

**Public Release Summary
on**

**Evaluation of the new active
PYRACLOSTROBIN
in the product
CABRIO FUNGICIDE**

Australian Pesticides and Veterinary Medicines Authority

September 2003

**Canberra
Australia**

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FOREWORD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Office of Chemical Safety), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (Worksafe Australia) and State departments of agriculture and environment.

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

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

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

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the APVMA. Alternatively, the reports can be viewed at the APVMA Library, 1st Floor, 22 Brisbane Avenue, Barton, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Program Manager—Pesticides Division, Australian Pesticides and Veterinary Medicines Authority, PO Box E240, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

AC	active constituent
ACR	Acute to chronic ratio
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose (for humans)
BBA	Biologische Bundesanstalt für Land – und forstwirtschaft
bw	bodyweight
CRP	Chemistry and Residues Program
d	day
DAT	Days After Treatment
DM	Dry Matter
DT₅₀	Time taken for 50% of the concentration to dissipate
DT₉₀	Time taken for 90% of the concentration to dissipate
EA	Environment Australia
E_bC₅₀	concentration at which the biomass of 50% of the test population is impacted
EC₅₀	concentration at which 50% of the test population are immobilised
EC	Emulsifiable Concentrate
EEC	Estimated Environmental Concentration
E_rC₅₀	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
FAO	Food and Agriculture Organisation of the United Nations
F₀	original parent generation
FW	Fresh Weight
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Haematocrit
HDPE	High-density polyethylene
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography <i>or</i> High Performance Liquid Chromatography
HPLC-UV	High Performance Liquid Chromatography with Ultra-Violet Detector
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC₅₀	concentration that kills 50% of the test population of organisms
LD₅₀	dosage of chemical that kills 50% of the test population of organisms
LC-MS/MS	liquid chromatography, mass spectroscopy
LOEC	Lowest Observable Effect Concentration
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified

mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration/Level
OC	Organic Carbon
OM	Organic Matter
PHED	Pesticide Handlers Exposure Database
PHI	Pre-harvest interval
po	oral
POEM	Predictive Operator Exposure Model (UK)
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TRR	Total Radioactive Residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
mg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHO	World Health Organisation
WHP	Withholding Period

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *CABRIO FUNGICIDE*, which contains the new active constituent pyraclostrobin. The product is proposed to be used for the control of leaf speckle and leaf spot/Yellow Sigatoka in bananas and downy and powdery mildew in grapevines.

Responses to this Public Release Summary will be considered prior to registration of the product. They will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling. Certain sections of this publication make reference to use of *CABRIO FUNGICIDE* on peanuts however the request for this use has been withdrawn. Comment is therefore not sought on this use.

Copies of full technical evaluation reports on pyraclostrobin, covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request (see order form on last page). They can also be viewed at the APVMA library located at the APVMA offices, First Floor, 22 Brisbane Avenue, Barton ACT 2604.

Written comments should be received by the APVMA by 30 September 2003. They should be addressed to:

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Applicant

BASF Australia Ltd

Product Details

It is proposed to register *CABRIO FUNGICIDE*, containing pyraclostrobin at 250g/L as an emulsifiable concentrate formulation. *CABRIO FUNGICIDE* will be imported fully formulated and packaged in 1 L, 5 L, 10 L and 20 L containers.

Pyraclostrobin is a new fungicide of the strobilurin group. It is closely related to azoxystrobin and trifloxystrobin, compounds which have been registered for use as fungicides in Australia for several years. With respect to fungicide resistance, pyraclostrobin is classed as a Group K Fungicide.

Application is as a foliar spray to control leaf speckle (*Mycosphaerella musae*) and leaf spot (*Mycosphaerella musicola*) of bananas and downy mildew (*Plasmopara viticola*) and powdery mildew (*Uncinula necator*) of grapevines.

Overseas registrations: Pyraclostrobin formulations are currently registered in the following countries; Argentina, Brazil, Colombia, EU, Germany, Great Britain, Paraguay, South Africa

and Switzerland. It is used for the control of various diseases of crops including bananas, cereals, grapevines and soybeans.

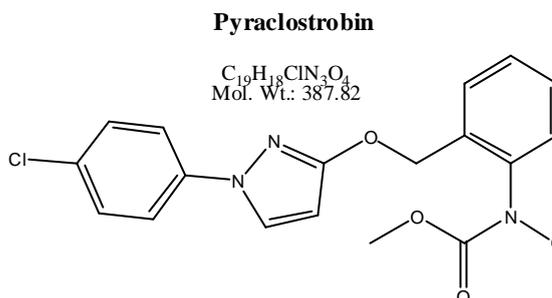
CHEMISTRY AND MANUFACTURE

Active Constituent

The chemical active constituent has the following properties:

Common Name:	Pyraclostrobin
Chemical Name (IUPAC):	methyl <i>N</i> -(2- {[1-(4-chlorophenyl)-1 <i>H</i> -pyrazol-3-yl]oxymethyl}phenyl)- <i>N</i> -methoxy carbamate
CAS Registry Number:	175013-18-0
Empirical Formula:	C ₁₉ H ₁₈ ClN ₃ O ₄
Molecular Weight:	387.82
Physical form:	Crystalline powder
Colour:	White to light beige
Odour:	Odourless
Melting Point:	63.7-65.2 °C
Density:	3.367 g/cm ³
Octanol/water partition coefficient (K _{OW}):	Log P _{0/w} =3.99
Vapour pressure at 25 °C:	Not applicable

Chemical Structure:



Summary of the APVMA's Evaluation of pyraclostrobin active constituent

The Chemistry and Residues Program has evaluated the chemistry aspects of pyraclostrobin active constituent (manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable.

Pyraclostrobin is a new active constituent and there is no compendial specification available for pyraclostrobin. On the basis of the data provided, the following minimum compositional standard has been established for pyraclostrobin:

Active constituent	Minimum content
Pyraclostrobin	Not less than 950 g/kg

Other characteristics of pyraclostrobin (toxicology, environmental fate etc) are covered in subsequent sections of this Public Release Summary.

Formulated Product

Distinguishing name: Cabrio Fungicide
Formulation type: Emulsifiable Concentrate (EC)
Active constituent concentration: 250 g/L pyraclostrobin

Physical and Chemical Properties of the Product

Physical state: Liquid
Colour: Dark yellow
Odour: Moderate naphthalene like odour
Density or specific gravity: 1.055 g/mL at 20 °C
Acidity, alkalinity or pH value: 6.4 (1% aqueous solution)
Flash point, flammability and auto flammability: 98 °C
Storage stability: Stable for at least 2 years when stored under ambient temperature.

Summary of the APVMA's Evaluation of Cabrio Fungicide

The Chemistry and Residues Program (CRP) has evaluated the chemistry aspects of Cabrio Fungicide (manufacturing process, quality control procedures, batch analysis results, analytical methods, storage stability, and specifications for containers for the product) and found them to be acceptable.

TOXICOLOGICAL ASSESSMENT

PYRACLOSTROBIN

Evaluation of Toxicology

The toxicological database for pyraclostrobin, 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 (ADI and ARfD) at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

In rats given an oral dose of 5 or 50 mg/kg bw of radiolabelled pyraclostrobin, about 50% of the dose was absorbed. An initial peak in blood or plasma levels after 30 minutes, was followed by a secondary peak at 8 or 24 hours after dosing. The gastrointestinal tract and contents had the highest levels of radioactivity 30 minutes after dosing, with only the liver, and to a lesser extent the kidneys, recording higher levels than plasma. Only a very small percentage of the administered dose was found in tissues 42 and 72 hours after administration of 5 and 50 mg/kg bw doses, respectively. In the first 48 hours after dosing, the majority of the ¹⁴C-dose was eliminated in the faeces (74-91%) and the urine (10-13%). In bile-cannulated animals, 35-38% of the dose was excreted in the bile within 48 hours after dosing. The elimination of pyraclostrobin was similar in rats pre-treated with non-radiolabelled compound for 2 weeks.

After 4 or 8 hours of dermal exposure of male rats to radiolabelled pyraclostrobin (0.8, 4 and 18 mg/kg bw), up to 2.6% of the dose was absorbed. Systemic absorption was not affected by increasing the dose per unit area of skin.

In an *in vitro* study, in which ¹⁴C-pyraclostrobin (15, 75 and 375 µg active ingredient/cm²) was applied to rat and human skin for 24 hours, 21-51% (rat) and 3-8% (human) of the dose was absorbed.

Acute Studies

Pyraclostrobin has low acute oral (LD₅₀ >5000 mg/kg bw, no deaths) and dermal (LD₅₀ >2000 mg/kg bw, no deaths) toxicity and has moderate inhalation toxicity (LC₅₀ 310–1070 mg/m³) in rats. It is a slight skin and eye irritant in rabbits, but is not a skin sensitiser in guinea pigs, using the Magnusson-Kligman Maximisation Test.

Cabrio Fungicide (250 g/L pyraclostrobin) was of moderate acute oral toxicity ($LD_{50} = 260$ mg/kg bw in females and was between 500 and 2000 mg/kg bw in males) and low acute inhalation ($LC_{50} = 3760$ mg/m³ in males and 3720 mg/m³ in females) and dermal ($LD_{50} >4000$ mg/kg bw) toxicity in rats. It was a moderate eye and skin irritant in rabbits and it was not a skin sensitiser in guinea pigs.

Short-Term Studies

There were no effects in mice given pyraclostrobin by oral gavage at doses of 0 and 4 mg/kg bw/day for 1 week or if it was administered in the diet at 0 and 18 ppm for males and 0 and 15 ppm for females for 1 week.

There were no effects in rats fed pyraclostrobin in the diet at 0 and 34 ppm or given pyraclostrobin by oral gavage at doses of 0 and 4 mg/kg bw/day for 1 week.

Pyraclostrobin was administered to rabbits by gavage at doses of 0 and 4 mg/kg bw/day for 1 week, and also in the diet at concentrations designed to provide 0 and 4 mg/kg bw/day for 1 week. There was no clear effect of treatment on food consumption and bodyweight gains.

Pyraclostrobin was administered to rats at 0, 20, 100, 500 and 1500 ppm in the diet for 4 weeks. There were no mortalities or treatment-related clinical signs. Body weight gain and food consumption were reduced at 500 and 1500 ppm and food efficiency was inferior at 1500 ppm. At 500 and/or 1500 ppm, erythrocyte counts, haemoglobin and mean corpuscular haemoglobin concentration were reduced, and mean corpuscular volume, platelet counts and prothrombin time were increased. Total bilirubin was increased and glucose, globulin, inorganic phosphate and total protein were slightly reduced at 1500 ppm. At 500 and/or 1500 ppm, alanine aminotransferase, alkaline phosphatase and serum cholinesterase were reduced. At 1500 ppm, urine volume was increased and urine specific gravity was decreased. Spleen weights were increased and the incidences of mucosal hyperplasia in the duodenum and extramedullary haematopoiesis in the spleen were increased at 500 and 1500 ppm. In the liver, hepatocellular hypertrophy was increased at 1500 ppm (males) and diminished fat storage occurred at 500 and 1500 ppm.

Pyraclostrobin was administered dermally to rats at 0, 40, 100 and 250 mg/kg bw/day for 4 weeks. There were no mortalities, but scale formation and erythema occurred on the treated skin at 250 mg/kg bw/day. In males, body weight gain was slightly reduced at 250 mg/kg bw/day and food efficiency was inferior at 100 and 250 mg/kg bw/day. There were no treatment-related effects on open field observations, haematology, clinical chemistry and urinalysis parameters. At 250 mg/kg bw/day, uterus weight was increased and was associated with an increase in dilation of the lumen. In the area of treated skin, epidermal thickening and hyperkeratosis were increased at 100 and 250 mg/kg bw/day.

