Public Release Summary
on

Evaluation of the new active

BOSCALID

in the product

FILAN FUNGICIDE

Australian Pesticides and Veterinary Medicines Authority

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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), Department of Environment and Heritage (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 Program, 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 Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
CRP	Chemistry and Residues Program
d	day
DAT	Days After Treatment
DM	Dry Matter
DT_{50}	Time taken for 50% of the concentration to dissipate
DT_{90}	Time taken for 90% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EC	Emulsifiable Concentrate
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
ESI	Export Slaughter Interval
EUP	End Use Product
FAO	Food and Agriculture Organisation of the United Nations
Fo	original parent generation
FW	Fresh Weight
g	gram
GAP	Good Agricultural Practice
GC/MS	gas chromatography/mass spectroscopy
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
HDPE	High-density polyethylene
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
HPLC-UV	High Performance Liquid Chromatography with Ultra-Violet Detector
HR	Highest Residue
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
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
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 dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
MSMS	mass spectroscopy/mass spectroscopy
NOAEC	No Observable Adverse Effect Concentration
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
STMR	Supervised Trials Median Residue
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
µg	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 *FILAN FUNGICIDE,* which contains the new active constituent boscalid. The product is proposed to be used for the control of bunch rot (*Botrytis cinerea*) 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.

Copies of full technical evaluation reports on boscalid, 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 12 May 2004. They should be addressed to:

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Applicant
BASF Australia Ltd

Product Details
It is proposed to register FILAN FUNGICIDE, containing boscalid at 500 g/kg as a wettable granule formulation. FILAN FUNGICIDE will be imported fully formulated and packaged in 2kg, 2.5kg, 5kg, 10kg, 15kg and 20kg containers.

FILAN FUNGICIDE is a new fungicide having protective and curative action. It inhibits spore germination, germ tube elongation, mycelial growth and sporulation. FILAN FUNGICIDE acts systemically. For resistance management boscalid is a member of the oxathiin group of fungicides. It is a Group G Fungicide.

Application is as a foliar spray to control Bunch rot (*Botrytis cinerea*) of grapevines.

Overseas registrations: Boscalid formulations are currently registered in the following countries: Argentina, Chile, Korea, UK, Germany, Switzerland, Israel, Macedonia, Canada and USA.

It is used overseas for the control of various diseases of many crops including grapevines, stone and pome fruits, vegetables and ornamentals.

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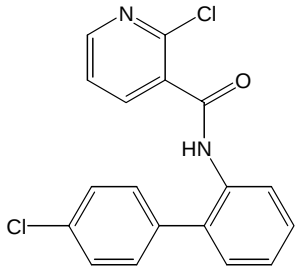
CHEMISTRY AND MANUFACTURE

Active Constituent

The chemical active constituent has the following properties:

Common Name:	Boscalid
Chemical Name (IUPAC):	2-Chloro-*N*-(4'-chlorobiphenyl-2-yl)nicotinamide
CAS Registry Number:	188425-85-6
Empirical Formula:	$C_{18}H_{12}Cl_2N_2O$
Molecular Weight:	343.21
Physical form:	Solid
Colour:	White
Odour:	Odourless
Melting Point:	142.8-143.8^{o}C
Density:	1.381 g/cm^3
Octanol/water partition coefficient (K_{OW}):	2.96
Vapour pressure at 25 °C:	2x10^{-8} hPa

Chemical Structure:



Summary of the APVMA's Evaluation of boscalid active constituent

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

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

Active constituent	Minimum content
Boscalid	Not less than 960 g/kg

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

Formulated Product

Distinguishing name:	Filan Fungicide
Formulation type:	Water Dispersible Granule (WG)
Active constituent concentration:	500g/kg boscalid

Physical and Chemical Properties of the Product

Physical state:	Solid
Colour:	Grey brown granules
Odour:	Faint aromatic odour
Acidity, alkalinity or pH value:	5.2-6.4
Density:	1.400
Flash point:	Not applicable
Flammability:	Not highly flammable
Auto flammability:	348^{o}C
Vapour pressure:	Not available
Storage stability:	Stable for at least 2 years when stored under ambient temperature.

Summary of the APVMA's Evaluation of Filan Fungicide

The Chemistry and Residues Program (CRP) has evaluated the chemistry aspects of Filan 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

BOSCALID

Evaluation of Toxicology

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

Toxicokinetics and Metabolism

In rats given a single gavage dose of 50 mg/kg/day ^{14}C-boscalid, there was an initial peak in the concentration of radiolabel in the plasma at 30 minutes. Lower levels from 1 to 4 hours were followed by a second peak plasma level at 8 hours. Excretion was around 16% in the urine and 39% in the bile, with approximately 80% recovered in the faeces and zero in expired air. The bioavailability was estimated to be 55%. Tissue distribution was widespread and highest levels were found in the fat, liver and kidney. About 30 to 40% of the dose was excreted unchanged in the faeces, but very little boscalid was detected in the tissues, urine or bile. The remainder was extensively metabolised, the major pathways were hydroxylation of the biphenyl group followed by conjugation with glucuronic acid and sulfhydryl substitution of the 2-chloropyridine moiety followed by conjugation with glucuronic acid.

The *in-vitro* epidermal absorption rate was 8 to 20 times faster through rat epidermis than through human epidermis. Although the amount absorbed was greater from the higher concentrations, the percentage absorbed was lower. Up to 11% was absorbed through rat skin *in-vivo* in 24 hours. Dermal absorption was not dose-proportional.

Acute Studies

In acute studies in rats, boscalid had an estimated oral LD_{50} of >5000 mg/kg, a dermal LD_{50} of >2000 mg/kg, and an inhalation LC_{50} of >6700 mg/m^3. It was not a skin irritant in rabbits or a skin sensitiser in guinea pigs, but was a slight eye irritant in rabbits.

Filan Fungicide had acute oral and dermal LD_{50}s of >2000 mg/kg and an inhalation LC_{50} of >5200 mg/m^3 in rats. Filan was not a skin irritant but was a slight eye irritant in rabbits and was non-sensitising to guinea pigs in a Buehler test.

Short-Term Studies

Rats received dermal applications of 0, 100, 250, or 1000 mg/kg/day boscalid for 6 hours/day, 5 days per week, for 4 weeks. There were reductions in serum total bilirubin at 1000 mg/kg/day, aspartate aminotrasferase in 1000 mg/kg/day females and in spleen weight at ≥250 mg/kg/day. There were no deaths or clinical signs of toxicity. Body weight gains, food consumption and efficiency, haematology, urinalysis, macro- and microscopic pathology were unchanged following treatment with boscalid.

Mice were fed 0, 150, 1000, 4000 or 8000 ppm boscalid in the diet for 3 months. Changes to serum chemistry included a slight increase in alanine aminotransferase in ≥4000 ppm females and decreases in total protein in ≥4000 ppm males and 8000 ppm females, in total bilirubin at 8000 ppm and in triglycerides in 8000 ppm females. There were decreases in cholesterol at ≥1000 ppm and in albumin and globulin at ≥4000 ppm, with a greater severity in males. Liver weights were increased at ≥1000 ppm and histopathology revealed an increase in the severity of diffuse fatty change in the livers of ≥4000 ppm males. The NOEL is 150 ppm (equivalent to 42 mg/kg/day).

Rats were fed 0, 100, 500, 2000, 5000 or 15000 ppm boscalid in the diet for 3 months. Prothrombin time was significantly reduced in 15000 ppm females. There were significant increases in serum gamma-glutamyl transpeptidase in ≥2000 ppm males and ≥5000 ppm females, in total protein in ≥5000 ppm males and in 15000 ppm females, in albumin and calcium in ≥5000 ppm males, and in globulin and cholesterol in 15000 ppm females. Significant decreases were observed in total bilirubin and triglycerides in ≥2000 ppm and 15000 ppm males respectively, and in alkaline phosphatase in ≥500 ppm females. Thyroid weight and liver weight were increased at ≥2000 ppm and ≥5000 ppm respectively and spleen weight decreased in 15000 ppm males. Histopathological changes included diffuse hyperplasia and follicular cell hypertrophy in male thyroids at ≥2000 ppm. Central hypertrophy in the liver at ≥5000 ppm was accompanied by reductions in midzonal fat storage. The NOEL is 100 ppm (equivalent to 8 mg/kg/day).

Dogs were fed 0, 250, 2500 or 25000 ppm boscalid in the diet for 3 months. Abnormal faeces were observed at ≥2500 ppm. Initial body weight losses were noted in 25000 ppm males and ≥250 ppm females. Overall, body weight gain was slightly reduced in 25000 ppm females. Haematological changes included decreases in haemoglobin levels and erythrocyte counts in 25000 ppm females. Increased serum alkaline phosphatase and reductions in alanine aminotransferase and aspartate aminotransferase were seen in 25000 ppm males and ≥2500 ppm females. Serum triglycerides increased at 25000 ppm. There were decreases in male kidney weights at 25000 ppm and increases in liver weights at ≥2500 ppm and in female thyroid weights at 25000 ppm, with no treatment-related changes at macroscopic or microscopic examination. The NOEL is 250 ppm (equivalent to 18 mg/kg/day).

