to the **Application in Apple and Pear Orchards and Vineyards** section.	This use is subject to an AVCARE anti-resistance strategy. Follow a complete disease management program for powdery mildew by rotating with fungicides from unrelated chemical groups as per the Avcare fungicide resistance management guidelines. Apply a block of three applications of *FLINT FUNGICIDE* at 14 day intervals. *FLINT FUNGICIDE* may be applied from early flowering till pre bunch closure. DO NOT apply more than three applications of *FLINT FUNGICIDE* per season (part of the Avcare anti-resistance strategy). Apply by dilute or concentrate spraying equipment. Apply the same amount of product to the target crop whether applying this product by dilute or concentrate spraying methods.

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

WITHHOLDING PERIODS:
Apples, Pears, Grapes: **DO NOT HARVEST FOR 35 DAYS AFTER APPLICATION.**

GENERAL INSTRUCTIONS
Mixing - Add the required amount of product directly to the spray tank and mix well.

Tank Mixing - When mixing *FLINT FUNGICIDE* and other water dispersible granule (WG) or wettable powder (WP) formulations, ensure they are added and mixed well prior to adding emulsifiable concentrate (EC) or suspension concentrate (SC) products. Wettable powder (WP) formulations should be pre-mixed separately and then added to the spray tank.

Application in Apple and Pear Orchards and Vineyards
Apply by high volume (dilute) sprayer or by concentrate sprayer as recommended in the Directions for Use.

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

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

EXAMPLE ONLY

1. Dilute spray volume as determined above: for example 1000 L/ha
2. Your chosen concentrate spray volume: for example 250 L/ha
3. The concentration factor in this example is: 4 X (ie, 1000L ÷ 250 L = 4)
4. If the dilute label rate is 10 mL/100L, then the concentrate rate becomes 4 x 10, that is 40 mL/ 100 L of concentrate spray.

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

Compatibility
DO NOT mix *Flint Fungicide* with surfactants as damage to flowers and russetting may occur. Before applying *Flint Fungicide* in mixtures with other fungicides and insecticides test a small amount of the mixture on a small area of the crop first to ensure the product are physically compatible and that no unacceptable phytotoxicity occurs.

Fungicide Resistance Warning

GROUP	*FUNGICIDE*
K	

Flint Fungicide is a member of the strobilurin group of fungicides. For fungicide resistance management *Flint Fungicide* is a Group K fungicide.
Some naturally occuring individual fungi resistant to *Flint Fungicide* and other Group K fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungi population if these fungicides are used repeatedly. These resistant fungi will not be controlled by *Flint Fungicide* and other Group K fungicides, thus resulting in a reduction in efficacy and possible yield loss.
Since the occurrence of resistant fungi is difficult to detect prior to use, Novartis Crop Protection Australasia Pty Limited accepts no liability for any losses that may result from the failure of *Flint Fungicide* to control resistant fungi.

PROTECTION OF LIVESTOCK
Low hazard to bees – product may be applied to plants at any time of day.
DO NOT allow stock to graze in any treated areas.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Dangerous to fish and other aquatic organisms. DO NOT apply under meteorological conditions or from spraying equipment which could be expected to cause spray to drift onto adjacent areas, particularly streams, rivers or other waterbodies.

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

INTEGRATED PEST MANAGEMENT

Flint Fungicide is suitable for use in IPM programmes. *Flint Fungicide* is harmless to predators in situations where integrated mite control is practised.

STORAGE AND DISPOSAL

Store in closed original container in a dry, well ventilated place as cool as possible out of direct sunlight.

Rinse containers before disposal. Add rinsings to the spray tank. DO NOT dispose of undiluted chemicals on site. Dispose of at a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

PRECAUTION

Re-entry Period: DO NOT allow entry into treated areas until the spray has dried. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist and a washable hat and chemical resistant gloves. Clothing must be laundered after each day's use.

SAFETY DIRECTIONS

Will irritate the skin. Avoid contact with skin. Wash hands after use.

When opening the container, preparing spray and using the prepared spray, wear:

- **cotton overalls buttoned to the neck and wrist,**
- **a washable hat and**
- **elbow-length PVC gloves.**

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

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone 131 126.

MATERIAL SAFETY DATA SHEET:

If additional hazard information is required refer to the Material Safety Data Sheet. For a copy phone 1800 025 931 or visit our website at *www.cp.au.novartis.com*

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY

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

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.

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NRA PUBLICATIONS ORDER FORM

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

David Hutchison
Agricultural and Veterinary Evaluation Section
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:
David Hutchison at (06) 6272 3218.

Name (Mr, Mrs, Ms, Dr)_____

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Company/organisation _____

Address _____

Contact phone number (___) _____

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Make cheques payable to 'National Registration Authority'.

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Card number _____/_____/_____/_____ Expiry date ...../...../.....

Signature_____ Date _____