Pyraclostrobin was administered to mice at 0, 50, 150, 500, 1000 and 1500 ppm in the diet for 3 months. There were no treatment-related mortalities or clinical signs. Since many effects occurred in a single sex, only the concentration at which these effects occurred has been stated, for simplicity. Body weight gain was reduced at 50 ppm and above and food efficiency was inferior at 1000 and 1500 ppm. Red blood cell values, haemoglobin, haematocrit, mean corpuscular volume and mean corpuscular haemoglobin were reduced at 1500 ppm and leucocyte counts, lymphocytes and monocytes were reduced at 500 ppm and above. Eosinophils were decreased at all doses and platelets increased at 500 ppm and above. At 1000 and/or 1500 ppm, cholesterol was increased and total protein and globulin were reduced. Urea was increased at 150 ppm and above and triglycerides were decreased at all doses. At 500 ppm and above, liver weight was reduced, and was accompanied by less fatty infiltration in the liver at 1500 ppm. The incidence and/or severity of thickening of the duodenal mucosa (500 ppm and above), erosions or ulcers in the glandular stomach, atrophy

of the thymus gland (150 ppm and above) and apoptotic bodies in follicles of the mesenteric lymph node (500 ppm and above) were increased. Decreased vacuolation in cells of the X-zone in the adrenal cortex (150 ppm and above) and fewer lipid vacuoles in the kidneys (500 ppm and above) also occurred. There was no NOEL.

Pyraclostrobin was administered to rats at 0, 50, 150, 500, 1000 and 1500 ppm in the diet for 3 months. There were no mortalities or treatment-related clinical signs. Since many effects occurred in a single sex, only the concentration at which these effects occurred has been stated, for simplicity. At 500 ppm and above, body weight gain and food consumption were reduced, with inferior food efficiency recorded at 1000 and 1500 ppm. At 1000 and/or 1500 ppm, erythrocyte counts, haemoglobin and haematocrit were reduced and reticulocytes, prothrombin time, leucocyte counts, polymorphonuclear neutrophils and lymphocytes were increased. Mean corpuscular volume was increased at 500 ppm and above. At 1000 and/or 1500 ppm, bilirubin and erythrocyte cholinesterase were increased and globulin, triglycerides, creatinine and serum cholinesterase were reduced. Albumin was increased and alanine aminotransferase, alkaline phosphatase and cholesterol reduced at 500 ppm and above. At 1000 and 1500 ppm, urine was discoloured and cloudy, urine volume was increased and urine specific gravity was decreased. The number of crystals in the urinary sediment was slightly increased at 1500 ppm. Adrenal gland (1500 ppm) weight was reduced, whereas ovary (1500 ppm) weight was increased. An increase in spleen weights at 500 ppm and above was associated with distension of sinusoids (1000 and 1500 ppm), extramedullary haematopoiesis and histiocytosis (150 ppm and above). Liver weight was increased in females at 1500 ppm, whereas in males a reduction in organ weight was seen at 150 ppm and above, which reflected opposing changes such as diminished fat storage in the liver and hepatocellular hypertrophy (500 ppm and above). An increase in the incidence and/or severity of mucosal hyperplasia in the duodenum occurred at 500 ppm and above. The NOEL was 50 ppm (4 mg/kg bw/day in males and females).

Pyraclostrobin was administered to dogs at 0, 100, 200 and 450 ppm in the diet for 3 months. There were no mortalities, but vomiting and diarrhoea occurred at 450 ppm. At 450 ppm, body weight gain and food consumption were reduced and food efficiency was inferior. There were no treatment-related effects on ophthalmology parameters. At 450 ppm, platelet counts were increased (females), whereas total protein, albumin, globulin (both sexes), glucose (females) and liver weights (females) were reduced. In the duodenum, thickening of the wall and mucosal hypertrophy occurred in both sexes at 450 ppm. The NOEL was 200 ppm (6 mg/kg bw/day in males and females).

Long- Term Studies

In a carcinogenicity study, pyraclostrobin was administered to mice at 0, 10, 30 and 120 ppm, and to females only at 180 ppm (0, 1, 4 and 17 mg/kg bw/day in males and 0, 2, 5, 21 and 33 mg/kg bw/day in females) in the diet for 18 months. There were no treatment-related mortalities or clinical signs, but body weight gain was reduced in males at 120 ppm and females at 180 ppm. There were no treatment-related effects on food consumption and efficiency or water consumption. Circulating monoblasts were increased in females at 180 ppm, but this parameter was not assessed in other treated females. Liver weights were reduced in males at 120 ppm. There were no treatment-related pathology or neoplastic findings. The NOEL was 30 ppm (4 mg/kg bw/day in males and 5 mg/kg bw/day in females).

In a chronic study, pyraclostrobin was administered to male and female rats at 0, 25, 75 and 200 ppm in the diet for 24 months. There were no treatment-related mortalities or clinical signs. Body weight gain was reduced in both sexes at 200 ppm, but there were no treatment-related effects on food consumption and efficiency. There were no treatment-related effects on haematology parameters, but alanine aminotransferase (males)

and alkaline phosphatase (both sexes) levels were reduced at 200 ppm. There were no treatment-related effects on organ weights and pathology. The NOEL was 75 ppm (3 mg/kg bw/day in males and 5 mg/kg bw/day in females).

In a carcinogenicity study, pyraclostrobin was administered to male and female rats at 0, 25, 75 and 200 ppm in the diet for 24 months. There were no treatment-related effects on mortality or clinical signs, but body weight gain (both sexes) and food consumption (females) were reduced at 200 ppm. There were no treatment-related effects on differential blood counts. At 200 ppm, absolute liver weight (females) was reduced and the incidences of liver necrosis (males), liver adenomas and erosion and ulcers in the glandular stomach (males) were increased. The NOEL was 75 ppm (3 mg/kg bw/day in males and 5 mg/kg bw/day in females).

Pyraclostrobin was administered to male and female dogs at 0, 100, 200 and 400 ppm in the diet for 12 months. There were no mortalities, but vomiting and diarrhoea occurred at 400 ppm. In females at 400 ppm, body weight gain and food consumption were reduced and food efficiency was inferior. There were no treatment-related effects on ophthalmology parameters. At 400 ppm, leucocyte (males) and platelet (both sexes) counts were increased, whereas total protein, albumin, globulin and cholesterol were reduced in both sexes. Liver weight was reduced in females at 400 ppm. There were no treatment-related pathology findings. The NOEL was 200 ppm (5 mg/kg bw/day in males and females).

Reproduction and Developmental Studies

Pyraclostrobin was administered to rats at 0, 25, 75 and 300 ppm (0, 3, 8 and 33 mg/kg bw/day) in the diet over 2 generations. There were no treatment-related mortalities or clinical signs, but body weight gain and food consumption were slightly reduced in adults at 300 ppm. There were no effects on fertility, gestation, parturition and pup survival in the F₀ or F₁ generation. There were no treatment-related effects on organ weights and pathology in adult rats. In F₁ and F₂ pups at 300 ppm, body weight gain was reduced. There was a slight delay in vaginal opening in F₁ pups at 300 ppm. The NOEL for general toxicity was 75 ppm (8 mg/kg bw/day) and for reproduction toxicity was 300 ppm (33 mg/kg bw/day), the highest concentration tested.

Pyraclostrobin was administered to female rats at 0, 10, 25 and 50 mg/kg bw/day by gavage on days 6-19 of gestation. There were no mortalities or treatment-related clinical signs. At 25 and/or 50 mg/kg bw/day, body weight gain, carcass weight and food consumption were reduced. There were no treatment-related findings on litter and foetal parameters. There were no treatment-related pathology findings in adult animals. The incidence of dilated renal pelves, incomplete ossification of sternebra and rudimentary cervical ribs were slightly increased on a foetal and litter basis at 50 mg/kg bw/day. The NOEL for maternal effects was 10 mg/kg bw/day and for developmental effects was 25 mg/kg bw/day.

Pyraclostrobin was administered to female rabbits at 0, 5, 10 and 20 mg/kg bw/day by gavage on days 7-28 of gestation. There were no treatment-related mortalities, but blood in the bedding and reduced defecation occurred at 10 and 20 mg/kg bw/day. Body weight gain and food consumption were reduced in does from all treated groups. Early resorptions were increased at 10 and 20 mg/kg bw/day, which was associated with a reduction in the number of live young at 20 mg/kg bw/day. Gravid uterus weight and foetal body weight were reduced at 10 and 20 mg/kg bw/day, but there were no visceral or skeletal abnormalities in foetuses. Maternotoxicity was observed at all doses and the NOEL for developmental effects was 5 mg/kg bw/day.

Pregnant rabbits were given pyraclostrobin by oral gavage at doses of 0, 1, 3 and 5 mg/kg bw/day on days 7-28 of gestation. Food consumption and bodyweight gain were transiently reduced immediately after dosing, but over the entire dosing period there was no difference between control and treated groups. Embryo/fetal growth and survival were unaffected by treatment with pyraclostrobin, but examination of fetuses was not undertaken. The overall NOEL for maternotoxicity was 3 mg/kg bw/day.

Genotoxicity

In the presence and absence of metabolic activation, pyraclostrobin was not mutagenic in the Ames Test (20-5000 µg/plate) in *Salmonella typhimurium* and *Escherichia coli* strains, or in a forward mutation assay (0.625-20 µg/mL) at the HGPRT locus in Chinese hamster ovary cells and did not cause an increase in chromosomal aberrations (0.005-25 µg /mL) in Chinese hamster V79 cells. Using rat hepatocytes *in vitro*, unscheduled DNA synthesis was not induced by pyraclostrobin at concentrations up to 0.5 µg/mL. In an *in vivo* study, pyraclostrobin was not genotoxic in the micronucleus assay in mouse bone marrow cells after single oral doses of 75, 150 and 300 mg/kg bw.

Neurotoxicity Studies

Pyraclostrobin (0, 100, 300 and 1000 mg/kg bw) was administered to rats as a single gavage dose. There were no mortalities, but diarrhoea (300 and 1000 mg/kg bw/day) and piloerection (females at 1000 mg/kg bw/day) were observed after dosing. Body weight gain was reduced in males at 1000 mg/kg bw/day. There were no treatment-related effects on behaviour and motor activity parameters on days 7 and 14, or neuropathology findings.

Pyraclostrobin was administered to rats at 0, 50, 250, 750 (males only) and 1500 ppm (females only) in the diet for 3 months. The equivalent doses of pyraclostrobin were 0, 4, 17 and 50 mg/kg bw/day in males and 0, 4, 20 and 112 mg/kg bw/day in females. There were no mortalities or treatment-related clinical signs. In males at 750 ppm and females at 1500 ppm, body weight gain and food and water consumption were reduced. Grip strength of the forelimbs was impaired in females at 1500 ppm. There were no treatment-related motor activity and neuropathology findings.

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 pyraclostrobin be included 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.

Acceptable Daily Intake (ADI)

The Acceptable Daily Intake is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOEL obtained in the most sensitive species. This NOEL is then divided by a safety factor, which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for pyraclostrobin was established at 0.03 mg/kg bw/day based on a NOEL of 3 mg/kg bw/day in a 24 month dietary study in rats and an overall NOEL of 3 mg/kg bw/day for maternal toxicity in rabbit developmental studies. A 100-fold safety factor was used in recognition of the extensive toxicological database available for pyraclostrobin.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event. The ARfD is derived from the lowest single or short term dose which causes no effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The highest acute dose of pyraclostrobin at which no evidence of toxicity was detected was 5 mg/kg bw in a rabbit developmental study. The ARfD was established at 0.05 mg/kg bw on the basis of this NOEL and using a 100-fold safety factor.

RESIDUES ASSESSMENT

Metabolism

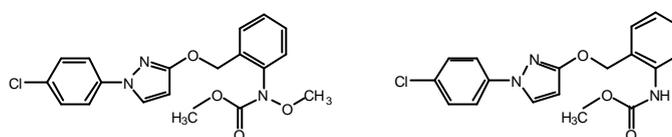
The metabolism of pyraclostrobin was investigated in rats, hens, goats, potatoes, wheat and grapes. In plants the predominant residue component was the parent compound with significant amounts of the N-desmethoxy metabolite also present. In animals pyraclostrobin was converted to a range of components including the N-desmethoxy metabolite and metabolites hydroxylated on the chlorophenyl ring. The analytical methods for residues in animal commodities measure the sum of pyraclostrobin and related metabolites following hydrolysis.