Long-Term Studies

In a carcinogenicity study, mice were fed 0, 80, 400, 2000 or 8000 ppm boscalid in the diet for 18 months. Body weight gain was reduced in ≥400 ppm males and in 8000 ppm females. There were increases in absolute liver weights at ≥2000 ppm and relative liver weights in ≥400 ppm males and ≥2000 ppm females. Histopathological changes in the liver included increased incidences of peripheral hypertrophy in 8000 ppm males and ≥2000 ppm females, oval cell proliferation in 8000 ppm females and a change from diffuse to centrilobular fatty infiltration in ≥400 ppm females. There were no increases in the types and incidence of tumours. The NOEL is 80 ppm (equivalent to 18 mg/kg/day).

In a carcinogenicity study, rats were fed 0, 100, 500, 2500 ppm boscalid in the diet for 24 months or 15000 ppm boscalid in the diet for 17 months (killed early due to significant reductions in female body weight gain). Body weight gain was significantly reduced in ≥2500 ppm females. There were increases in liver weight at 2500 ppm, in thyroid weight in 2500 ppm males, and in ovary weight at ≥500 ppm. In males, cystic degeneration in the testes and smaller seminal vesicles occurred at ≥500 ppm. In the liver, there were increases in the incidence of centrilobular hypertrophy at 2500 ppm and in eosinophilic foci in ≥500 ppm males. The incidence of adenomas, diffuse hypertrophy and focal hyperplasia increased in thyroid follicular cells at 2500 ppm. Diffuse papillary transitional cell hyperplasia in the urinary bladder increased slightly in 2500 ppm males. The NOEL is 100 ppm (equivalent to 6 mg/kg/day).

In a chronic study, rats were fed 0, 100, 500, or 2500 ppm boscalid in the diet for 24 months or 15000 ppm boscalid in the diet for 17 months (killed early due to significant reductions in body weight gain). A mild anaemia was suggested by slight reductions in haemoglobin, haematocrit, mean corpuscular volume and mean corpuscular haemoglobin in 15000 ppm females. Prothrombin time decreased in 15000 ppm females and erythrocyte counts increased and leucocyte counts decreased in 15000 ppm males. There were reductions in serum alkaline phosphatase at ≥500 ppm, in alanine aminotransferase in 15000 ppm males and in ≥2500 ppm females and in aspartate aminotransferase in 15000 ppm females. Serum gamma-glutamyl transpeptidase increased in ≥2500 ppm males and 15000 ppm females. Decreases occurred in total bilirubin at ≥2500 ppm and triglycerides at 15000 ppm. There were increases in total protein at ≥2500 ppm and in cholesterol in ≥2500 ppm females, with slight increases in albumin in 15000 ppm males and in globulin at ≥2500 ppm. There were increases in liver weight with centrilobular hypertrophy and necrosis at 2500 ppm, eosinophilic foci increased in ≥500 ppm males and a reduction in peripheral fatty infiltration occurred at 2500 ppm. Thyroid weight increased in 2500 ppm males. In thyroid follicular cells, adenomas were present at ≥500 ppm and diffuse hypertrophy and focal hyperplasia increased at 2500 ppm. Cystic degeneration in the testes was seen at 2500 ppm. The NOEL is 100 ppm (equivalent to 6 mg/kg/day).

Dogs were fed 0, 200, 800, 2000 or 20000 ppm boscalid for approximately 12 months. At 20000 ppm, soft, light-brown faeces were observed and almost daily vomiting was noted in one 20000 ppm female over the last 3 months. Body weight gain was reduced in 2000 ppm males and females and in 20000 ppm females, but not in 20000 ppm males. Food efficiency decreased in ≥2000 ppm females. Platelet counts were slightly increased in 20000 ppm females. Serum alkaline phosphatase increased in ≥2000 ppm males and 20000 ppm females. At 20000 ppm, there were increases in triglycerides, in total protein in females and in cholesterol (slight). Serum alanine aminotransferease decreased in ≥2000 ppm males and 20000 ppm females and slight decreases in aspartate aminotransferase occurred at 20000 ppm. Liver weight increased at ≥2000 ppm and thyroid weight increased in ≥2000 ppm males and 20000 ppm females, with no treatment-related changes at macroscopic or microscopic examination. The NOEL is 800 ppm (equivalent to 22 mg/kg/day).

Reproduction and Developmental Studies

In a two generation study, rats received 0, 100, 1000, or 10000 ppm of boscalid in their diet. At 10000 ppm, there were reductions in body weight gain in F_0 females during gestation and in F_1 males during pre-mating. Food consumption was reduced in 10000 ppm F_1 females during lactation. There were no effects on male or female fertility indices, or on reproduction data other than an increase in post-implantation losses in 10000 ppm F_1 females. In parental rats there were increases in liver weights at 10000 ppm and zone 3 hypertrophy and degeneration in the liver, with a reduction in peripheral fatty infiltration at ≥1000 ppm. The numbers of pups dying on the day of birth increased in F_2 litters at 10000 ppm. Pup body

weight gain was reduced during lactation at 10000 ppm and in 1000 ppm F_2 males. There were no effects on sexual maturation, or at necropsy. The NOEL for adults is 100 ppm (15 mg/kg/day). The NOEL for reproductive performance is 1000 ppm (155 mg/kg/day). There were no effects on fertility at up to 10000 ppm (at least 1457 mg/kg/day). The NOEL for neonates is 100 ppm (15 mg/kg/day).

Pregnant female rats received oral gavage doses of 0, 100, 300, or 1000 mg/kg/day boscalid on gestation days 6 to 19. There was no evidence of maternal toxicity. In foetuses, the incidence of incomplete ossification of the thoracic centrum increased at 1000 mg/kg/day. The maternal NOEL is at least 1000 mg/kg/day and the NOEL for foetal toxicity is 300 mg/kg/day.

Artificially inseminated female rabbits received oral gavage doses of 0, 100, 300, or 1000 mg/kg/day boscalid on gestation days 7 to 28. The incidence of abortion increased and maternal body weight gains decreased at 1000 mg/kg/day. In foetuses, incomplete ossification of the sacral arch, talus and thoracic centrum increased at 1000 mg/kg/day. The NOEL for both maternal and foetal toxicity is 300 mg/kg/day.

Genotoxicity

Boscalid was non-genotoxic in the following studies; a bacterial reverse mutation assay with *S. typhimurium* and *E. coli*, a mammalian cell mutation assay (CHO-HGPRT), an *in vitro* chromosome aberration assay in Chinese hamster V79 cells, a mouse micronucleus test and an *in-vitro* UDS assay in primary rat hepatocytes.

Neurotoxicity Studies

Rats received single oral gavage doses of 0, 500, 1000, or 2000 mg/kg boscalid. Piloerection was noted in two 2000 mg/kg/day females on the day of administration in the functional observation battery (FOB). There were no effects on other FOB indices, survival, body weight gain, macroscopic or neurohistopathological investigations.

Boscalid at 0, 150, 1500, or 15000 ppm was fed to groups of 10 male and 10 female rats in their diet for 3 months. There were no treatment-related effects on survival, clinical signs, body weight and food consumption, FOBs, motor activity, macroscopic necropsy or neurohistopathology.

Pregnant female rats were fed 0, 100, 1000 or 10000 ppm boscalid in their diet on gestation days 6 to 21. There were no effects on the dams, or on reproductive performance or fertility at any dose (at least 1853 mg/kg/day). Pup body weight gains were reduced at 1000 ppm on days 1-4 of lactation and at 10000 ppm throughout lactation. Auditory startle response was slightly reduced in 10000 ppm females. The NOEL for growth of pups is 100 ppm (18 mg/kg/day) and the NOEL for developmental neurotoxicity is 1000 ppm (186 mg/kg/day).

Special Studies

Rats received 0 or 15000 ppm boscalid in their diet for 2 weeks. There were increases in pentoxyresorufin-O-dependentylase (PROD) and TBA-reactive material (indicative of lipid peroxidation) in treated males and increases in liver weight and cytochrome P450 in treated rats. Liver electron microscopy revealed proliferation of the smooth endoplasmic reticulum

(SER), accompanied by glycogen depletion in severe cases, in centrilobular hepatocytes in treated rats.

Rats received 0 or 15000 ppm boscalid in their diet for 4 weeks. Blood levels of total triiodothyronine (T_3) were reduced on days 21-28 in treated males and at day 7 and on days 21-28 in treated females. Total thyroxine (T_4) was reduced from day 2 in treated males. Blood levels of thyroid stimulating hormone (TSH) increased from day 7 in treated males and from day 2 in treated females. Phase II biotransformation enzymes in the liver (p-nitrophenol-glucuronyltransferase (p-NP-GT), 4-methylumbeliferone-glucuronyltransferase (MUF-GT) and 4-hydroxybiphenyl-glucuronyltransferase (HOBI-GT)) were increased following boscalid treatment.

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.

The NDPSC has determined that boscalid is exempt from scheduling on the basis of its toxicological profile. There are provisions for appropriate safety directions on the product label.

NOEL/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 boscalid was established at 0.06 mg/kg/day based on the NOEL of 6 mg/kg/day in 2-year rat dietary studies and using a 100-fold safety factor in recognition of the extensive toxicological database available for boscalid.

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.

In developmental studies in rats, the NOEL for foetotoxicity was 300 mg/kg/day and this is an appropriate endpoint to use in establishing an ARfD. Using a safety factor of 100, the ARfD is 3 mg/kg.

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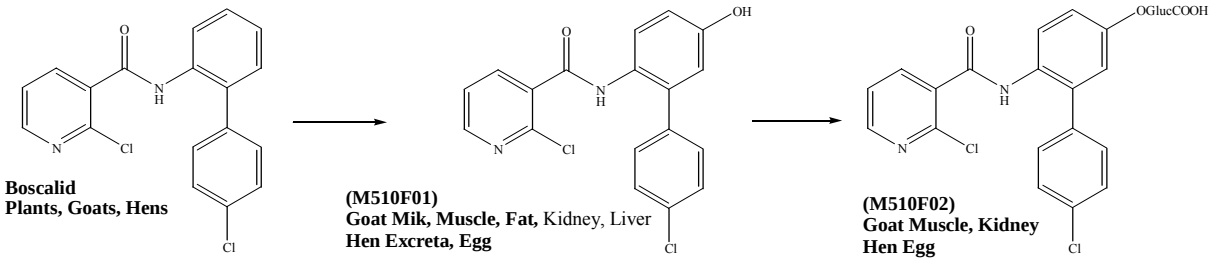
RESIDUES ASSESSMENT

Metabolism

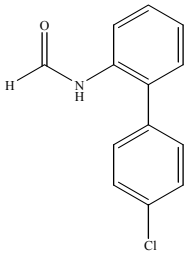
Grapevines were treated with a foliar application of ^{14}C-boscalid. Total radioactive residues (TRR) were predominantly found on the leaves of the grapevines (75-77% TRRs). In lettuce treated with ^{14}C boscalid, the majority of the extractable TRRs were similarly located in the leaves. Less than 5% of the labelled residues in bean plants were present in the green beans, bean pods or bean seeds. Boscalid was essentially not metabolised by the plant, comprising over 92%, 99% and 78% of the TRRs in grapes, lettuce and bean plants, respectively.

Laying hens were dosed at 1.875 mg/kg bw for 10 consecutive days with ^{14}C-boscalid. Excretion of radioactivity over the period of the study was greater than 97%. Radioactivity in eggs accounted for 0.11% of the total dose. Radioactive residues in tissues were highest in liver (0.169 mg equiv./kg) followed by fat (0.025 mg equiv/kg), and muscle (0.0025 mg equiv/kg). The extraction of residues from the liver proved to be quite difficult as much of the radiolabel was bound to the hepatic matrix. A significant amount of the radiolabel not initially extracted was released by microwave treatment.

Boscalid was the major residue in the fat (93%). However, a metabolite was observed as a result of hydroxylation of the phenol and its subsequent glucuronide conjugate, accounting for 76% and 44% in the excreta and egg, respectively.



Two **lactating goats** were dosed with ^{14}C-boscalid at 1.41-1.80 mg/kg bw for 5 consecutive days. Total radioactive residues in excreta were over 90% of the administered dose. Total ^{14}C-residues in milk and tissues accounted for less than 1% of the administered dose. Of these, the total radioactivity was 0.43-0.61 mg equiv./kg in liver, 0.06-0.15 mg equiv./kg in milk and <0.02 mg. equiv./kg in each of the bile, kidney, fat and muscle tissues. The parent compound was the major residue in urine, faeces, milk, fat, muscle and kidney. Metabolites accounting for greater than 10% of the TRR were again the hydroxylated biphenyl moiety and its glucuronide conjugate. An acetamide metabolite was identified as a result of the microwave treatment of the liver, and may be considered as a marker metabolite for boscalid in this matrix only.



N-(4'-chlorobiphenyl-2-yl)acetamide

Analytical methods

Analytical methods to determine boscalid residues in grapes, animal tissues and milk were provided.

Boscalid and metabolite residues in fruit and animal tissues are determined by HPLC with MS/MS detection following extraction in aqueous acidic methanol. The LOQ was 0.05 mg/kg in plant tissues, 0.025 mg/kg in animal muscle, fat, kidney and liver, and 0.01 mg/kg in milk and eggs.

Boscalid residues in the hepatic matrix and milk were liberated by treatment with an acidic acetonitrile solution in a microwave oven (170 °C, 30 mins). Determination was undertaken using GC/MS, liberating the acetamide, which may be considered a marker metabolite for the presence of boscalid residues in the liver only.

Storage stability

Storage stability data for homogenised grape samples indicated that the residues are stable upon frozen storage for up to 24 months (-20 °C). Storage stability information was also provided for animal tissues. Residues of boscalid in fortified samples of bovine muscle, liver, and kidney were stable after frozen storage for over five months.

Residue definition

Metabolism studies provided for boscalid in plants showed that the parent compound was not absorbed or translocated by the plant. The parent was not metabolised in the plant to any significant extent.

In animal studies, over 90% of the residues attributable to boscalid were excreted. In the edible tissues, the TRRs were primarily the parent compound, and a hydroxylated metabolite (M510F01) that exhibited some conjugation, especially in the kidney and liver. Extractable TRRs were were identified as the parent compound and the hydroxy metabolite.

Therefore, in plant material, the residue definition of boscalid is the parent compound *per se*. In animal tissues, the recommended residue definition for boscalid is "*sum of boscalid, 2-chloro-N-(4'-chloro-5-hydroxybiphenyl-2-yl) nicotinamide and the glucuronide conjugate, expressed as boscalid equivalents"*.

Residue trials

A total of 45 residue trials for grapes were provided. Five Australian trials where the treatment regime was consistent with proposed GAP were presented. The data were supplemented with trials conducted in Europe (Northern and Southern Germany, Northern and Southern France and Northern Italy).

When boscalid was used according to proposed GAP, residues in grapes were (median underlined) 0.53, 0.71, 0.95, 1.09, 1.38, 1.45, <u>1.61</u>, 1.65, 2.00, 2.25, 2.33, 2.80 and 2.95

mg/kg (600 g ai/ha, 2 non-consecutive applications, 28-day WHP). The STMR (underlined above) is 1.61 mg/kg, and the HR is 2.95 mg/kg.

Based on the data shown above an MRL of 4.0 mg/kg is appropriate for grapes with a 28-day withholding period.

As a result of two trials, the mean processing factor determined for the conversion of grapes → wet pomace was 2.6. Applying the average processing factor for wet pomace to the STMR (1.61 mg/kg) and HR (2.95 mg/kg) for grapes, gives a pomace HR-P of 7.67 mg/kg for wet grape pomace. The STMR-P for wet grape pomace is calculated as 3.86 mg/kg. As pomace is approximately 40% dry matter, the expected HR-P for dry pomace is 19.17 mg/kg, and the STMR-P is 10.48 mg/kg. An MRL of 25 mg/kg is appropriate for grape pomace, dry.

The US EPA has published a drying factor of 4.7 for grapes → raisins. Applying this concentration to the STMR and HR for the conversion of grapes → raisins would give residues of 7.57 and 13.87 mg/kg, respectively. In a processing study, a concentration factor of 2.4 was estimated for residues of boscalid from grapes → raisins. As no detailed information on the drying process was provided, the recommended MRL for dried grapes is 15 mg/kg.

Animal commodity MRLs

Grape pomace is a potential animal feed commodity, formed as a by-product of juice and wine manufacture.

In a cow transfer study, fourteen dairy cows were fed 0, 0.05, 0.164 and 0.655 mg/kg bw of boscalid once daily for 28 days. The highest residues for boscalid were noted to be present in the cream, kidney, fat and liver of cows dosed at 0.655 mg/kg bw at levels of 0.381, 0.318, 0.292 and 0.182 mg/kg, respectively. Residues of 0.096 mg/kg were detected in whole milk on Day 18 of the study. No residues were detected in skim milk. Residues of 0.058 mg/kg were detected in the muscle of the cow after feeding for 28 days.