Potato plants were treated with 6 foliar applications of [¹⁴C-tolyl]- or [¹⁴C-chlorophenyl]-pyraclostrobin. Total radioactive residues (TRR) of the chlorophenyl labelled test substance in green plant matter were 19.6 mg equiv./kg and 69.6 mg equiv./kg 7 days after the third and sixth applications respectively. Total radioactive residues of the tolyl labelled test substance in green plant matter were 9.9 mg equiv./kg and 47.8 mg equiv./kg 7 days after the third and sixth applications respectively. TRRs in tubers collected 7 days after 3 or 6 applications were 0.01-0.05 mg equiv./kg for both label positions. Greater than 90% of the radiolabels were extracted from green plants with methanol. Approximately 40% of the tolyl radiolabel was extracted from tubers using methanol, compared to 50-70% of the chlorophenyl label. The lower extractability of the tolyl label was explained by the incorporation of the label into natural products via tryptophan. The extractability of the radiolabels from tubers was comparable or slightly better using methanol:water (70:30) as the extraction solvent. The parent compound was the predominant residue component in foliage accounting for 50-60% of the TRR. The parent compound was also a significant residue in tubers of plants treated with the chlorophenyl label (20-30% of TRR), although only small amounts were observed in tubers from plants treated with the tolyl label. The desmethoxy metabolite accounted for up to 21% of the TRR in foliage and 6% of the TRR in tubers. L-Tryptophan accounted for up to 30% of the TRR (tolyl label) in tubers. In potatoes the proposed metabolic transformations included desmethoxylation at the oxime ether bond, hydroxylation of the tolyl or chlorophenyl rings to give glucosides or methoxy metabolites, cleavage of the ring system to give a chlorophenyl pyrazole metabolite or formation of L-tryptophan via an anthranilic acid derivative.

Wheat plants were treated with 2 foliar applications of pyraclostrobin uniformly labelled with ¹⁴C in either the tolyl or chlorophenyl ring at stem elongation and beginning of flowering. Total radioactive residues in mature samples harvested 41 days after the last treatment were highest in straw followed by chaff, forage and grain. Total radioactive residues following application of the tolyl- or chlorophenyl label were comparable, except in grain where the TRR was approximately 4-fold higher following application of the tolyl label. It was postulated that certain metabolites containing the tolyl portion of the molecule were preferentially translocated into grain after cleavage of the parent molecule. Extractability of the radiolabels in methanol/water was typically 70-80% for forage and straw and 50-70% for grain. Pyraclostrobin was a significant residue component accounting for up to 57%, 56% and 36% of the TRR in forage, straw and grain respectively. The desmethoxy metabolite accounted for up to 13%, 15% and 10% of the TRR in forage, straw and grain respectively. Tryptophan accounted for 23% of the TRR in grain. Metabolism of pyraclostrobin in wheat occurred mainly by N-desmethoxylation. Both pyraclostrobin and the desmethoxy metabolite were hydroxylated and further converted to glucoside conjugates. In grain, cleavage of the parent compound was an important pathway with incorporation of the tolyl fragment into tryptophan. A structural isomer of pyraclostrobin was identified and postulated to be a product of photolysis rather than enzymatic transformation. The metabolite accounted for <5% of the TRR and or <0.1 mg equiv./kg in all cases.

Grapevines were treated with 6 foliar applications of pyraclostrobin uniformly labelled with ^{14}C in either the tolyl or chlorophenyl ring, with the last spray applied at berry ripening. Total radioactive residues in grapes sampled 40 days after the last application were 0.95-1.56 mg equiv./kg. The extractability of the radiolabels in methanol was 84-87%. The parent compound was the major residue in fruit accounting for 56-62% of the TRR. The desmethoxy metabolite accounted for 11-17% of the TRR in fruit. Up to 3 minor metabolites were characterised, although none accounted for >5% of the TRR. The proposed metabolic pathways involved N-desmethoxylation of the tolyl side chain and methoxylation of the tolyl ring. The chlorophenylpyrazole portion of the molecule was also N-hydroxylated and converted to a glucoside conjugate.

In plants the predominant residue component was the parent compound. Smaller amounts of the N-desmethoxy metabolite were present, usually at levels greater than 10% of the TRR. In potato tubers and wheat grain a significant amount of the tolyl portion of the molecule was incorporated into the naturally occurring amino acid tryptophan. Smaller amounts of radioactivity were incorporated into other endogenous substances such as cellulose and lignin.



Pyraclostrobin (BAS 500F) N-desmethoxy metabolite (BF 500-3)

Laying hens were dosed orally for 7 consecutive days with pyraclostrobin uniformly labelled with ^{14}C in either the tolyl or chlorophenyl ring. The dose levels were equivalent to 12 ppm in the diet. The hens were sacrificed 23 hours after the last dose. Approximately 87-93% of the totally administered radioactivity was recovered in the excreta. Radioactivity in eggs was only 0.05% of the total dose. Total residues were highest in liver (0.32-0.47 mg equiv./kg) followed by kidney (0.12-0.29 mg equiv./kg), fat (0.055-0.058 mg equiv./kg) and muscle (0.007-0.009 mg equiv./kg). The extractability of the radiolabels in organic solvents and water was approximately 50% for liver, 54-66% for eggs and 96-99% for fat. Treatment of liver with pronase and acid hydrolysis released a significant portion of the previously unextracted radiolabel. The majority of the unextracted radiolabel appeared to be bound to liver proteins. The parent compound accounted for 9-15% of the TRR in fat and eggs, however it was not present in liver. The desmethoxy metabolite was a significant metabolite in fat and eggs accounting for 27-39% and 8-11% of the TRRs respectively. The desmethoxy metabolite was not observed in liver. A glucuronide metabolite of the desmethoxy metabolite accounted for 11-13% of the liver TRR. A number of minor metabolic pathways were also identified including:

- Hydroxylation of the ring systems followed by glucuronidation
- Oxygenation of the parent compound at the chlorophenyl ring para-position with shift of the Cl-atom to the meta-position
- Cleavage of the parent compound at the methylene bridge

Lactating goats were dosed orally for 5 consecutive days with pyraclostrobin uniformly labelled with ^{14}C in either the tolyl or chlorophenyl ring. The dose levels were equivalent to 12 ppm in the diet (low dose) or 50 ppm in the diet (high dose). The goats were sacrificed 23 hours after the last dose. Approximately 60-74% and 62-66% of the totally administered doses were recovered in the excreta of low dose goats and high dose goats respectively. Excretion in milk accounted for 0.1-0.3% (low dose) and 0.2-0.5% (high dose) of the total dose. Total radioactive residues were highest in liver, followed by fat which was comparable to kidney and then muscle. The parent compound was the predominant residue in fat and muscle accounting for greater than 75% of the TRRs. In milk and kidney extracts the parent compound could not be separated from the desmethoxy metabolite and the two components

were quantified as a sum. The sum of parent compound and desmethoxy metabolite accounted for approximately 20% of the TRRs in milk and kidney. The parent compound accounted for only 2-9% of the liver TRR with the desmethoxy metabolite accounting for 1-2%. A number of minor metabolites were identified in milk, liver and kidney. The 3 key transformations in the goat were:

- N-desmethoxylation
- Hydroxylation of the chlorophenyl, tolyl and/or pyrazole rings
- Cleavage of the molecule at the methylene bridge between the ring systems.

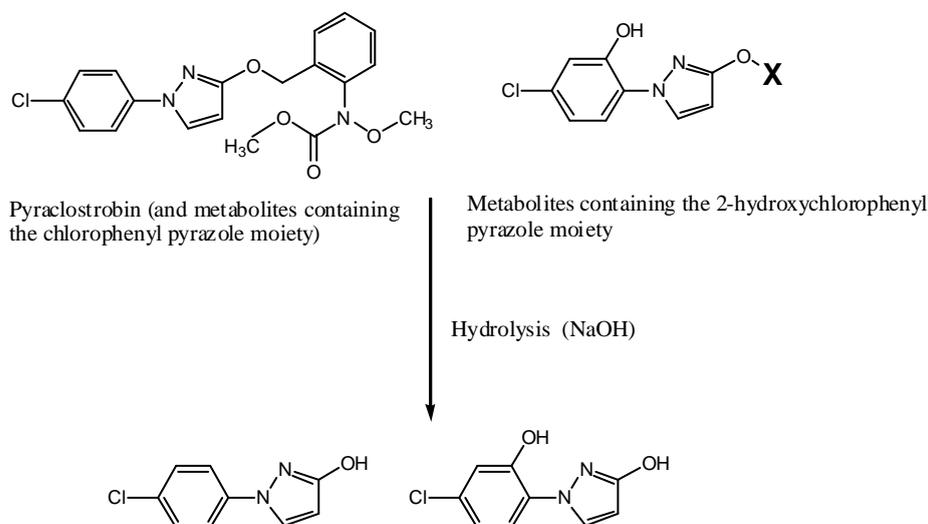
Acid hydrolysis of liver samples containing the chlorophenyl label converted the majority of the radioactivity to two chlorophenylpyrazole compounds. The results of the acid hydrolysis indicated a useful approach to a common moiety analytical method.

Analytical methods

Residues of pyraclostrobin and the desmethoxy metabolite in plant matrices are determined by HPLC-UV following solvent extraction and clean-up by column chromatography on C18 and silica gel. The parent compound and its metabolite are resolved by HPLC and quantitated by comparison with external standards. The validated LOQ for each analyte is 0.02 mg/kg.

Residues of pyraclostrobin in eggs, fat, kidney, liver, milk and muscle are determined by HPLC-UV following solvent extraction and cleanup-up on a silica gel column. The validated LOQ for tissues and eggs is 0.05 mg/kg and the validated LOQ for milk is 0.01 mg/kg.

Residues of pyraclostrobin and its metabolites containing the chlorophenylpyrazole moiety or the 2-hydroxychlorophenylpyrazole moiety in cattle tissues and milk can also be determined by a common moiety method. Samples of fat, kidney, liver, milk and muscle are hydrolysed under basic conditions. The extracts are then cleaned up by silica gel chromatography. The target analytes of 1-(4-chloro-phenyl)-1H-pyrazol-3-ol and 1-(4-chloro-2-hydroxy-phenyl)-1H-pyrazol-3-ol are determined by LC-MS-MS (all matrices) and GC-MS (milk only). The method was validated by analysing samples fortified with pyraclostrobin and a model metabolite hydroxylated at the 2-position on the chlorophenyl ring. For each target analyte the validated LOQ for tissues is 0.05 mg/kg and the validated LOQ for milk is 0.01 mg/kg. Residues of the target analytes are expressed as parent compound equivalents and summed to give a total residue. The LOQ for the total residue expressed as pyraclostrobin is 0.02 mg/kg for milk and 0.1 mg/kg for tissues.



Residues in poultry tissues and eggs are determined by a similar common moiety method. The target analytes in the poultry method are 1-(4-chloro-phenyl)-1H-pyrazol-3-ol and 1-(3-

chloro-4-hydroxy-phenyl)-1H-pyrazol-3-ol. The LOQs for total residues expressed as parent equivalents are 0.1 mg/kg for eggs and tissues.

Storage stability

Storage stability data were generated for a range of plant commodities including peanut nutmeat, peanut oil, wheat grain, wheat straw, sugarbeet tops, sugarbeet roots, tomatoes and grape juice. Fortified residues of pyraclostrobin and BF 500-3 were stable for at least 19 months when samples were stored frozen. Samples from residue trials were stored frozen for less than 19 months prior to analysis. The results obtained in the crop residue trials are considered an accurate reflection of the residues present at sampling.

Residues of pyraclostrobin and the metabolite BF 500-10 (model compound for metabolites with 2-hydroxylation in the chlorophenyl ring) were stable in fortified liver, muscle and milk when samples were stored frozen for up to 8 months. Samples from the dairy cow transfer study were stored frozen for a maximum of 3 months (milk) and 6.5 months (tissues). The results from the cow transfer study are considered to be an accurate reflection of the residues present at sampling.

Residue definition

Based on the metabolism data, residues data and analytical methodology the following residue definitions are appropriate:

Commodities of plant origin: Sum of pyraclostrobin and the N-desmethoxy metabolite, expressed as pyraclostrobin.

Commodities of animal origin [mammalian only]: Sum of pyraclostrobin and metabolites hydrolysed to 1-(4-chloro-phenyl)-1H-pyrazol-3-ol and 1-(4-chloro-2-hydroxy-phenyl)-1H-pyrazol-3-ol, expressed as pyraclostrobin.

Commodities of animal origin [poultry only]: Sum of pyraclostrobin and metabolites hydrolysed to 1-(4-chloro-phenyl)-1H-pyrazol-3-ol, expressed as pyraclostrobin.

Residue trials

Australian and overseas residue data for bananas, grapes and peanuts were evaluated. The residue data were adequate to allow the establishment of MRLs for bananas, grapes and related animal feeds. Adequate data were provided to allow the establishment of MRLs for commodities of animal origin at the limits of analytical quantitation.