Depuration data were given for a single cow, sacrificed 7 days following dosing at 0.655 mg/kg bw in the feed. The data show that quantifiable residues were not detected in the milk, muscle, liver, kidney and fat of the cow. Boscalid is rapidly depleted from the cow after removing the animal from dosing for 7 days.

The anticipated dietary exposure is approximately 0.08 mg/kg bw, which is approximately half that of the 3 × feeding level of 0.164 mg/kg bw in the dairy cattle feeding study. On the basis of the data from the feeding studies, the expected maximum residues are as follows:

Table 1.

Commodity	Residues of Boscalid and M510FO1 (mg/kg)	Residues of M510F53 (mg/kg)
Whole Milk	<0.02	
Skim Milk	<0.02	
Cream	0.063	
Muscle	<0.05	
Liver	0.032	<0.05
Kidney	0.044	
Fat	0.062	

It is therefore considered appropriate to establish MRLs for mammalian animal commodities at the following limits:

MO 0105	Edible offal [Mammalian]	0.05 mg/kg
MM 0095	Meat [Mammalian] (in the fat)	0.1 mg/kg
ML 0106	Milks	*0.02 mg/kg

Estimated dietary intakes

The chronic dietary exposure to boscalid is estimated by the National Estimated Daily Intake 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 boscalid is equivalent to 2.1% of the ADI. It is concluded that the chronic dietary exposure 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.

The NESTIs for all relevant commodities are less than the ARfD. It is concluded that the acute dietary exposure is acceptably low, as seen in the following table:

Commodity		**2-6 years**	**2+ years**
MM 0095	Meat (mammalian)	0.023	0.013
ML 0106	Milks	0.040	0.010
MO 0105	Edible Offal [mammalian]	0.001	0.003
DF 0269	Dried grapes (sultanas, currants, raisins)	0.610	0.017
FB0269	Grapes (excluding wine)	1.770	0.753
	Wine only	0.004	0.309

Recommendations

MRL changes

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

Table 1

Compound		**Food**	**MRL (mg/kg)**
Add:			
Boscalid			
DF	0269	Dried grapes (sultanas, currants, raisins)	15
FB	0269	Grapes (including wine)	4
MO	0105	Edible offal, mammalian	0.05
ML	0012	Milks	*0.02
MM	0095	Meat [mammalian] [in the fat]	0.1

Table 3

Add:		
	Boscalid	Commodities of plant origin: Boscalid Commodities of animal origin: Sum of boscalid, 2-chloro-N-(4'-chloro-5-hydroxybiphenyl-2-yl) nicotinamide and the glucuronide conjugate, expressed as boscalid equivalents

Table 4

Compound	**Animal Feed Commodity**	**MRL (mg/kg)**
Add:		
Boscalid		
	Grape pomace, dry	25

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 period statements are recommended in conjunction with the above MRLs:

Grapes (Harvest): DO NOT harvest for 4 weeks after application

Grapes (Grazing): DO NOT treat vineyards that will or may be grazed by livestock

Export Slaughter Interval (ESI)

DO NOT feed treated produce to livestock for 7 days before slaughter

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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 boscalid 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.

Commodities exported and main destinations

The applicant has indicated that as of November 2003, fungicides containing boscalid have been submitted for use on food crops in Germany, UK, France, Italy, the Netherlands, USA, Brazil, Chile, Argentina, Canada, Japan, Croatia, Romania and Yugoslavia. Definite registrations have been in place in Argentina, Chile, Korea, the UK, Germany, Switzerland, Israel, Macedonia, Canada, and the USA.

Risks to Australian trade from boscalid residues arise when the importing countries have not set tolerances for residues in food commodities, or when tolerances in the importing countries are lower than the corresponding Australian MRLs.

The following MRLs/tolerances have been proposed overseas for the use of boscalid on grapes (as of November 2003):

Commodity	**Overseas MRLs/tolerances (mg/kg) (PHI)**				**Proposed Australian MRL (mg/kg) (PHI)**
	Europe	**USA**	**Brazil**	**Japan**	
Grapes	5 (28)[1-3]	3.5	3 (7)	15	4 (28)
Dried Grapes		3.5, 7.7[3]			15

1. Tolerance is pending.
2. Value in parentheses is the PHI
3. Switzerland has established an MRL of 5 for grape and 1 for wine.
4. MRL of 7.7 mg/kg for raisins.

The applicant has stated in the financial year 1999-2000, over $A1.3 million of wine (comprising 284.9 million litres), $A74 million of table grapes (33 485 tonne) and $A13 million of dried grapes (71% sultanas, 22% currants, 4 929 tonne) of dried grapes were exported to overseas destinations. These countries include Belgium (dried grapes), Canada (wine, dried grapes), the EU (wine), Germany (wine, dried grapes), Hong Kong (fresh grapes), Indonesia (fresh grapes), Japan (wine, dried grapes), Luxembourg (dried grapes), Malaysia (fresh grapes), New Zealand (wine, fresh and dried grapes), Norway (wine), Switzerland (wine), UK (wine, dried grapes), USA (wine) and Vietnam (fresh grapes), amongst others.

The applicant proposes to mitigate the risk to trade by the inclusion of the following statements on the label:

"*Grapes and grape products intended for export: Consult your peak industry body or BASF for recommended withholding period*"

"*EXPORT OF TREATED PRODUCE*
Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all export markets for grapes treated with FILAN fungicide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing fruit for export (either fresh, dried or as a wine) please check with your industry spray diary, peak industry body (such as the Australian Wine Research Institute http://www.waite.adelaide.edu.au/AWRI/) or BASF for the latest information on MRLs and import tolerances before using FILAN Fungicide."

*Animal Commodities***.**
It is expected that animals consuming produce treated with boscalid according to label directions could potentially contain residues of up to 0.1 mg/kg for meat fat, 0.05 mg/kg in edible offal and *0.02 mg/kg in milks. Consequently, it is likely that animal commodities may contain residues, however given that depuration data show negligible amounts of residues in animal commodities following the cessation of feeding treated produce for 7 days, it is not likely that residues would be detected in animal commodities. As such a period of 7 days between the cessation of feeding treated produce and slaughter of the animals destined for export is recommended.

The APVMA welcomes comment with regard to whether the proposed use of boscalid on grapes, processed commodities or animals exposed to produce treated with boscalid poses an undue prejudice to Australia's trade in these commodities.

Assessment of Occupational Health & Safety

Boscalid is not listed on the NOHSC *List of Designated Hazardous Substances.* Boscalid is determined to be hazardous according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* with the following risk phrase: R40 Limited evidence of a carcinogenic effect. Based on the concentration of boscalid in the product, Filan Fungicide is classified as hazardous according to the NOHSC *Approved Criteria for Classifying Hazardous Substances.*

Filan Fungicide has low acute oral, dermal and inhalation toxicity in rats. The product is a slight eye irritant in rabbits, but was not a skin irritant in rats or a skin sensitiser in guinea pigs.

Formulation, Packaging, Transport, Storage and Retailing

The product will be imported into Australia as a finished product packaged in 2, 2.5, 5, 10, 15 & 20 kg packages packed in HDPE bottles.

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

Use and Exposure

Filan Fungicide is a water dispersible granule formulation which will be used for the control of bunch rot (*Botrytis cinerea*) in grapevines.

The product will be applied as a concentrated or dilute spray at the maximum rate of 1.8 kg/ha in spray volumes of 500-1500 L/ha with approximately 5-15 hectares treated/day by tractor-mounted commercial vineyard sprayers which will be motor-driven with enclosed cabs using airblast sprayers. The duration of application is expected to be 2-3 hours/day.

Workers may be exposed to the product when opening containers, preparing spray, applying spray, maintaining equipment and cleaning up spills. Workers may also be exposed to product residues when entering treated areas to carry out various crop activities.

There were no worker exposure studies available for assessment. In the absence of worker exposure data, NOHSC used the UK Predictive Operator Exposure Model (POEM) and the Pesticide Handlers Exposure Database (PHED) to estimate worker exposure to boscalid during mixing/loading and application using tractor-driven airblast equipment.

Worker exposure estimated using the UK POEM indicated unacceptable exposure for workers using airblast concentrated spraying with and without the use of gloves, and for dilute spraying without the use of gloves. Exposure was found to be acceptable for dilute spraying while using gloves.

Worker exposure estimated using PHED indicated acceptable exposure for workers open mixing/loading with and without the use of gloves, and for applicators with and without the use of gloves while using open cabs. Total exposure for mixer/loader/applicator were acceptable for workers in open cabs with and without the use of gloves, and in enclosed cabs while using gloves.

The risk assessment indicates that cotton overalls buttoned to the neck and wrist (or equivalent clothing), a washable hat and elbow-length PVC gloves should be worn when opening the container, preparing the spray and using the prepared spray.