The reported residue levels in the following section refer to residues measured as the sum of pyraclostrobin and BF 500-3, as per the residue definition for commodities of plant origin.

Bananas

Three trials were conducted in Australia on bananas that had bunch covers in place for most or all of the applied sprays. Residues of pyraclostrobin in whole bananas harvested 0 days after 3-8 applications at 100 g ai/ha were <0.02, <0.02 and 0.24 mg/kg. Residues of BF 500-3 (N-desmethoxy metabolite) were all <0.02 mg/kg.

A total of 10 trials were conducted on bananas in Costa Rica, Ecuador, Colombia, Guatemala, Mexico, and on the island of Martinique. Residues in whole bananas from covered and uncovered bunches were investigated in all trials. The product was applied in significantly lower volumes compared to the Australian trials (20-34 L/ha compared to 220-240 L/ha) to simulate aerial application spray volumes. Residues of pyraclostrobin and BF 500-3 in whole bananas from covered or uncovered bunches harvested 0 days after 8 applications at 100 g ai/ha were all <0.02 mg/kg.

An MRL of *0.02 mg/kg is suitable for bananas, provided they are bagged at the time of application. The label should clearly indicate that the approved use is for bagged bananas only. A withholding period is not required (ie. 0 days).

Grapes

Residue trials conducted in Australia and overseas were evaluated.

Residues in grapes harvested 21 days after application at rates consistent with Australian GAP were 0.10, 0.11, 0.12, 0.14, 0.43, 0.48, and 0.93 mg/kg. The STMR is 0.14 mg/kg and the HR is 0.93 mg/kg.

An MRL of 2 mg/kg is appropriate for grapes when Cabrio Fungicide is applied at 10 g ai/100L with a 21 day withholding period.

The mean processing factor for wet grape pomace was 4× (n=4). Based on the 21 day PHI data the HR for wet pomace is 3.7 mg/kg and the STMR is 0.56 mg/kg. Assuming a dry matter content of 40%, the HR for dry pomace is 9.3 mg/kg and the STMR is 1.4 mg/kg. An MRL of 10 mg/kg is appropriate for grape pomace expressed on a dry weight basis.

A total of 4 wine-making studies were conducted on red and white grapes containing incurred residues of pyraclostrobin and BF 500-3. Grapes were processed into red and white wine. In each study a subsample of the must was heated prior to fermentation. Total residues in red and white wine were <0.04 mg/kg. The processing factors for conversion of grapes to wine were <0.04 to <0.1. A separate MRL is not required for wine as residues will be adequately covered by the entry for grapes.

Livestock dietary exposure and animal commodity MRLs

Lactating dairy cows were fed pyraclostrobin in the diet for 28 consecutive days at levels equivalent to 8.8, 27.2 and 89.6 ppm in the diet.

Residues of the parent compound were <LOQ (<0.01 or <0.05 mg/kg) in whole milk, skim milk, muscle, fat, kidney and liver of cows from all dose groups. Finite residues of the parent compound (0.016-0.044 mg/kg) were only observed in cream of cows dosed at the 89.6 ppm level.

Total residues of pyraclostrobin and metabolites convertible to the chlorophenylpyrazole and 2-hydroxychloropyrazole analytical targets were <LOQ (<0.1 mg/kg) in muscle and fat at all feed levels. Finite residues were observed in liver at all dose levels and kidney at the highest dose level only. Total residues in liver were <0.1-0.32 mg/kg, 0.46-0.61 mg/kg and 2.1-2.8 mg/kg for the 8.8 ppm, 27.2 ppm and 89.6 ppm dose groups respectively. Total residues in kidney were 0.37-0.40 mg/kg for the 89.6 ppm dose group and <0.1 mg/kg for the lower dose groups.

In the highest dose group the total residues in milk plateaued within 7 days of dosing. Total residues in milk were all <LOQ (<0.02 mg/kg) for the 8.8 ppm dose group. Total residues in milk peaked at 0.024 mg/kg and 0.18 mg/kg for the 27.2 ppm and 89.6 ppm dose groups respectively.

Total residues in cream were 0.021-0.33 mg/kg, <0.02-0.056 mg/kg and 0.13-0.26 mg/kg for the 8.8 ppm, 27.2 ppm and 89.6 ppm dose groups respectively. In skim milk finite residues were only observed in the 89.6 ppm dose group at 0.039-0.10 mg/kg.

The results of the dairy cow transfer study are in contrast to those observed in the goat metabolism study, particularly in relation residues observed in fat. The residues of parent compound are compared in the following table:

Study	¹⁴ C label position	Dose, ppm in feed (mg/kg bw)	Pyraclostrobin in fat, mg equiv./kg or mg/kg
Goat	Chlorophenyl	12.23 (0.95)	0.069
	Chlorophenyl	78.13 (2.72)	0.819
	Tolyl	12.19 (0.7)	0.061
	Tolyl	69.86 (1.37)	0.318
Cow	-	8.8 (0.22)	<0.05
	-	27.2 (0.67)	<0.05
	-	89.6 (2.40)	<0.05

The goat study indicates significant fat solubility of the parent compound, however, residues >0.05 mg/kg were not reported in cow fat, even at the highest dose level. The goat metabolism study is therefore used as a conservative estimate of potential residues in mammalian fat.

Sample	Observed HR, mg/kg	Study feed level, ppm	Expected residue ¹ , mg/kg, from stated dietary exposure	
			0.28 ppm in diet ²	4.65 ppm in diet ³
Liver	0.32	8.8	<0.1	0.17
Kidney	<0.1	8.8	<0.1	<0.1
Milk	<0.02	8.8	<0.02	<0.02
Cream	0.033	8.8	<0.02	<0.02
Muscle	<0.1	8.8	<0.1	<0.1
Fat	0.819	78.1	<0.05	<0.05

1. Estimated residue in fat is for parent compound only based on goat metabolism study. Residues in other tissues are based on the cow transfer study and are expressed as pyraclostrobin following analysis by the common moiety method.
2. Assumes grape pomace containing pyraclostrobin at the STMR consumed at 20% of the diet
3. Assumes grape pomace containing pyraclostrobin at the HR consumed at 50% of the diet

Based on the expected dietary burden of livestock the following MRLs are recommended:

Edible offal, mammalian *0.1 mg/kg
 Meat, mammalian [in the fat] *0.1 mg/kg
 Milks *0.02 mg/kg

Laying hens were dosed with pyraclostrobin at 3 ppm in the diet for 30 consecutive days. Total residues of pyraclostrobin and metabolites convertible to the chlorophenyl pyrazole and the 3-hydroxychlorophenylpyrazole analytical targets were <0.1 mg/kg in eggs, liver, muscle and fat.

The maximum expected dietary burden for poultry is 42× lower than the feed level that resulted in <LOQ residues in the feeding study. Total residues in poultry commodities are expected to be <LOQ (<0.1 mg/kg). The following MRLs are appropriate:

Poultry meat [in the fat] *0.1 mg/kg
 Poultry, edible offal *0.1 mg/kg
 Eggs *0.1 mg/kg

Spray drift

The APVMA is currently developing formal operating principles and registration requirements in relation to spray drift [see http://www.apvma.gov.au/chemrev/APVMA_spray_drift_proposal.pdf].

Although a formal guideline for risk assessment is still in development, the following is considered to be a conservative assessment of the spray drift risk associated with Cabrio Fungicide.

The product is to be applied by ground application only. If it is assumed that the application rate for bananas and grapes is 100 g ai/ha and 5% of the application rate (5% of 100 g ai/ha = 5 g ai/ha) drifts onto adjacent grazing land with a density of 1500 kg DM/ha then the potential residue on the pasture is 3.3 mg/kg DM.

Sample	Observed HR, mg/kg	Study feed level, ppm	Expected feed level, ppm	Expected residue, mg/kg
Liver	0.32	8.8	3.3	0.12 (common moiety)
Kidney	<0.1	8.8	3.3	<0.1 (common moiety)
Milk	<0.02	8.8	3.3	<0.02 (common moiety)
Cream	0.033	8.8	3.3	<0.02 (common moiety)
Muscle	<0.1	8.8	3.3	<0.1 (common moiety)
Fat (goat)	0.819	78.1	3.3	<0.05 (parent compound)

Total residues are predicted to be <LOQ in milk and all tissues except liver. The predicted total residue in liver (0.12 mg/kg) is above the LOQ for total residue when measured by the common moiety method. The available residue decline information indicates that total residues in liver should decline with a half life of approximately 3 days. Given that liver residues are rapidly depleted and the assumption of 5% drift by ground application is likely to be a conservative over estimate, it is concluded that the risk of finite residues in animal tissues through spray drift contamination is low.

Estimated dietary intakes

The chronic dietary exposure to pyraclostrobin is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and dietary intake data from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with *Guidelines for predicting dietary intake of pesticide residues (revised)* [World Health Organisation, 1997].

The NEDI for pyraclostrobin is equivalent to 1% of the ADI. It is concluded that the chronic dietary exposure is small and the risk is acceptably low.

The acute dietary exposure is estimated by the National Estimated Short Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR using 97.5th percentile food consumption data from the 1995 National Nutrition Survey of Australia.

Commodity	NESTI as % of ARfD	
	2-6 years old	2 years old and above
Meat (mammalian) [in the fat]	2.7	1.6
Edible offal (Mammalian)	0.2	0.6
Milks	3.1	1.2
Banana	1.3	0.4
Dried grapes	14.0	3.9
Grapes	33.5	14.2
Wine	0.02	1.4
Poultry meat [in the fat]	2.4	1.3
Poultry, Edible offal of	0.1	0.7
Eggs	0.8	0.3

The NESTIs for all relevant commodities are less than the ARfD for the population groups 2-6 years old and 2 years and above. It is concluded that the acute dietary exposure is small and the risk is acceptably low.

Bioaccumulation potential

The log $P_{o/w}$ for pyraclostrobin is 3.99 indicating some potential for preferential accumulation in fat. In the lactating goat study total radioactive residues were approximately 4 times higher in fat compared to muscle.

Detectable residues are not expected to occur in animal commodities based on a conservative assessment of livestock dietary exposure and animal transfer factors.

Recommendations

MRL changes

The following changes will be made to the *MRL Standard*:

Table 1

Compound	Food	MRL (mg/kg)
Add:		
Pyraclostrobin	FI 0327 Banana	*0.02
	MO 0105 Edible offal (Mammalian)	*0.1
	PE 0112 Eggs	*0.1
	DF 0269 Dried grapes	5
	FB 0269 Grapes	2
	MM 0095 Meat [mammalian] [in the fat]	*0.1
	ML 0106 Milks	*0.02
	PM 0111 Poultry, Edible offal of	*0.1
	PM 0110 Poultry meat [in the fat]	*0.1

Table 3

Add:	Pyraclostrobin	Commodities of plant origin: Sum of pyraclostrobin and the N-desmethoxy metabolite, expressed as pyraclostrobin. Commodities of animal origin [mammalian only]: Sum of pyraclostrobin and metabolites hydrolysed to 1-(4-chloro-phenyl)-1H-pyrazol-3-ol and 1-(4-chloro-2-hydroxy-phenyl)-1H-pyrazol-3-ol, expressed as pyraclostrobin. Commodities of animal origin [poultry only]: Sum of pyraclostrobin and metabolites hydrolysed to 1-(4-chloro-phenyl)-1H-pyrazol-3-ol, expressed as pyraclostrobin.
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Table 4

Compound	Animal Feed Commodity	MRL (mg/kg)
Add: Pyraclostrobin	Grape pomace, dry	10

The MRL recommendations indicated above will be conveyed to Food Standards Australia New Zealand (FSANZ) for consideration for incorporation into Standard 1.4.2 of the Food Standards Code and consequent adoption into the State/Territory food legislation.

Withholding periods

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

BANANAS: NOT REQUIRED WHEN USED AS DIRECTED

GRAPES: DO NOT HARVEST FOR 21 DAYS AFTER APPLICATION

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ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Relevant Export Commodities, Overseas Registration Status and MRLs, and Potential for Undue Risk to Australian Trade

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

As pyraclostrobin is a relatively new chemical, very few overseas registrations have been achieved in relevant importing countries. Pyraclostrobin formulations are currently registered in the following countries; Argentina, Brazil, Colombia, EU, Germany, Great Britain, Paraguay, South Africa and Switzerland. There are no Codex MRLs for pyraclostrobin.

Bananas

The volume of bananas exported in 1999/2000 (12.5 tonnes) accounted for less than 0.01% of the total production volume for 1999 (225,166 tonnes).

Major export markets for bananas in 1999/2000 are shown below (Australian Horticultural Statistics Handbook 2000/2001)

Country	Volume, tonnes	Value, \$
New Zealand	1.3	14,600
Brunei	8.1	32,300
Indonesia	3.1	3,900
Total	12.5	50,800

Residue data showed that residues were <LOQ in 12 out of 13 trials where bunch covers were in place at the time of spraying. It is common practice to use bunch covers when cultivating bananas in Australia and the use of the product will be limited to bagged bananas.

Residues of pyraclostrobin in commodities exported to New Zealand would be covered by an appropriate MRL entry in the Food Standards Code. There is no indication that other export markets would have suitable residue tolerances in place. Relevant registrations to date are bananas, Colombia and an application for an import tolerance is included in an application for registration in USA.

The volume of bananas exported from Australia accounts for only a very small proportion of total domestic production of each commodity. It is concluded that the risks to export trade in bananas are small.

Wine

The total exports of Australian wine in 2001-2002 were 417 ML valued at \$2 billion (Australian Commodity Statistics 2002).

The 10 largest export markets for Australian wine by value are shown below (Australian Commodity Statistics 2002).

Destination	Value, \$ million
United Kingdom	843
United States	583

Canada	124
New Zealand	85
Germany	48
Ireland	43
Netherlands	33
Japan	30
Switzerland	30
Sweden	25

The Australian wine industry has mechanisms in place to advise growers on the use of pesticides in wine grapes and manage potential residues in wine. The Australian Wine Research Institute makes recommendations on export harvest intervals for Australian growers. Individual wineries may also make specific recommendations on pesticide use to contracted growers.

Relevant registrations to date are grapevines, Germany and Switzerland. The EU submission includes an application for an MRL of 2 mg/kg to cover imported wine. This level is the same as the proposed Australian MRL.

Overseas processing studies indicate that residues of pyraclostrobin are not expected to occur in wine produced from grapes treated with Cabrio Fungicide. Given that detectable residues are not expected to occur and that the industry has residue management strategies in place, the use of Cabrio Fungicide is unlikely to unduly prejudice export trade in wine.

Table Grapes

Total exports of table grapes in 1999/2000 were 35,129 tonnes valued at approximately \$74 million (The Australian Horticultural Statistics Handbook). The 5 largest export markets for Australian table grapes in 1999/2000 are shown below:

Destination	Volume, tonnes	Value, \$ million
Hong Kong	11,279	24,809
Singapore	9,718	16,958
Malaysia	4,306	9,352
New Zealand	1,941	4,544
Indonesia	1,531	3,371

Finite residues are likely to occur in table grapes. There are no import tolerances for pyraclostrobin residues in/on table grapes in the major export markets (Hong Kong, Singapore and Malaysia). In contrast to the wine industry, the table grape industry does not have the same programs in place to manage chemical residues in exported produce. The table grape industry should be made aware that residues of pyraclostrobin may present a risk to Australia's export trade in this commodity.

The Applicant has included the following statement on the draft product label:
Export of Treated Fruit or Wine:

Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for fruit treated with Cabrio Fungicide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing fruit for export

(either fresh, dried or for wine production), please check with BASF Australia Ltd or the Australian Wine Research Institute <http://www.waite.adelaide.edu.au/AWRI/> for the latest information on MRLs and import tolerances BEFORE using *Cabrio Fungicide*.

Dried Vine Fruits

Total exports of dried vine fruits in 1999/2000 were 4,592 tonnes valued at approximately \$12 million (The Australian Horticultural Statistics Handbook). The 5 largest export markets for Australian dried vine fruits in 1999/2000 are shown below:

Destination	Volume, tonnes	Value, \$ million
Germany	1,471	3,821
United Kingdom	888	2,698
New Zealand	888	2,441
Canada	680	1,827
Belgium-Luxembourg	227	621

Finite residues are likely to occur in dried grapes. There are no import tolerances for pyraclostrobin residues in/on dried grapes in the major export markets. The dried grape industry should be made aware that residues of pyraclostrobin may present a risk to Australia's export trade in this commodity. The export label statement includes a reference to dried grapes.

Animal Commodities

Residues in animal commodities may be determined as the parent compound only or as the sum of pyraclostrobin and metabolites converted to two target chlorophenylpyrazole compounds.

A full discussion of the expected residues in animal tissues was presented in the Residues Assessment (see Livestock dietary exposure and animal commodity MRLs). When *Cabrio Fungicide* is used as directed, finite residues are not expected to occur in animal tissues or milk.

The overall risk to export trade in animal commodities is considered to be low.

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

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OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Assessment of Occupational Health & Safety

Pyraclostrobin is not on the NOHSC *List of Designated Hazardous Substances*. Based on the available information NOHSC has classified pyraclostrobin as hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances*. NOHSC has classified Cabrio Fungicide as hazardous according to the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

Pyraclostrobin will be manufactured overseas. It has low acute oral and dermal toxicity but moderate inhalation toxicity in rats. Pyraclostrobin is not a skin or eye irritant in rabbits and not a skin sensitiser in guinea pigs.

Cabrio Fungicide will be manufactured overseas. It has moderate acute oral and low acute dermal and inhalation toxicity. It is a moderate skin and eye irritant in rabbits but not a skin sensitiser in guinea pigs.

Formulation, Packaging, Transport, Storage and Retailing

The end-use product (EUP) will be imported into Australia fully packaged and ready for sale in 1, 5, 10 and 20 L containers.

Transport workers, store persons and retailers will handle the packaged product and could only become contaminated if the packaging were breached.

Use and Exposure

Cabrio Fungicide is indicated for the control of certain fungal diseases in banana, grapes and peanut crops. It will be used mostly either as a dilute (1500 L/ha in grapes) or concentrate spray with air-blast sprayer. The maximum application rate is 0.6 L/ha and suggested spray volumes are between 50 to 1500 L/ha. Number of applications is not specified but will be determined by the disease pressure. A withholding period of 21 days is recommended for grapes and peanuts.

The main routes of exposure are dermal, inhalation and ocular. Categories of workers that can be exposed to the product are mixer/loaders, ground applicators, clean-up personnel and re-entry workers.

There are no available worker exposure data on Cabrio Fungicide. NOHSC used the UK Predictive Operator Exposure Model (POEM) and Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate applicator exposure to Cabrio Fungicide.

These estimates in conjunction with toxicology data demonstrated that the use of clothing, gloves and face shield or goggles during mixing/loading and, clothing and gloves during ground application is necessary to protect workers from acute and repeated exposure.

Entry into Treated Areas

Workers entering treated areas can be exposed to product residues and degradation products during crop management activities and harvesting.

Using the US Occupational Post-Application Risk Assessment Calculator (US Policy 003.1) and based on the toxicity profile and use pattern of Cabrio Fungicide, NOHSC does not recommend a specific re-entry period. However, in accordance with good occupational health and safety practices, re-entry to treated areas should not be allowed until the spray has dried. If prior entry is required, the recommended Personal Protective Equipment (PPE) should be worn.

Recommendations for Safe Use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of cotton overalls buttoned to the neck and wrist (or equivalent clothing), a washable hat, elbow-length PVC gloves and face shield or goggles when preparing the spray and cotton overalls buttoned to the neck and wrist, a washable hat and elbow-length PVC gloves when using the prepared spray for ground application.

The recommended PPE should meet the relevant Australian Standards.

Re-entry statement

NOHSC recommends the following re-entry statement on the product label:

RE-ENTRY

“Do not allow entry into treated areas until the spray has dried. If prior entry is necessary, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day’s use.”

Conclusion

NOHSC supports the registration of pyraclostrobin in Cabrio Fungicide at 250 g/L as an emulsifiable concentrate, for use on banana, grapes and peanut crops.

Cabrio Fungicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available in the Cabrio Fungicide MSDS.

ENVIRONMENTAL ASSESSMENT

Environmental Exposure

CABRIO FUNGICIDE, containing the technical grade active constituent pyraclostrobin at 250 g a.i.(active ingredient)/L, is a Group K fungicide. Cabrio Fungicide will be applied to bananas and grapevines by ground spraying only. Application is as a foliar spray to control leaf speckle (*Mycosphaerella musae*) and leaf spot/Yellow Sigatoka (*Mycosphaerella musicola*) of bananas and downy mildew (*Plasmopara viticola*) and powdery mildew (*Uncinula necator*) of grapevines.

The application rate for bananas is 300 to 400 mL plus 3 to 5 L of water miscible oil per ha, utilising airblast sprayer or misting machine. The higher rate should be used under conditions favouring disease infection and up to four sprays per season may be used as part of a preventive disease control programme. In common with Good Agricultural Practice (GAP) for banana production in Australia, application will only be made to bananas utilising bunch covers (i.e. bagged bananas).

For grapevines the application rate is 40 mL per 100 L water and application by either dilute or concentrate methods may be used. Up to three sprays per season may be applied as part of a complete disease programme. Ideally, these should be applied in a block of three sprays at 10 to 14 day intervals, commencing at flowering. The shorter interval should be used under conditions favouring disease infection.

Environmental Chemistry and Fate

Hydrolysis

Hydrolysis was not observed at 25°C after 30 days at pH 5 or 7 but there was slight degradation at pH 9 after 30 days. At 50°C, there was no degradation at pH 4, 5 or 7 after 5 days. At pH 9 and 50°C there was some degradation of pyraclostrobin (12%) with formation of several metabolites. A half-life was not determined due to the limited degradation. Under typical environmental conditions, hydrolysis will not be expected.

Photolysis

The UV spectrum of pyraclostrobin showed there was adsorption at wavelengths that correspond to the solar spectrum at ground level. Therefore direct photolysis is possible. Aqueous irradiation of pyraclostrobin with a simulated solar spectrum showed that parent was totally degraded after 1 day and an average half-life of 1.44 hours was determined. There was extensive cleavage and hydroxylation-type degradates formed together with mineralisation of the chlorophenyl side ring.

In soil photolysis studies, using a microbially active soil, ¹⁴C-labelled pyraclostrobin was applied to the thin layers of soil and irradiated with a simulated solar spectrum. The results indicate that soil photolysis does not have a significant effect on the rate of degradation of pyraclostrobin compared to the dark control samples. The half-lives were calculated to be 42.2 and 31.5 days (tolyl and chlorophenyl labels respectively) and for the corresponding dark controls were 41 and 22.3 days respectively. With increasing moisture in the soil (80% MWC) the half-lives were 8.9 and 10.4 days for irradiated and dark exposures respectively. However, the distribution of metabolites was different between irradiated and the dark controls, possibly indicating that there are different pathways in the irradiated samples compared to dark controls.

Metabolism

Aerobic soil

The metabolism of pyraclostrobin was studied under aerobic conditions in an agricultural soil classified as a sandy loam. Metabolism was fast early but slowed over time, with the DT50 calculated as 15 days and DT90 of 152 days. There was only one metabolite that exceeded 10% applied active with non-extractable soil bound products the majority of the products.

The degradation of the pyraclostrobin was also studied in 4 soils (3 loamy sands and a loam). After 120 days of incubation under a range of temperature and moisture conditions, the DT50s were calculated as between 38 to 137 days. There was no significant degradation at low temperature (5°C) or under sterile conditions. The study supports the previous study in showing that pyraclostrobin degrades in soil under aerobic conditions and the pathway gives mainly bound residues. Reducing the temperature or moisture levels reduces the degradation rate.

Aerobic aquatic metabolism

The aerobic aquatic metabolism of pyraclostrobin was conducted using two sediment-water systems, one from the Rhine River and the other from a pond. In the pond system, dissipation from water was rapid initially then slowly decreased to be 2.1% after 100 days. There was a corresponding increase in the sediment. Analysis showed that the majority was parent in both water and sediment with a metabolite (BF 500-3) but at just 11.6% after 100 days. Mineralisation was slow. The DT50 for dissipation from water compartment was 3 days and half-life for degradation in sediment was 33 days.