Entry into Treated Areas

There were no worker exposure data available to assess exposure during re-entry activities. Workers entering treated areas may be exposed to product residues and degradation products during crop irrigation, scouting, grape girdling, manual harvesting or other crop management activities. In the absence of re-entry data, NOHSC estimated risk for re-entry workers by using the US EPA Occupational Post-Application Risk Assessment Calculator Version 1 (8/9/00)-US EPA Policy 003.1.

The risk assessment indicated that re-entry workers for various crop activities should not enter treated crops until the spray has dried. If prior entry is required the PPE recommended below should be used.

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, and elbow-length PVC gloves when opening the container, preparing spray and using the prepared spray.

The PPE recommended should meet the relevant *Standards-Australia*.

NOHSC recommends the following re-entry & precaution statements on the product label:

RE-ENTRY
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), chemical resistant gloves and footwear. Clothing must be laundered after each day's use.

PRECAUTION

NOHSC recommends a 5-day re-entry interval for grape girdling.

Conclusion

NOHSC supports the registration of Filan Fungicide, containing 500 g/kg of boscalid, as a water dispersible granule formulation, for the control of bunch rot (*Botrytis cinerea*) in grapevines.

Filan Fungicide can be safely used by workers when handled in accordance with the instructions on the product label and any other control measures described above.

Additional information is available in the MSDS provided for Filan Fungicide.

ENVIRONMENTAL ASSESSMENT

Environmental Exposure

BASF Australia Pty Ltd has applied for the registration of a new product Filan Fungicide containing a new ingredient boscalid at 500 g ai/kg (formulated as a wettable granule, WG). Filan Fungicide is to be used for the control of the fungal disease bunch rot (*Botrytis cinerea*) in grapevines as per the directions for use on the label.

Environmental Chemistry and Fate

Hydrolysis

In a study conducted to meet both US EPA and EC Guidelines there was no hydrolysis at 25°C after 30 days at pH 5 and 7 or in tests conducted at 50°C. A half-life was not determined and it was concluded that under typical environmental conditions hydrolysis is not expected.

Photolysis

In a test conducted to meet US EPA and EC requirements, aqueous irradiation of boscalid with a simulated solar spectrum showed that there was no degradation. The UV spectrum of boscalid showed that there was very limited absorption over the range 290 to 800 nm, indicative of no absorption in the solar spectrum. Therefore, direct photolysis is unlikely.

In soil photolysis studies, conducted to US EPA and EC Guidelines using a microbially active soil, radiolabelled boscalid was applied to the thin layers of soil and irradiated with a simulated solar spectrum. The results indicate that soil photolysis has only a slight effect on the rate of degradation of boscalid compared to the dark control samples. A half life of 135 days was determined but as this exceeds the duration of the study it is not reliable. The report concluded that light might slightly increase the rate of degradation of boscalid in soil.

The photochemical oxidative degradation in the atmosphere was determined based on the chemical structure of the molecule. The half-life of boscalid was calculated to be 27.3 h for photochemical degradation by hydroxyl radicals and < 3.5 d (24 h day) for degradation by ozone. It was concluded that if boscalid reaches the troposphere it will be degraded fast by photochemical processes.

Metabolism

Aerobic soil

The metabolism of boscalid was studied in an agricultural soil, classified as sandy loam under aerobic conditions according to US EPA and BBA Guidelines. Metabolism was slight, with the DT_{50} calculated as 108 days. There were 2 minor metabolites none of which exceeded 1% applied active with non-extractable soil bound products reaching 60% after 1 year.

The degradation of the boscalid was studied in 4 agricultural soils (3 loamy sands and a loam) according to BBA Guidelines. After 120 days of incubation under a range of temperature and moisture conditions, the DT_{50}s were calculated as ranging from 133 to 348 days. There was no significant degradation at low temperature (5°C), dry conditions or under sterile conditions. The study supports the previous study in showing that boscalid degrades slowly in soil under aerobic conditions and the pathway gives mainly bound residues. Reducing the temperature or moisture levels reduces the degradation rate.

The rate of degradation of boscalid was determined in two German soils that had been previously treated with boscalid for up to three years. The DT_{50} ranged from 141 to 201 days

in one soil and 87 to 6600 days in the other. There was no significant effect from the pre-treatments and it was concluded that the degradation of boscalid in pre-treated soil had little influence on the degradation rate of boscalid.

The biodegradability of boscalid was determined according to OECD Test Guidelines 301F. There was limited degradation throughout the study (<10%) and it was concluded that boscalid is not readily biodegradable.

Aerobic aquatic metabolism

The aerobic aquatic metabolism of boscalid was conducted according to US EPA and BBA Guidelines using two sediment-water systems, one from the Rhine River and the other from a pond. In the pond system, dissipation from water was initially rapid then decreased to be 17.4% of applied radioactivity after 100 days. There was a corresponding increase in the sediment, and bound residues slowly increased to reach 12.9% of AR at 100 DAT. Analysis showed that the parent was the only product in both water and sediment without any other metabolites being detected. Mineralisation was negligible. The DT_{50} for dissipation from water compartment was 9 days.

Results for the river system again showed loss of radioactivity from the water phase with just 33% remaining after 7 days and 6% by 100 days, faster than in the pond system. Again only parent was detectable in both the water and sediment and bound residues slowly increased to reach 10% after 100 days. The DT_{50} for loss from the water compartment was 3 days.

The study showed that boscalid was adsorbed to the sediment but there was limited degradation after 100 days in the sediment with soil bound material the only 'degradation' noted. In the sterile systems the distribution of radioactivity at the end of the study was very similar to the viable systems.

Aerobic Aquatic metabolism under outdoor conditions

Boscalid, radiolabelled with ^{14}C at the diphenyl ring, was incubated in an aerobic aquatic system under outdoor conditions. The sediment-water system was taken from a pond; the water was aerobic and the sediment was anaerobic.

The results clearly showed that boscalid slowly dissipates from the water phase to the sediment where it slowly degrades, with just 22% of applied remaining in the former after 120 days. The half-life for dissipation to the sediment ranged from 21 days (first order, r^2 0.94) to 16 days using a more complex multi-compartment model. The half-life for degradation in sediment was 66 days. There was only one metabolite detected which reached a maximum of 9.5% of applied. It was concluded that this study clearly shows that boscalid dissipates from the water phase relatively quickly and is then found in the sediment where it slowly degrades.

Anaerobic soil metabolism

The metabolism of boscalid (^{14}C-labelled in the diphenyl or pyridine ring) was studied under anaerobic conditions in a sandy loam soil according to BBA Guidelines. The soil was flooded with water then after anaerobic conditions were established the soil was treated with boscalid before being anaerobically incubated for 120 days.

The majority of the applied radioactivity appeared as parent by the end of the study and there was little mineralisation from either label. The DT_{50} value was 345 days with the pyridine label (r^2 0.91) and 261 days with the diphenyl label (r^2 0.94). With either label only trace amounts of metabolites could be detected.

Mobility

Volatility

In a study conducted according to the BBA Guidelines the levels of volatilisation of radiolabelled boscalid within 24 h after application to a loamy sandy soil surface and bush bean surface were below 1 % in either case. The study demonstrated that volatilisation is not a relevant pathway for dissipation of boscalid.

Adsorption/desorption

The adsorption/desorption of boscalid was studied by the batch equilibrium method using 6 agricultural soils. Boscalid was moderately to strongly adsorbed onto all soils with K_{oc}s ranging from 507 to 1110 and was classified as having low to medium mobility (McCall classification). There was desorption with Koc_{des} ranging from 1243 to 2977.

Column leaching

A leaching column study was conducted using a sandy soil in accordance with BBA Guidelines. 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 boscalid and of its metabolites.

Field Dissipation

Dissipation at 2 German sites.

The dissipation of boscalid was studied under field conditions at two 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 3 rates, 300, 600 and 1200 g ai/ha using a suspension concentrate. The results of the chemical analysis (HPLC) showed that boscalid was mainly detected in the 0-10 cm layer and occasionally minor amounts (~10% of total recovered) were detected in the 10-25 cm soil sections. It was only detected lower down (25-50 cm) once at 0.02 mg/kg (DU2 site; 1200 g ai/ha 176 DAT). There were no metabolites detected. The DT_{50} of boscalid was determined as between 28 to 208 days in the total system using a multiple compartment model. The dissipation rates showed a decreasing trend with increasing application rates.

Dissipation at 4 European sites.