Results for the river system showed that loss of radioactivity from the water phase was just 8.8% remaining after 7 days and 0.8% by 30 days, faster than in the pond system. The degradation of pyraclostrobin gave one metabolite, BF 500-3 (found in the sediment only), which peaked at 67.7% after 14 days and then decreased. Sediment bound residues slowly increased to reach 54.1% after 100 days. The DT50 for loss from the water compartment was 3 days and the DT50 for degradation in sediment was calculated as 9 days. The half life for BF500-3 in the sediment was 55 days.

The study showed that pyraclostrobin was rapidly adsorbed to the sediment and was degraded in the sediment with half-life of 33 days (pond) and 9 days (Rhine River). The rapid degradation in the river system was due to the high anaerobic conditions in the sediment in this system. In the sterile systems degradation was very slow with 83 and 92% of AR recovered as parent for pond and river systems respectively, again almost exclusively in the sediment. Bound residues were 15 and 4.9% respectively.

Aerobic Aquatic metabolism with photolysis

Pyraclostrobin, radiolabelled with ¹⁴C at either the chlorophenyl ring or tolyl ring, was incubated in an aerobic aquatic system in the presence of light. The systems were incubated exposed to the air under conditions to simulate the climate in central Europe. The light intensity was adjusted daily to give the natural day light cycle. In addition, water only samples were prepared and incubate at the same time.

The results clearly showed that pyraclostrobin follows two major disappearance and degradation pathways in a natural sediment/water system in light. On reaching water there is both a fast photolysis degradation, to give a number of products, and adsorption to sediment with subsequent degradation to mainly BF 500-3. The photolytic metabolites are formed in the aquatic phase are not readily adsorbed to sediment and under go further degradation. The DT50s for parent were determined by modelling the total system using a multiple compartment model and the determining the DT50. The DT50 for loss from water compartment was 5 days and half-life for degradation in sediment was 4 days.

Anaerobic soil metabolism

The metabolism of pyraclostrobin (¹⁴C-labelled in the tolyl and chlorophenyl ring) was studied under anaerobic conditions in a sandy loam soil. The soil was flooded with water, then after anaerobic conditions were established the soil was treated with pyraclostrobin before being anaerobically incubated for 120 days.

The majority of the applied radioactivity appeared as non-extractable soil bound products by the end of the study and there was little mineralisation from either label. The metabolite BF 500-3 was formed very quickly and represented 86% of applied after 7 days. The DT50 value was 1.5 days and the DT90 5.1 days.

Mobility

Volatility

The levels of volatilisation of radiolabelled pyraclostrobin within 24 h after application to a loamy sandy soil surface and bush bean surface were below 1 and 3% respectively. The study demonstrated that volatilisation is not a relevant pathway for dissipation of pyraclostrobin.

Adsorption/desorption

The adsorption/desorption of pyraclostrobin was studied by the batch equilibrium method using 6 agricultural soils. Pyraclostrobin was strongly adsorbed onto all soils with K_{oc}s ranging from 6000 to 16000 and was classified as immobile (McCall classification). There was limited desorption.

The adsorption/desorption of the 3 principal metabolites of pyraclostrobin, BF 500-3, BF 500-6 and BF 500-7 was also studied by the batch equilibrium method using the same (or similar) agricultural soils. The study demonstrated that BF500-3 is strongly adsorbed to all but one soil tested and was classified as of low mobility to immobile in these soils. The study demonstrated that BF500-6 is strongly adsorbed to all soil tested and was classified as immobile in these soils. BF500-7 was also strongly adsorbed to all but one soil tested, and was classified as slightly mobile to immobile in these soils.

Column leaching

A leaching column study was conducted using 4 soils. Following leaching, most of the applied residues were retained in the first two column segments and there was no leaching through the 30 cm soil column. The experiments showed that there is limited leaching potential of pyraclostrobin and of its metabolites.

Aged leaching

An aged leaching column study was conducted using a sandy soil. The experiment showed that there is limited leaching potential of pyraclostrobin and of its 30-day aged residues.

Field Dissipation

Dissipation at 3 German sites.

The dissipation of pyraclostrobin was studied under field conditions at three locations in the Federal Republic of Germany that had been arably farmed for a number of years. Application was carried out on fallow land without vegetation at 250 g ai/ha using the proposed emulsion concentrate. The results of the chemical analysis (HPLC) showed that there were no residues of pyraclostrobin detected below 10 cm at anytime at any site. There were no metabolites detected except for BF500-6 at low concentrations at one site trial on two occasions. The DT50 of pyraclostrobin was determined as 25-37 days in the total system using a multiple compartment model.

Dissipation at 3 European sites.

The dissipation of pyraclostrobin was studied under field conditions at three locations in Europe, two in Spain and one in Sweden. The results of the chemical analysis (HPLC) were similar to previous and showed that there was no pyraclostrobin detected below 10 cm and no metabolites detected in any soil section above the limit of quantification. The half-life of pyraclostrobin was 2-8 days in Spain and 31 days in Sweden again using the total system, multiple compartment model. Given the similarity between the Spanish and Australian environments, rapid degradation could be expected under Australian conditions.

Bioaccumulation

The bioaccumulation of ¹⁴C pyraclostrobin in bluegill sunfish fish was conducted under flow through conditions. The average bioaccumulation factors (BCF) for edibles, viscera and whole fish were calculated as 247, 1195 and 691 respectively. Analysis of the fish showed that the majority of the accumulated residues were parent compound. These accumulated residues were rapidly eliminated with DT50 values of < 1.0 days in edibles, viscera and whole fish.

The bioconcentration potential of the metabolites BF 500-11, BF 500-13, and BF 500-14 were examined by determining the octanol/water partition coefficient (log P_{ow}). As these degradation products have relatively low log P_{ow} values, 1.87, 1.71 and 2.54 for BF 500-11, BF 500-13, and BF 500-14 respectively, they are unlikely to accumulate in fish.

Soil Accumulation

Accumulation potential in soils is low. The field studies showed that degradation can be very quick at higher temperatures, and at 250 g ai/ha there were no detectable residues after approximately 100 days.

Environmental Toxicology

Avian

Pyraclostrobin was practically non-toxic to bobwhite quail by the single oral dose route with an LD50 value greater than 2,000 mg ai/kg bw. This was also true with 5-day dietary exposures resulting in an LC50 > 5000 mg ai/kg bw for bobwhite quail chicks and for mallard ducklings. In the one generation dietary studies to bobwhite quail and mallard duck, the NOECs were 1000 mg ai/kg food, the maximum treatment used.

Aquatic

Under static conditions technical pyraclostrobin is rated as very highly toxic to fish with 96 h LC50s between 4.53-10.1, 19.6-33.5 and 12.1-25.8 µg/L for rainbow trout, bluegill sunfish and carp respectively. The dose response curves were very steep with NOECs of 3.3, 10.9 and 12.1 µg/L, respectively. The proposed formulated product containing 250 g ai/L of pyraclostrobin was also rated as very highly toxic with the 96 h LC50 for 6 species of fish ranging from 12.3-27.4 to 32.5-88.5 µg/L, again all result are ranges due to the very steep dose response curves.

The toxicity of the 3 major metabolites to rainbow fish was also determined and the results show that these metabolites had limited toxicity, with LD50s > 50 mg/L and were rated at being slightly toxic to practically non-toxic to rainbow trout.

A short term sublethal and two early life stage studies were conducted using rainbow trout and technical pyraclostrobin under flow-through conditions. The NOEC in the sublethal study was 3.1 µg/L and for the first early life stage study the no observable adverse effects levels (NOAEL) was 2.35 µg/L, with lethality the most sensitive effect. A second early life stage study was conducted but exposure concentrations followed a saw tooth shaped exposure with

14 days between peak concentrations and with increasing concentrations toward the end of the study to reflect the expected field exposure pattern. The NOEC was determined as 5 µg/L (nominal).

For aquatic invertebrates, the acute 48 h daphnia toxicity test gave an EC50 of 15.7 µg ai/L and pyraclostrobin was rated as very highly toxic. In the chronic 21 days study the NOEC for daphnia was 4 µg ai/L with effects on reproduction and growth in the parent generation being the effects observed in the study. Using the proposed formulated product, the acute 48 h daphnia toxicity test gave an EC50 of 56-100 µg/L, equivalent to 14-25 µg ai/L, and was rated as very highly toxic. The toxicity of the 3 major metabolites to daphnia was also determined and the results show that these metabolites had limited toxicity, with LD50 > 50 mg/L and were rated as being slightly to practically non-toxic to daphnia. Based on a 96 h LC50 of 4.16 µg/L, technical pyraclostrobin is very highly toxic to the mysid. For midge larvae, a sediment dwelling organism, the 28 d NOEC was 40 µg ai/L and the EC50 was calculated as 377 µg/L.

Technical pyraclostrobin was rated as highly toxic to the green alga *Pseudokirchneriella subcapitata* (syn. *Selenastrum capricornutum*) with a 96-h E_rC50 of > 842 µg/L and an E_bC50 of 152 µg/L. The acute 96-h toxicity of the proposed formulated product containing pyraclostrobin at 250 g/L using the green alga *Selenastrum capricornutum* Prinz was E_rC50 of 3.32 mg ai/L and an E_bC50 of 1.37 mg/L.

The toxicity of the 3 major metabolites to green algae was also determined and the results show that they had limited toxicity, with 72-h E_rC50 of > 46 mg/L and E_bC50 of > 100 mg/L and were rated as being slightly to practically non-toxic to green algae.

When duckweed was exposed to various concentrations of pyraclostrobin, the EC50 based on frond numbers was greater than 1.72 mg/L, the highest tested concentration and the approximate limit of the test substance in water, and 1.72 mg/L when calculated on plant biomass. The 14 day NOEC, based on number of normal, non-chlorotic fronds and plant biomass was set at 0.896 mg/L.

Mesocosm

An outdoor mesocosm study was conducted with reference to several guidance documents in Germany. There were 15 ponds, each with water depth of 100 cm with the bottom 30 cm of sediment, some of which was natural. Sediment and water in the ponds originated from natural species rich lake.

The spray drift from vineyard applications was simulated (considered to be worst-case for Europe) with eight applications of pyraclostrobin in 14-day intervals and with rates increasing from 60 to 160 g ai/ha during the season. The application rate was based on spraydrift from an orchard sprayer at 5 m distance together with concentrations of a third, three and nine times this with correspondingly lower rate from the early applications.

Standard statistical procedures were used as well as elaborated new techniques to analysis biological responses.

Analytical measurements of test substance concentrations in the spraying solutions and directly in the water (for the highest test concentration only) shortly after spraying generally ranged from 83 to 122% of nominal and decreased to 23 to 6.6% of nominal after 14 days. This is in agreement with standard and extended laboratory studies on the environmental fate of pyraclostrobin.

The concentration in the sediment (highest treatment) shortly after the last application corresponded to 16% of the amount applied 1 week before sampling and less than 4% of the total amount applied. At the next measurement some 73 days later, when the test substance had nearly completely disappeared from the water ($< 0.5 \mu\text{g/L}$), less than 2% was found in the sediment.

There were no significant effects between treatments on the standard physical water measurements (pH, oxygen concentration, diurnal pH or oxygen changes, conductivity, ion-concentrations) or on total chlorophyll concentration, indicative of total algae and primary producers concentrations. A large number of different species was observed in this mesocosm study at varying abundances during the course of the experiment. The important freshwater phytoplankton groups were present with ~65 different taxa and there were no significant, concentration related effects on the total density of phytoplankton or on the number of different taxa in the various treatments. In addition, there was neither a significant change in species composition, biodiversity and similarity indices and multivariate statistical methods (Principal Response Curves) did not indicate any treatment related effects.

Zooplankton showed a large biodiversity and a number of important groups were present in large numbers, ie Rotifera, Phyllozoa, Copepoda. The analysis of the data showed no effect of treatments on the number of species, total abundances, species biodiversity or similarity indices. Multivariate statistical techniques did not indicate significant treatment related effects. However, within the group Daphniidae, the species *Daphnia longispina* appeared significantly inhibited in all treatments during the time of the 4th and subsequent applications. During this period the populations in all treatments fell to very low levels such that the variability between samples could also be due to sampling errors.

The same was true for Copepoda, which were dominated in numbers by nauplia larvae. Population levels were often higher in the control than in most treatment groups, significantly so during the early applications and there appears to be a dose response. However, the highest treatment group showed higher densities than the other groups, and in the same range as the controls, during the time of the highest test substance applications. The report indicates that the occasional differences in nauplia population densities must be attributed to variability and was not caused by pyraclostrobin treatments. That the early responses may have been toxic effects with consequent selection of a resistant population having occurred has not been ruled out.