The dissipation of boscalid was studied under field conditions at four locations in Europe, two in Spain and one each in Germany and Sweden. The results of the chemical analysis (HPLC) were similar to previous and showed that boscalid was mainly detected in the 0-10 cm layer and occasionally minor amounts were detected in the 10-25 cm soil sections. It was not detected lower at any time at any site. The DT_{50} of boscalid was 27 and 78 days for the 2 sites in Spain and 144 days in Germany again using the total system, multiple compartment model. At the Swedish site, a DT_{50} could not be determined as there was little degradation after 1 year when there was ~75% of applied remaining. It was noted that the DT_{50} calculations used the *in situ* petri dishes rather than the analysed soil result for the initial amount in the soil and resulted in an improved correlation. Given the similarity between the Spanish and Australian environments, similar degradation rates could be expected under Australian conditions.

Bioaccumulation

The bioaccumulation and elimination of ^{14}C-boscalid in rainbow trout was investigated in a dynamic flow-through system accordance with US EPA and OECD Guidelines. The average bioaccumulation factors (BCF) for edibles, viscera and whole fish were calculated as 40, 95 and 64 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.

Soil Accumulation

3 year vineyard – interim report

The accumulation behaviour of boscalid in a vineyard was investigated over a three-year period according to the BBA Guidelines. Boscalid was applied to grapes vines at application rates of between 680-735 g ai/ha 3 times a year using a SC formulation containing a nominal concentration of 500 g ai/L. Typical agricultural management practices were used with leaves and plant material cut from the vines left on the plots.

The highest amounts of residues of boscalid were detected in the 0–10 cm soil layer at all sampling dates. Residue levels in the 10–25 cm layer increased slightly to be approximately 5-10% of the level in the 0-10 cm layer 3 years after the first application. The report claims that is was considered to be due to agricultural engineering of the plots, which is possible but questionable given that only shallow mechanical treatment (<10 cm) or glyphosate was used to keep the trial area weed free.

The residues during the 3-year study did not plateau, a requirement for the BBA. Modeling was used to determine the plateau level and it was considered that the observed data after 3 years are in good agreement with this predicted concentration range. The Department of the Environment and Heritage notes that the 1st year data is below the theoretical and the 3rd year data is above and therefore questions where this could be considered to be a good agreement for the data at all. In addition, given the field studies were not analysed on a first order basis, averaging half-lives and assuming a first order degradation curve to determine the minimum and maximum levels in soil may not be valid and the results need to be treated with caution. In any future extension of use, the 5-year report from this study (which BASF state are currently being written) should be presented.

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3 years vegetables – interim report

The accumulation behaviour of boscalid in vegetables was investigated over a three-year period according to the BBA Guidelines. Boscalid was applied to vegetables (1st year lettuce, then green bean; 2nd year carrots and cauliflowers) at application rates of between 300-500 g ai/ha, 5 times a year. Total amounts applied were 2.1 kg ai/ha in the first year and 1.7 kg ai/ha in the second year. In the 3rd year a cereal crop (spring wheat) was grown and there was no application of boscalid. The report indicates that this is typical agricultural practice in Germany.

The highest amounts of residues of boscalid were detected in the 0–10 cm soil layer in the first 2 years but in the 3rd year the highest residues are found in the 10-25 cm layer. The residue level in the 10–25 cm layer increased after the 1st year and was higher than in the 0-10 cm layer. The report claims that is was due to agricultural engineering of the plots, including ploughing once a year to 35 cm deep. It is not possible to drawn any conclusion from this study. Clearly the residues did not reach a plateau after 2 years of applications and there remained significant residues in the soil one year after the last application. As for the grape accumulation study above, the expected minimum and maximum residue levels in soil were modeled using the same assumptions and the results need to be treated with caution. However, the report considers that the observed data up to 3 years are in good agreement with this predicted concentration range. In any future extension of use, any available updates to this report should be presented.

Environmental Toxicology

Avian

Boscalid was practically non-toxic to bobwhite quail by the single oral dose route with an LD_{50} 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 300 and 1000 mg ai/kg diet for quail and ducks respectively.

Aquatic

Under static conditions in a test conducted to meet US EPA requirements, technical boscalid is rated as moderately toxic to rainbow trout with a 96 h LC_{50} of 2.7 mg/L but less toxic to bluegill sunfish with a LC_{50} of >4.0 mg/L and the NOEC = 4.0 mg/L, the maximum solubility of boscalid in the test water. It is also only moderately toxic to sheepshead minnow with a LC_{50} of >3.86 mg ai/L and the NOEC = 2.33 mg/L. The formulated product Filan is rated as slightly toxic to rainbow trout with 50% mortality at 100 mg/L and the LC_{50} is approximately 100 mg/L (equivalent to 50 mg ai/L).

A short term sublethal and an early life stage study were conducted using rainbow trout and technical boscalid according to OECD guidelines under flow-though conditions. The NOEC in the sublethal study was 0.93 mg ai/L and LOEC 1.98 mg ai/L. For the early life stage study the no observable adverse effects level (NOAEL) was 0.166 mg/L and LOEC 0.241 mg/L, with lethality the most sensitive effect.

For aquatic invertebrates the acute 48 h daphnia toxicity test conducted according to OECD Guidelines using technical boscalid gave an EC_{50} of 5.33 mg ai/L and boscalid was rated as moderately toxic. Using the formulated product Filan, again tested according to OECD Guidelines, the acute 48 h daphnia toxicity test gave an EC_{50} of 60.3 mg/L, equivalent to 30 mg ai/L, and was rated as slightly toxic. In the chronic 21 days study, conducted according to OECD guidelines, the NOEC and LOEC for daphnia were 1.3 and 2.63 mg ai/L respectively with effects on reproduction being the effect observed in the study. For midge larvae, a sediment dwelling organism tested according to BBA guidelines, the 28 d NOEC and LOEC were 2.3 and 4.31 mg ai/L respectively based on initial measure concentrations. Using mysid shrimp boscalid was rated at worst as moderately toxic with an EC_{50} of >3.81 mg ai/L and the NOEC = 3.81 mg ai/L, the maximum water solubility. It did affect shell growth in Eastern oysters with an EC50 of 1.66 mg ai/L and the NOEC <0.42 mg ai/L.

Technical boscalid was rated as moderately toxic to the green alga *Pseudokirchneriella subcapitata* (syn. *Selenastrum capricornutum*) with a 96-h E_rC50 of 3.75 mg/L and an E_bC50 of 1.34 mg/L in a test conducted according to OECD Guidelines. It did not affect blue-green algae or marine diatoms with EC50s of >4.2 and >3.5 mg ai/L respectively, the maximum test concentrations and water solubility. An acute 72-h toxicity test using the formulated product Filan (50% ai) and the same green alga gave an E_rC50 of 4.5 mg/L and an E_bC50 of 3.37 mg/L of Filan.

Non-Target Terrestrial Invertebrates

The NOEC for boscalid (technical) to bees was greater than 100 µg/bee by both the oral and contact exposure routes, tested according to EPPO Guidelines. The formulated product Filan was also rated as harmless to bees with a NOEC of 100 µg/bee by both the oral and contract toxicity. There were no effects on parasitic wasps, green lacewings, ladybirds and predatory mites when tested according to BBA test Guidelines to dry residues of Filan on glass (36 µg ai/cm^2 equivalent to 3.6 kg ai/ha). When tested against beetles and wolf spiders according to BBA Guidelines (direct overspray) at 2.4 kg/ha, Filan was non-toxic to these organisms. In a field test on grapevines, there was no ecologically 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 boscalid technical on earthworms conducted according to OECD Guidelines using artificial soil, the LC_{50} was determined as > 1000 mg ai/kg and the NOEC as 1000 mg ai/kg. In the same OECD test using Filan the acute LC_{50} was determined as > 1000 mg/kg and the NOEC, based on reduced body weight of the worms compared to control as 667 mg/kg soil.

In a chronic test conducted according to BBA Guidelines, Filan sprayed at 1.8-18 kg/ha caused no effect on the parent generation but the number of juvenile worms was statistically significantly lower than control at rates 9 and 18 kg/ha. The NOEC for reproduction was 3.6 L/ha, corresponding to 1.8 kg ai/ha.

The effect of Filan (50.8% ai), on earthworms in grasslands under field conditions was determined according to BBA guidelines at two sites. The test concentrations used corresponded to the full rate expected to be used in grapevines in Europe (1.2 kg/ha), similar to the Australian rate and half this rate. Three applications 14 days apart were made. At one site, 21 days after the 3rd application, there was a decline in earthworm abundance in the highest exposure group but this was not seen at the other site. It was concluded that the studies show that 3 applications at the maximum application rate in grapevines could affect earthworm populations within the treated area but any effects are likely to be minor.

Soil invertebrates

The effect of Filan, formulated at (50.8% ai), on the reproduction and growth of the collembola (springtails species *Folsomia candida*) was determined according to ISO Guidelines in artificial soil. The results showed statistically significant acute toxic effects of Filan to the springtails at concentrations of 250 and 1000 mg/kg but as there were no mortalities at 500 mg/kg, the high mortality at 250 mg/kg (64%), may not be treatment related. No abnormal behaviour or conditions were observed with the surviving Collembola. The LC_{50} was determined as approximately 1000 mg/kg of Filan with 48% mortality at 1000 mg/kg. The NOEC is 500 mg/kg. There was no statistically significant effect on reproduction but the variability between treatments was high.