The abundance of benthic organisms was determined in sediment and artificial substrate samples at only three occasions during the course of the experiment. For most of the many taxa found in this study - Nematoda, Turbellaria, Oligochaeta, Crustacea, Insecta and Arachnida - no clear treatment related effects were observed. Examination of biodiversity and similarity indices and multivariate statistical methods (Principal Response Curves) did not indicate any treatment related effects. Two snail species and one mussel species appeared affected at the highest treatment level only. The NOEC was determined as $8 \mu\text{g/L}$.

No treatment related effects were observed for aquatic insects as measured in emergence, plankton and benthos samples.

Parallel to the mesocosm study, the effects on fish under outdoor conditions were assessed using the same application scheme in separate small ponds. Toxic effects were only observed at the highest treatment level at the last application (during a period of high temperatures and low oxygen concentrations) causing fish mortality (5 fish died out of 7; all fish initially showed symptoms). No sublethal effects (behaviour, growth, gross pathological findings) were observed in any of the other treatments.

After the last treatment the ponds were drained and the number of surviving fish determined. There were 7, 4, 6 and 3 fish recovered in control and the 3 lowest treatments respectively. The report considered that these losses were not treatment related as there were no fish showing symptoms in these treatments. The LOEC and NOEC were determined as 24 and 8 µg/L respectively and therefore the EAC (ecologically acceptable concentration) is ≥ 8 but < 24 µg/L.

It was concluded that the results of a complex mesocosm study shows that pyraclostrobin can have effects on a few species at concentrations of 24 µg ai/L (equivalent to the nine-fold of the 5% drift scenario) and higher. Fish and molluscs may be affected at this concentration, too. For all planktonic species the effects were found to be reversible. No clear statistically significant treatment related effects were observed at 8 µg ai/L. The multitude of endpoints and species and environmental conditions in this mesocosm study show clearly that at this (8 µg ai/L and lower) concentration no adverse effects on aquatic communities can be expected after 2 applications at this level. The ecologically acceptable concentration (EAC) is thus between 8 µg ai/L and 24 µg ai/L, the NOEC and LOEC respectively.

Non-Target Invertebrates

The LD50 for pyraclostrobin (technical) to bees was greater than 100 µg/bee by both the oral and contact exposure routes. There were effects on parasitic wasps, green lacewings, ladybirds and predatory mites when exposed to dry residues on glass (3.2 µg/cm² equivalent to 320 g ai/ha). When tested using plants as spray target at 320 g ai/ha, pyraclostrobin as an EC formulation was non-toxic to parasitic wasps and ladybirds, and slightly toxic to green lacewings. When tested against beetles and wolf spiders, direct overspray at 320 g ai/ha, pyraclostrobin (EC formulation) was non-toxic to these organisms. In field tests on grapevines, there was no statistically significant effect on endemic populations of predatory mites. It can be rated as harmless to bees, parasitic wasps, green lacewings, ladybirds, predatory mites and ground beetles and presumably to other terrestrial insects in the field.

Earthworms

In tests on the effect of pyraclostrobin technical on earthworms using artificial soil, the LD50 was determined as 556 mg ai/kg and the 14 day NOEC as 151 mg ai/kg. A study was designed to investigate the possible release of soil-bound residues by earthworms and the potential toxicity of the bound residues for these soil-living animals. It was concluded that the results shows that pyraclostrobin is bound in the soil very tightly to the humic substances and cannot be released even by digestive processes of soil-eating animals.

In a chronic test, the EC formulation (250 g ai/L) sprayed at 1-10 L/ha caused no effect on the parent generation but the number of juvenile worms was statistically significantly lower than control at rates higher than 1 L/ha. The NOEC for reproduction was 1 L/ha, corresponding to 250 g ai/ha. Earthworm tests on the two principal soil metabolites showed that there was no effect at 1000 mg/kg soil.

The effect of pyraclostrobin, formulated as the proposed EC (250 g ai/L), on earthworms in grasslands under field conditions was determined in three trials conducted at two sites in Germany. The test concentrations used in two of the trials corresponded to the full rate expected to be used in grapevines in Europe (160 g ai/ha), similar to Australian rates and half this rate with eight applications in both trials. In the third trial, there were two applications at 1.7 times the proposed maximum Australian rate of 150 g ai/ha. At one site where multiple applications were applied, after the 3rd application, there was a decline in earthworm abundance in both the “50 and 100%” concentration groups. At the final evaluation after 8 treatments, no statistically significant differences compared to the control were observed in any of the treatments. For the other site where both two and multiple application trials were applied, there were no statistically significant differences between numbers of any dominant

species or total earthworm abundance in control compared to the treatments applied at any of the in-treatment and post-treatment evaluations. It was concluded that the studies shows that repeated application at likely application rate in grapevines could affect earthworm populations within the treated area but any effects are transitory.

Soil invertebrates

The effect of pyraclostrobin, formulated as the proposed EC (250 g ai/L), on the soil invertebrate activity under field conditions was determined using a bait-lamina test according to EU guidance. The study was conducted as a follow-up study following the previous field study with earthworms. 12 weeks after the last application soil cores were taken and the feeding activity of the soil invertebrates was determined. Based on the results of this study there were no treatment-related (adverse) effects on the feeding activity of soil invertebrates.

The effect of pyraclostrobin, formulated as the proposed EC (250 g ai/L), on collembolan species (springtails) under field conditions was determined. The study was conducted as a follow-up study to the previous field study with earthworms. Based on the results of this study, there were no treatment-related effects on the Collembola biocenosis. There was no effect from the treatments on springtail populations and it was concluded that fluctuations in population densities are mainly influenced by abiotic parameters such as soil moisture. Sustained adverse effects following application of pyraclostrobin were considered to be highly unlikely.

Soil microorganisms

Investigations into the effects of pyraclostrobin (as the proposed EC at 250 g ai/L) on soil microbial activity at the field rate and 10X that rate showed there was no statistically significant effect on respiration or on nitrogen turnover at either rate.

The effect of two principal soil metabolites on soil microbial activity was determined and showed no statistically significant effect on respiration, nitrogen mineralisation or nitrification. There were slight but negligible effects but these not considered as treatment-related since no clear dose-response relationship could be observed.

Non-target vegetation

A phytotoxicity study conducted at 160 or 480 g ai/L demonstrated no or limited effects on the mono and dicotyledonous plants treated with visual plant injury not greater than 15% of that seen in the controls. There were no significant differences in the biomasses of the treated and untreated plants.

Environmental Hazard

Registration of Cabrio fungicide is sought for the control of the fungal diseases in bananas (leaf speckle, leaf spot and black sigatoka), grapevines (downy and powdery mildew) and peanuts (early leaf spot, late leaf spot, rust and net blotch) as per the directions for use on the label. Orchard air blaster sprayers or boom sprayers fitted with hollow cone nozzles will apply it at between 75-150 g ai/ha in water. The label gives direction to use water miscible spraying oil when used for bananas. Residues from application would be expected on plant surfaces and soil. Surface water, uncultivated land and nearby non-target plants may be contaminated through overspray, spray drift and/or run-off.

Concentration in soil

The maximum application rate is 150 g ai/ha. Given a direct application to bare soil at 150 g ai/ha, incorporation into the top 5 cm and a soil bulk density of 1.3 g/mL, the estimated environmental concentration (EEC) of pyraclostrobin in treated soil would be 0.23 mg ai/kg soil per application. With up to 4 applications per year, the yearly application could be as

high as 600 g ai/ha and a soil EEC of 0.92 mg ai/kg soil. However, using the longest field dissipation half-life of 37 days and first order calculations, after 4 applications at 21 days apart, the maximum concentration is 0.56 mg/kg in the first 5 cm of soil and there is no year-to-year carry over.

Concentration in water

In a worst-case scenario of a direct overspray to a 15 cm deep body of water at the maximum single application rate of 150 g ai/ha, the EEC is 100 µg ai/L. As up to 4 applications per season/year could be made and the dissipation DT50 in natural water-sediment systems is fast (DT50 4-5d) accumulation in water is unlikely as shown in the mesocosm study submitted with the application.

Birds

Based on the typical diet of northern bobwhite quail and the EEC of pyraclostrobin in food items, the concentration of pyraclostrobin in the diet was calculated as 16 mg ai/kg food or 64 mg ai/kg food for four applications. As the most sensitive chronic NOEC for quail of 1000 mg ai/kg food is significantly higher, no avian hazard is expected.

Earthworms

The 14-d LC50 for the earthworm was 566 mg ai/kg soil and is at least 1000 times higher than the worst case soil EEC of 0.56 mg ai/kg soil for pyraclostrobin in the top 5 cm of soil following 4 applications. Thus the proposed use of pyraclostrobin is not expected to pose an acute hazard to earthworms. The studies on chronic toxicity to earthworms showed no direct toxic effects; however, there were effects on reproduction at 500 g ai/ha [0.77 g ai/kg soil] and a hazard to earthworm reproduction cannot be ruled out. However, plant interception will reduce the soil concentration and field studies showed no effects on earthworms and other soil dwelling invertebrates when repeatedly sprayed with Cabrio at a maximum application rate of 160 g ai/ha or at 250 g ai/ha and two applications.

Beneficial arthropods

The hazard to honey bees is expected to be relatively low as the single application rate of 150 g ai/ha (equivalent to 1.5 µg ai/cm²) is 100 times lower than the most sensitive contact NOEC of > 100 µg ai/bee assuming that a honeybee is approximately 1 cm² in surface area. In the laboratory, ladybird beetles were affected when exposed to dry residues of pyraclostrobin at 320 g ai/ha with 100% mortality of larvae. There was no effect on ladybird beetles when vegetation was sprayed at a lower rate of 64 g ai/ha. While effects on ladybird beetles cannot be ruled out when oversprayed at 150 g ai/ha, there are unlikely to be serious long-term effects on the overall populations of ladybird beetles. Ground beetles are not expected to be adversely affected at the proposed rate of 150 g ai/ha as no effect was seen when oversprayed at 320 g ai/ha. Effects on other species such as parasitic wasps, green lacewing, wolf spiders and predatory mites are not expected as applications at higher rates had no or limited effect.

Soil Micro-organisms

The information presented on the effect of pyraclostrobin on soil micro-organisms showed these organisms were not affected at 3.8 kg/ha and therefore a hazard to soil micro-organism and soil processes is unlikely at the proposed rates.

Non-target vegetation

A phytotoxicity study conducted at 160 or 480 g ai/L [cf. 150 g ai/ha, the maximum rate proposed for Australia] demonstrated no or limited effects on the six species of plants treated which is indicative of hazard to plants not being expected to be of significance at the proposed rates.

Hazard to aquatic organisms

Water bodies adjacent to sprayed areas may be contaminated through direct overspray while spray drift can result in contamination of areas outside the target area. Runoff of material dissolved in the water or sorbed to soil and organic particles can also result in movement of pyraclostrobin into waterbodies.

The potential for direct overspray on water bodies is expected to be limited by the use of ground application and by using best agricultural management practices. The greater potential hazard to aquatic environments through spray drift and was assessed using the Ganzelmeier and AgDrift models. As specific models for banana and peanuts were not available, the models for hops and orchards were selected as a surrogate for bananas and for peanuts field crops. Based on several worst-case scenarios, the proposed use of Cabrio Fungicide is not expected to pose an unacceptable hazard to fish, waterfleas or algae via spraydrift provided there is at least 10 metres between the site of application and a downwind waterbody for bananas and peanuts and 5 metres for grapes.

The strong binding of pyraclostrobin to soil particles is expected to limit the run-off of residues from treated areas to that adsorbed to eroded soil particles. Further, current land management practices such as planting across the slope and grass between grapevines rows, minimises erosion and thus the amount of pyraclostrobin entering the aquatic environment via runoff. The risk from erosion is expected to be low and acceptable when pyraclostrobin is used in accordance with the proposed label and good farm management practices. The hazard to the aquatic environment is further mitigated by adsorption to sediment and dilution from non-treated areas in the catchment.

The chronic hazard is low with pyraclostrobin being both rapidly adsorbed to sediment and rapidly degrading to less toxic metabolites. Studies showed that this degradation is very rapid under anaerobic conditions and in the field.

Conclusion

The extensive environmental data provided for the submission are sufficient to conclude that the proposed use as a fungicide on banana, grape and peanut crops, according to the proposed label, including use of a 10 metre buffer if waterbodies, watercourses or wetlands are downwind of the application area, and good farm management practices, will not lead to unintended effects on animals, plants, things or the environment.

EFFICACY AND SAFETY ASSESSMENT

Justification for use and Mode of Action

Pyraclostrobin is a new fungicide of the strobilurin group. It is closely related to azoxystrobin and trifloxystrobin, compounds which have been registered for use as fungicides in Australia for several years. With respect to fungicide resistance, pyraclostrobin is classed as a Group K fungicide. As a Group K fungicide, Cabrio Fungicide offers the potential to introduce a new Mode of Action to banana disease control programmes, thereby reducing the selection pressure on widely used Group C (DMI) products. The introduction of Cabrio, which has good activity for the control of both powdery and downy mildew of grapes, will be a useful addition to the fungicides presently used in this crop, as strains of powdery mildew resistant to Group C (DMI) fungicides have recently been reported in Australia.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Cabrio Fungicide will be applied to bananas and grapevines by ground spraying only. Application is as a foliar spray to control leaf speckle (*Mycosphaerella musae*) and leaf spot/Yellow Sigatoka (*Mycosphaerella musicola*) of bananas and downy mildew (*Plasmopara viticola*) and powdery mildew (*Uncinula necator*) of grapevines.

The application rate for bananas is 300 to 400 mL plus 3 to 5 L of water miscible oil per ha, utilising airblast sprayer or misting machine. The higher rate should be used under conditions favouring disease infection and up to four sprays per season may be used as part of a preventive disease control programme. In common with Good Agricultural Practice (GAP) for banana production in Australia, application will only be made to bananas utilising bunch covers (i.e. bagged bananas).

For grapevines the application rate is 40 mL per 100 L water and application by either dilute or concentrate methods may be used. Up to three sprays per season may be applied as part of a complete disease programme. Ideally, these should be applied in a block of three sprays at 10 to 14 day intervals, commencing at flowering. The shorter interval should be used under conditions favouring disease infection.

Use is proposed for all State and Territories.

It is proposed the product will be available in 1L, 5L, 10L or 20L co-extruded PE/PA packs.

The following Withholding Period statements are recommended for the product:

Bananas (bagged)- Not required when used as directed.

Grapes- Do not harvest for 21 days after application.

Evaluation of efficacy

The data presented supported the claim for control of leaf speckle (*Mycosphaerella musae*) and leaf spot/Yellow Sigatoka (*Mycosphaerella musicola*) of bananas and downy mildew (*Plasmopara viticola*) and powdery mildew (*Uncinula necator*) of grapevines. Detailed efficacy data was presented including results from a range of Australian and overseas field trials.

Bananas

Data from 10 Australian field trials conducted over two seasons were presented in support of the application. Trial layout, design and number of data plants were satisfactory. Trials were conducted in suitable locations and, in most cases, the commencement dates were related to weather conditions. Disease levels in some trials were too low to demonstrate the efficacy of the product as claimed in the trial reports. However, in general the data demonstrate efficacy of Cabrio when applied in a program for control of the banana diseases, leaf spot/Yellow Sigatoka and leaf speckle.

Grapevines

Data from 12 Australian trials conducted over two seasons, and from nine overseas trials were presented in support of the application. These trials were conducted in plantings of vines such as Shiraz, Chardonnay, Semillon and other varieties that are susceptible to both powdery and downy mildews. The majority of trials were well designed, conducted, analysed and reported. The trials were conducted in commercial vineyards subject to normal levels of disease pressure and spray volumes and spray intervals were similar to those used under commercial production conditions. The data support the claims.

Crop Safety

Applications of Cabrio did not cause phytotoxicity to bananas or grape varieties including Chardonnay, Shiraz and Verdelho in any of the submitted trials at rates up to twice the proposed label rate.

Resistance management

Pyraclostrobin has been included in Fungicide Resistance Group K. For bananas, it is recommended to alternate applications of Cabrio with sprays from other fungicide groups in a resistance management programme. Similarly, application to grapevines should be in accordance with the Avcare resistance management strategy.

Conclusion

Sufficient statistically analysed data from suitably designed and scientifically conducted trials has been presented to substantiate the claims for use shown on the draft labels. As long as the product is used according to label instruction and Good Agricultural Practice it should be suitable for the proposed purposes.

LABELLING REQUIREMENTS

PACK LABEL

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

CABRIO[®] Fungicide

ACTIVE CONSTITUENT: 250 g/L PYRACLOSTROBIN
SOLVENT: 705 g/L HYDROCARBONS, LIQUID

GROUP	K	FUNGICIDE
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For the control of leaf speckle and leaf spot in bananas and downy and powdery mildew in grapevines,
as specified in the DIRECTIONS FOR USE table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE.

BASF

BASF Australia Ltd
ABN 62 008 437 867
Norwest Business Park, 7 Maitland Place
Baulkham Hills NSW 2153

1, 5, 10, 20 L

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STORAGE AND DISPOSAL

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

Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do NOT dispose of undiluted chemicals on-site. If recycling, replace cap and return clean containers to recycler or designated collection point.

If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should NOT be burnt.

SAFETY DIRECTIONS

Harmful if swallowed. Will irritate the eyes and skin. Avoid contact with eyes and skin. If product on skin, immediately wash area with soap and water. If product in eyes, wash it out immediately with water. Wash hands after use. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length PVC gloves and face shield or goggles. When using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow-length PVC gloves. After each day's use, wash gloves, face shield or goggles and contaminated clothing.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Telephone 131126 Australia-wide. If skin contact occurs, remove contaminated clothing and wash skin thoroughly. If in eyes, wash out immediately with water.

MSDS

Additional information is listed in the Material Safety Data Sheet.

CONDITIONS OF SALE

All conditions and warranties rights and remedies implied by law or arising in contract or tort whether due to the negligence of BASF Australia Ltd or otherwise are hereby expressly excluded so far as the same may legally be done provided however that any rights of the Buyer pursuant to non excludable conditions or warranties of the Trade Practices Act 1974 or any relevant legislation of any State are expressly preserved but the liability of BASF Australia Ltd or any intermediate Seller pursuant thereto shall be limited if so permitted by the said legislation to the replacement of the goods sold or the supply of equivalent goods and all liability for indirect or consequential loss or damage of whatsoever nature is expressly excluded. This product must be used or applied strictly in accordance with the instructions appearing hereon. This product is solely sold for use in Australia and must not be exported without the prior written consent of BASF Australia Ltd.

EMERGENCY INFORMATION PANEL
PESTICIDE, LIQUID, TOXIC, N.O.S. (CONTAINS PYRACLOSTROBIN); UN No. 2902; PG III; HAZCHEM 2X
IN A TRANSPORT EMERGENCY DIAL: 000 POLICE OR FIRE BRIGADE
FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY PHONE 1 800 033 111 TOLL FREE - ALL HOURS - AUSTRALIA WIDE

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NRA Approval No.:

Product No.:

Batch No.:

Date of Manufacture:

LABEL LEAFLET

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

CABRIO[®] Fungicide

ACTIVE CONSTITUENT: 250 g/L PYRACLOSTROBIN
SOLVENT: 705 g/L HYDROCARBONS, LIQUID

GROUP	K	FUNGICIDE
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For the control of leaf speckle and leaf spot in bananas and downy and powdery mildew in grapevines,
as specified in the DIRECTIONS FOR USE table.

THIS LEAFLET IS PART OF THE LABEL.

BASF

BASF Australia Ltd
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DIRECTIONS FOR USE:**RESTRAINTS:**

DO NOT use by aerial application.

DO NOT apply CABRIO Fungicide if waterbodies, watercourses or wetlands are within 10 metres downwind of the application area.

CROP	<u>DISEASE</u>	<u>RATE</u>	<u>WHP</u> (Days)	CRITICAL COMMENTS
Bananas (bagged)	Leaf speckle (<i>Mycosphaerella musae</i>), leaf spot (<i>Mycosphaerella musicola</i>)	300 to 400 mL plus 3 to 5 L of water miscible oil/ha.	-	Maintain good crop hygiene by regularly removing old and diseased leaves to reduce the source of disease inoculum. DO NOT use on bananas unless bunch covers are in place. Ground application only: Apply by airblast sprayer or misting machine. Use the higher rates under conditions favouring disease infection. Apply up to four sprays per season, as part of a preventive disease control programme, commencing early in the season and using alternative mode-of-action products in between CABRIO applications. Do NOT apply consecutive sprays of CABRIO or other Group K fungicides. This use is subject to an AVCARE resistance management strategy.
Grapevines	Downy mildew (<i>Plasmopara viticola</i>), powdery mildew (<i>Uncinula necator</i>),	<u>Dilute spray</u> 40 mL/100 L water <u>Concentrate spray</u> Refer to the "Application" section.	21	Also see 'CAUTION' section re export commodities. Apply up to three sprays per season as part of a complete disease control programme. Ideally, apply in a block of three sprays at 10 to 14 day intervals, commencing at flowering. Use the shorter intervals under conditions favouring disease infection. Apply by dilute or concentrate spraying equipment. Apply the same total amount of product to the target crop whether applying this product by dilute or concentrate spraying methods. This use is subject to an AVCARE resistance management strategy.

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.**WITHHOLDING PERIODS:****HARVEST:** BANANAS (BAGGED) - NOT REQUIRED WHEN USED AS DIRECTED.

GRAPES - DO NOT HARVEST FOR 21 DAYS AFTER APPLICATION.

GENERAL INSTRUCTIONS

MIXING

To ensure even mixing, half-fill the spray tank with clean water and add the required amount of product.

If required, add compatible products and agitate thoroughly, then add the remainder of the water. Agitate again before spraying commences.

APPLICATION

Apply by ground application equipment only.

Bananas:

Apply by airblast sprayer or misting machine to ensure even coverage.

Grapevines:

Dilute Spraying

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

Concentrate Spraying

- ◆ 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

Dilute spray volume as determined above: For example 1500 L/ha

Your chosen concentrate spray volume: For example 500 L/ha

The concentration factor in this example is: 3 X (i.e. $1500 \text{ L} \div 500 \text{ L} = 3$)

If the dilute label rate is 40 mL/100 L, then the concentrate rate becomes 3 x 40, that is 120 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.

◆

For concentrate application, use a spray volume of at least 200 litres per hectare.

For dilute application, apply to run-off. See ***Dilute spraying*** above.

COMPATIBILITY

For information on compatibility please contact your local BASF representative.

FUNGICIDE RESISTANCE WARNING

GROUP	K	FUNGICIDE
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CABRIO Fungicide is a member of the strobilurin group of fungicides. For fungicide resistance management, CABRIO Fungicide is a Group K fungicide.

Some naturally-occurring individual fungi resistant to CABRIO Fungicide and other Group K fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungal population if these fungicides are used repeatedly. These resistant fungi will not be controlled by CABRIO Fungicide or 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, BASF Australia Ltd accepts no liability for any losses that may result from the failure of CABRIO Fungicide to control resistant fungi.

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 (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

CAUTION

Export of treated fruit or wine

Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for fruit treated with CABRIO Fungicide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing fruit for export (either fresh, dried or for wine production), please check with BASF Australia Ltd or the Australian Wine Research Institute <http://www.waite.adelaide.edu.au/AWRI/> for the latest information on MRLs and import tolerances BEFORE using CABRIO Fungicide.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

HIGHLY TOXIC TO AQUATIC ORGANISMS. Do NOT contaminate streams, rivers or waterways with the chemical or used containers.

STORAGE AND DISPOSAL

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

Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do NOT dispose of undiluted chemicals on-site. If recycling, replace cap and return clean containers to recycler or designated collection point.

If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should NOT be burnt.

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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 octanol water partitioning co-efficient.
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light.
Photolysis	Breakdown of chemicals due to the action of light.
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

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Footnote:

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

APVMA PUBLICATIONS ORDER FORM

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

David Hutchison
Pesticides Division
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
David Hutchison, Pesticides Division at (02) 6272 3218.

Name (Mr, Mrs, Ms, Dr) _____

Position _____

Company/organisation _____

Address _____

Contact phone number (____) _____

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

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

___ Bankcard ___ Visa ___ Mastercard

Card number ____/____/____/____ Expiry date/...../.....

Signature _____ Date _____