The effect of Filan (50.8% ai) on the soil invertebrate activity under field conditions was determined. The study was conducted in parallel to the previous field study with earthworms with 3 applications at 1.2 kg/ha. 22 weeks after the last application soil cores were taken and the number of the collembola was determined. The collembola biocenosis was determined to be composed of 31 taxa representing 5 different families. Statistical analysis revealed no effect on overall numbers of springtails but there were statistical differences in numbers of springtails in two families at the maximum rate (3 X 1.2 kg/ha).

Soil microorganisms

Investigations into the effects of Filan on soil microbial activity were conducted according to BBA Guidelines at the field rate and 10X that rate. There was no statistically significant effect on respiration or on nitrogen turnover at either rate.

The effect of Filan on breakdown of organic matter in grassland was determined as part of a previous earthworm field study with 3 applications at 1.2 kg/ha. The test follows a draft BBA Guidance document. There were no treatment related, ecologically relevant effects on the organic matter breakdown under the conditions tested, thus long-term adverse effects are highly unlikely to occur. A second field study was conducted with one application at 3.6

kg/ha of Filan. In this case statistical analysis indicated that there were significant differences between control and the test substance at all evaluation dates but as deviations from control were <25%, it was concluded that long-term adverse effects are highly unlikely to occur.

Non-target vegetation
The effect of Filan on non-target plants was evaluated in a 14-day vegetative vigour study limit test at 2 concentrations, 1.2 and 3.6 kg/ha, the maximum single field rate and 3-fold the rate. Some symptoms of phytotoxicity were noted for carrots only and were small. There were no other significant differences. The report clearly shows that Filan exhibits no relevant herbicidal activity up to 3 times maximum field rate.

Hazard to Terrestrial Organisms
Birds
Based on the typical diet of northern bobwhite quail and the calculated of boscalid in food items, the concentration in the diet was calculated. As the single oral dose LD_{50} for quail of >2000 mg ai/kg bw and a NOEC of 2000 mg ai/kg bw were significantly above the dietary estimated environmental concentration (EEC), there is no hazard from the worst-case single oral dose. As the maximum number of applications per year is 2 and the worst-case dietary EEC remained below the chronic NOEC for quail, the hazard was considered very low. Similar calculations with mallard ducks, with a different diet to quail, also indicated no expected hazard.

Earthworms
As the worst case soil EEC for boscalid in the top 5 cm of soil following 2 applications was calculated as at least 500 times lower than the LD50 for earthworms, the proposed use of boscalid is not expected to pose an acute hazard to earthworms. The maximum soil concentration is 2.14 mg ai/kg (plateau level) is lower than the NOEC in the chronic earthworm tests and a hazard to earthworm reproduction is unlikely. As the application will be directed into the foliage rather than towards the ground, it is unlikely that the soil will receive the full application rate, further reducing the hazard.

The field studies generally showed no effects on other earthworms or other soil dwelling invertebrates when sprayed with Filan 3 times for a total application rate of 3.6 kg/ha, more than twice the proposed maximum Australian yearly rate.

Beneficial arthropods
The hazard to honey bees is expected to be low. Calculations showed that direct overspray of bees at the single application rate was 10 times lower than the most sensitive contact NOEC, assuming that a honeybee is approximately 1 cm^2 in surface area. Effects on other beneficial species such as parasitic wasps, green lacewing, wolf spiders and ladybird or ground beetles are not expected as applications at higher rates had no or limited effect. There were no effects on predatory mites in laboratory tests and no significant effect in field test conduct in grapevines.

Soil Micro-organisms
The information presented on the effect of boscalid on soil micro-organisms showed these organisms were not affected at 12 kg/ha in laboratory test and there was no effect on organic matter degradation in field studies at 3.6 kg/ha of Filan. Therefore a hazard to soil micro-organisms and soil processes is unlikely at the proposed rates.

Hazard to Aquatic Organisms
The label specifies that all applications of Filan Fungicide will be by ground application using air blaster sprayers. Droplets are likely to be fine with a volume mean diameter (vmd) of 100-

200 µm. Water bodies adjacent to treated vineyards may be contaminated through direct overspray although this is considered very unlikely.

Direct overspray
The worst-case scenario of direct overspray of a 15 cm deep body of water with the maximum single application rate of Filan Fungicide (750 g ai/ha) gave a calculated EEC of 0.5 mg ai/L. Using the most sensitive acute adverse effect on fish (rainbow trout with the 96-h LC_{50} of between 1.88-3.0 mg ai/L) calculations show a slight risk to fish and a potential hazard for chronic exposure. Acute effects on water fleas were are unlikely, with a 48 hour EC_{50} of 5.33 mg ai/L. The chronic NOEC of 1.3 mg ai/L for daphnia and 2 mg ai/L for midge larvae indicates that chronic exposure is unlikely to pose a hazard to these aquatic invertebrates from direct overspray. The EC50 of 1.66 mg/L for eastern oyster indicate slight effects on other shelled invertebrates (bivalves, snails etc) are possible.

For algae, the lowest EC_{50} (biomass) was 1.34 mg ai/L showed that acute effects on algae are possible from direct overspray. The hazard to aquatic plants is unlikely as the NOAEC was 0.99 mg ai/L, approximately twice the EEC from direct overspray.

Spray drift
There is potential for Filan Fungicide to contaminate surface waters via spray drift. However, the resulting EEC is expected to be considerably lower than that from direct overspray. Assuming a worst-case scenario of 10% of a single application reaching the aquatic environment via spray drift, the resulting EEC would be 0.05 mg ai/L. The risk to fish, daphnia, algae and oysters would be reduced and effects on these organisms from spray drift are unlikely. In addition, the actual spray drift is expected to be significantly less than 10% of the application rate and therefore the risk is considered below the level of concern.

Multiple applications
The label recommends maximum of 2 applications in a 4-spray program. The label also directs that applications are not sequential. Given that boscalid dissipates in natural water to the sediment, with a half-life of 21 days, and with 14 days between applications, the maximum concentration in water from direct overspray was calculated as 0.8 mg/L. With 10% spray drift the maximum concentration is therefore 0.08 mg/L, significantly below the acute chronic endpoints for all aquatic species tested. Considering that the actual spraydrift will be lower than 10%, the overall hazard from 2 applications per year is considered very low and acceptable.

Runoff
Boscalid has high K_{ocs} in a range of soils and the moderately strong binding will limit the run-off to that adsorbed to eroded soil. From the column leaching studies it is immobile in soil and is unlikely to leach. In a worst case scenario, assuming the maximum application rate of 1.5 kg ai/ha (2 X at 750 g ai/ha) of boscalid is applied to a 1 ha field shortly followed by 100 mm of rainfall with 10% of runoff of boscalid, the EEC in a pond receiving runoff was estimated as 58 µg ai/L, not allowing for adsorption. This assumes the dilution results from the 15 cm deep water, 100 mm of rain and 10 mm of runoff water, total depth of 26 cm. This EEC indicates a low hazard for fish, daphnia, oysters (bivalves) and algae. The figure of 58 µg/L is also below the chronic NOEC for all tested species. The hazard to aquatic organisms is considered to be low and acceptable.

Overall the risk from runoff and erosion is expected to be low and acceptable when boscalid is used in accordance with the proposed label and good farm management practices.

Chronic hazard

Boscalid is unlikely to be a chronic toxicant. Concentrations in the aquatic environment will be adsorbed to sediment, where they will not be bioavailable, and slowly degraded in the sediments. Given the low hazard already, boscalid (Filan) is not expected to cause a chronic hazard despite of the relative slow degradation in aquatic systems and in soil.

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EFFICACY AND SAFETY ASSESSMENT

Justification for use and Mode of Action

Filan Fungicide is a fungicide having protective and curative action. It inhibits spore germination, germ tube elongation, mycelial growth and sporulation. Filan acts systemically. After penetration through the leaf surface, the active ingredient is translocated acropetally within the plant. Boscalid inhibits fungal respiration through its inhibition of the enzyme succinate ubiquinone reductase, also known as complex II, in the mitochondrial electron transport chain. Boscalid has a double activity because complex II, in addition to delivering electrons for energy production also forms an essential junction where components of the TCA cycle can be diverted to build amino acids and lipids. Through its inhibition of complex II boscalid disrupts fungal growth by preventing energy production. In this respect it resembles the strobilurins, but there is no risk of cross-resistance due to its different site of action in the electron transport chain. It also inhibits fungal growth by eliminating the availability of the chemical building blocks for the synthesis of other essential cellular components.

Boscalid differs from strobilurins and other fungicides both in its Mode and site of Action. Pathogens which have developed resistance to other chemical classes of fungicides may be controlled by boscalid. For resistance management boscalid is a member of the oxathiin group of fungicides. It is a Group G fungicide.

Bunch rot or *Botrytis* as it is commonly known, is a major fungal disease of grapevines in the cooler grape growing areas of Australia. It causes major yield losses where humid, wet conditions prevail over flowering and more importantly after veraison. Young shoots, leaves, flowers and fruit can be infected. Bunch rots develop in late summer and autumn as the sugar content in berries increases. If wet weather persists during this time, losses exceeding 40% can occur. *Botrytis* bunch rot is a difficult disease to control and in recent years management of the disease has been complicated by the development of strains of the fungus resistant to benzimidazole and dicarboximide groups of fungicides.

Filan Fungicide has been shown to give excellent results against *Botrytis* and allows growers an alternative in their spray programs. It will play an important role in any resistance management program.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Filan Fungicide will be applied to grapevines by ground spraying only. Application is as a foliar spray to control bunch rot (*Botrytis cinerea*) of grapevines.

For grapevines the application rate is 120g per 100 L water and application by either dilute or concentrate methods may be used. Up to two sprays per season may be applied at either 5% capfall, 80% capfall, pre-bunch closure, veraison or at 4 weeks prior to harvest. When applied as part of a 3-spray program, only one spray of Filan should be applied. In a 4-spray program, two sprays of Filan may be applied. Consecutive applications of Filan may not be made. Up to five times concentration (5X concentration factor) may be used and application may not be made in volumes lower than 250 L/ha.

Use is proposed for all State and Territories.

It is proposed the product will be available in 2kg, 2.5kg, 5kg, 10kg, 15kg or 20kg HDPE containers.

The following Withholding Period statements are recommended for the product:

Harvest:
Do not harvest for 4 weeks after application.
Grazing:
Do not treat vineyards that will or may be grazed by livestock.
Export Slaughter Interval:
Do not feed treated produce to livestock for 7 days before slaughter.
Grapes and Grape Products Intended for Export:
Consult your peak industry body or BASF for the recommended withholding period.

Evaluation of efficacy

The data presented supported the claim for control of bunch rot (*Botrytis cinerea*) of grapevines. Detailed efficacy data was presented including results from a range of Australian field trials.

Grapevines
Data from 8 Australian trials were presented in support of the application. These trials were conducted in plantings of vines such as Chardonnay, Pinot noir, Rhine Reisling, Sauvignon blanc and Semillon which are susceptible to *Botrytis*. The treatments were applied to panels of vines with each treatment replicated 4 times and arranged in randomised block design. Different rates of Filan were compared with one or two commercial products and all rated against an untreated control. Most trials were conducted in commercial vineyards subject to natural levels of disease pressure. Although the disease development differed between sites, the levels were sufficient to detect differences between treatments. At one site berry clusters were artificially inoculated with *Botrytis* to produce high levels of disease in the plots prior to treatment. Spray volumes and spray intervals were similar to those used under commercial production conditions. The data support the claims.

Crop Safety

No phytotoxicity was observed in any of the 8 efficacy trials where Filan was applied in different climatic areas and to several grape cultivars.

Resistance management

Boscalid has been included in Fungicide Resistance Group G. It is recommended to alternate applications of Filan with sprays from other fungicide groups in a resistance management programme.

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

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

FILAN® Fungicide

ACTIVE CONSTITUENT: 500 g/kg BOSCALID

GROUP	G	FUNGICIDE

For the control of bunch rot (*Botrytis cinerea*) in grapevines,
as specified in the DIRECTIONS FOR USE table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE

Net Contents: 2 kg, 2.5 kg, 5 kg, 10 kg, 15 kg, 20 kg

BASF

STORAGE AND DISPOSAL

Keep out of reach of children. 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

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

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Telephone 131126 Australia-wide.

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.

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APVMA Approval No.: 56362/ /

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Label version: V260304

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Batch Number:
Date of Manufacture:
Fax on Demand: 0500 544 044
Website: www.agro.basf.com.au

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

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DIRECTIONS FOR USE

CROP	DISEASE	RATE	CRITICAL COMMENTS
Grapevines	Bunch rot (*Botrytis cinerea*)	Dilute spray 120 g/100 L water Concentrate spray Refer to the Application section.	Apply as part of a *Botrytis* bunch rot program: In a 3 spray program, apply only 1 spray of FILAN. In a 4 spray program, apply only 2 sprays of FILAN. Do NOT apply consecutive sprays of FILAN. The ideal timing for the first spray is 5 % capfall. Applications can also be made at 80 % capfall, pre-bunch closure, veraison or 4 weeks prior to harvest. 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. Do NOT use in equipment that requires rates greater than 600 g/100 L (5X concentration). Do not apply in volumes less than 250 L/ha

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

WITHHOLDING PERIOD

HARVEST:
DO NOT HARVEST FOR 4 WEEKS AFTER APPLICATION

GRAZING:
DO NOT TREAT VINEYARDS THAT WILL OR MAY BE GRAZED BY LIVESTOCK

EXPORT SLAUGHTER INTERVAL (ESI):
DO NOT FEED TREATED PRODUCE TO LIVESTOCK FOR 7 DAYS BEFORE SLAUGHTER

GRAPES AND GRAPE PRODUCTS INTENDED FOR EXPORT:
CONSULT YOUR PEAK INDUSTRY BODY OR BASF FOR THE RECOMMENDED WITHHOLDING PERIOD

GENERAL INSTRUCTIONS

FUNGICIDE RESISTANCE WARNING **GROUP G FUNGICIDE**

FILAN Fungicide is a member of the oxathiin group of fungicides. For fungicide resistance management, FILAN Fungicide is a Group G fungicide. Some naturally-occurring individual fungi resistant to FILAN Fungicide and other Group G 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 FILAN Fungicide or other Group G 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 FILAN Fungicide to control resistant fungi.

EXPORT OF TREATED PRODUCE

Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all export markets for grapes treated with FILAN Fungicide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing fruit for export (either fresh, dried or as wine) please check with your industry spray diary, peak industry body (such as the Australian Wine Research Institute http://www.waite.adelaide.edu.au/AWRI/) or BASF for the latest information on MRLs and import tolerances before using FILAN Fungicide.

MIXING
Partly fill the spray tank with water and add the required amount of product while stirring. If required, add compatible products and agitate thoroughly. Continue agitation as filling of the tank is completed. Agitate again before spraying commences.

If tank mixing with other water dispersible granule (WG) or wettable powder (WP) formulations, ensure they are mixed in well before adding emulsifiable concentrate (EC) or suspension concentrate (SC) products. WP formulations should be pre-mixed separately prior to adding to the spray tank.

APPLICATION
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 L ÷ 500 L = 3)
As the dilute label rate is 120 g/100 L, then the concentrate rate becomes 3 x 120, that is 360 g/ 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 concentrate application, do NOT use in equipment that requires rates greater than 600 g/100 L (5X concentration). Do NOT apply in volumes less than 250 L/ha.
- For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training and follow industry Best Practices.

COMPATIBILITY
FILAN is compatible with a wide range of agricultural chemicals commonly applied to grapes during the periods specified for Botrytis control. For further information on compatibility please contact your local reseller or BASF representative.

RE-ENTRY PERIOD
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.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Toxic to Aquatic organisms. Do NOT contaminate streams, rivers or waterways with the chemical or used containers.

STORAGE AND DISPOSAL

Keep out of reach of children. 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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APVMA Approval No.: 56362/ /

Label version: V260304

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Batch Number:
Date of Manufacture:
Fax on Demand: 0500 544 044
Website: www.agro.basf.com.au

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

References

Felton, J.C., Oomen, P.A. & Stevenson, J.H. 1986, 'Toxicity and hazard of pesticides to honeybees: harmonisation of test methods', *Bee World*, vol. 67, no. 3, pp. 114-24.

Goring, C.A.I. et al. 1975, 'Principles of pesticide degradation in soil', in *Environmental Dynamics of Pesticides*, edited by R. Haque and V.H. Freed, Plenum Press, New York, pp 135-72.

Matthews, G.A. 1992, *Pesticide Application Methods*, 2nd ed., Longman, London.

Australian Pesticides and Veterinary Medicines Authority 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, APVMA, Canberra.

Australian Pesticides and Veterinary Medicines Authority 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, APVMA, Canberra. (See footnote below)

Australian Pesticides and Veterinary Medicines Authority 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, APVMA, Canberra. (See footnote below)

Australian Pesticides and Veterinary Medicines Authority 2001, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, APVMA, Canberra. (See footnote below)

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 boscalid in the product *FILAN 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:
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