Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active pyriofenone in the product Kusabi 300 SC Fungicide

AUGUST 2016

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This publication is available from the APVMA website: www.apvma.gov.au.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator 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 Office of Chemical Safety (OCS) from the Department of Health, Department of Environment (DoE), and State Departments of Primary Industries.

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 products containing new active constituents.

The information and technical data required by the APVMA to assess the safety of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website at: www.apvma.gov.au.

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from 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.

About this document

This is a Public Release Summary.

It indicates that the Australian Pesticides and Veterinary Medicines Authority (APVMA) is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of Kusabi 300 SC Fungicide should be granted. Submissions should relate only to matters that the APVMA is required, by legislation, to take into account in deciding whether to grant the application. These matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on 20 September 2016 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments 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.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be *confidential commercial information (CCI)*[1] contained in submissions will be treated confidentially.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the grounds for registration should be addressed in writing to:

Case Management and Administration Unit
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

[1] A full definition of 'confidential commercial information' is contained in the Agvet Code.

Further information

Further information can be obtained via the contact details provided above.

Further information on public release summaries can be found on the APVMA website at www.apvma.gov.au.

1 INTRODUCTION

1.1 Applicant

Ishihara Sangyo Kaisha Ltd.

1.2 Details of the product

It is proposed to register Kusabi 300 SC Fungicide, containing 300 g/L pyriofenone, as a suspension concentrate (SC) for use as a fungicide for the control of powdery mildew (*Podosphaera xanthii*) in cucurbits and powdery mildew (*Erysiphe necator*) in grapes. The proposed use for Kusabi 300 SC Fungicide will involve up to three applications to cucurbits at a maximum application rate of 500 ml product/ha and up to two applications on grapevines, at a maximum dilute spray concentration of 30 ml product/100 L.

Kusabi 300 SC Fungicide is the first pyriofenone based product to be introduced in the Australian market. The active constituent pyriofenone belongs to the aryl phenyl ketone chemical family (group U8 fungicides), which has an unknown mode of fungicidal action. This is the second fungicide with active constituent from this chemical family to be registered in Australia.

Both pyriofenone and Kusabi 300 SC Fungicide will be manufactured and formulated overseas. Kusabi 300 SC Fungicide will be available in 1 L, 2 L, 5 L and 100 L High density polyethylene (HDPE) containers.

1.3 Overseas registrations

Pyriofenone as a 300 g/L suspension concentrate is currently registered for use in France, Italy, Portugal, Hungary, Slovenia, Kosovo, Macedonia, Montenegro and Bulgaria. Applications for registration have been made in USA and Canada, with approvals expected later in 2016.

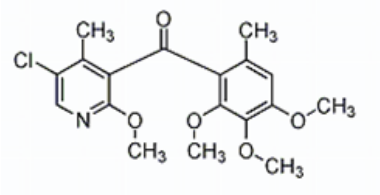
This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Kusabi 300 SC Fungicide, and approval of the new active constituent, pyriofenone.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The chemical active constituent pyriofenone is manufactured by Isihhara Sangyo Kaisha. Table 1 and 2 summarise key properties of this chemical.

TABLE 1: NOMENCLATURE, CHEMISTRY AND KEY IDENTIFIERS OF THE ACTIVE CONSTITUENT PYRIOFENONE

COMMON NAME (ISO):	Pyriofenone
IUPAC NAME:	5-chloro-2-methoxy-4-methylpyridin-3-yl 2,3, 4-trimethoxy-6-methylphenyl ketone
CAS REGISTRY NUMBER:	688046-61-9
EMPIRICAL FORMULA:	C18H20ClNO5
MOLECULAR WEIGHT:	365.8
STRUCTURAL FORMULA:	
CHEMICAL FAMILY:	Aryl phenyl ketone

Physico-chemical properties of active constituent

TABLE 2: SUMMARY OF KEY PHYSICO-CHEMICAL PROPERTIES OF THE ACTIVE CONSTITUENT PYRIOFENONE

PHYSICAL FORM:	Beige powder
ODOUR:	Odourless
MELTING POINT:	93–95^{o}C
RELATIVE DENSITY AT 20OC:	1.33 g/mL at 20^{o}C
DISSOCIATION CONSTANT (PKA):	4.02
SURFACE TENSION (90% SATURATED SOLUTION):	72 mN/m
SOLUBILITY AT 20OC:	Dichloromethane: >250 g/L Methanol: 23.6 g/L n-hexane: 9.2 g/L n-octanol: 17.8 g/L Water: 1.56 mg/L
STABILITY:	In metals and metal ions: Stable in aluminium, iron and zinc and their corresponding acetate salts Compatible with common oxidising and reducing agents such as KMnO4 and Zn

2.2 Formulated product

The product Kusabi 300 SC Fungicide will be manufactured and formulated overseas, imported into Australia in HDPE containers.

Kusabi 300 SC Fungicide

TABLE 3: KEY DETAILS OF THE PRODUCT KUSABI 300 SC FUNGICIDE

DISTINGUISHING NAME:	Kusabi 300 SC Fungicide
FORMULATION TYPE:	Suspension Concentrate (SC)
ACTIVE CONSTITUENT CONCENTRATION:	300 g/L pyriofenone

Physical and chemical properties of product

TABLE 4: SUMMARY OF KEY PHYSICO-CHEMICAL PROPERTIES OF THE PRODUCT KUSABI 300 SC FUNGICIDE

PHYSICAL FORM:	Beige liquid
ODOUR:	Odourless
PH VALUE:	6.0 (1% w/v dispersion)
RELATIVE DENSITY:	1.08 at 20°C
SURFACE TENSION:	44.5 mN/m (for 0.06 g a.i. dilution; 35.0 mN/m (for 0.3 g a.i./L dilution)
VISCOSITY:	Test substance show pseudoplastic flow behaviour Measured range: 190–6900 mPa.s at 20°C 93–5100 mPa.s at 40°C
FLASH POINT:	None determined before the test substance boiled at 99°C
OXIDISING PROPERTIES:	Non-oxidising
EXPLOSIVE PROPERTIES:	Not explosive
FLAMMABILITY:	Auto-ignition temperature: 380°C
CORROSIVE HAZARD:	Not corrosive to High density polyethylene (HDPE) containers
PACK SIZES:	1 L, 2 L, 5 L or 10 L
PACKAGING MATERIAL:	HDPE
PRODUCT STABILITY:	The product should remain within specifications for at least 2 years under normal conditions in HDPE packaging

2.3 Recommendations

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

On the basis of the data provided, and the toxicological assessment, it is proposed that the following APVMA Active Constituent Standard shown in table 5 be established for pyriofenone active constituent:

Table 5: APVMA active constituent standard proposed for active constituent pyriofenone

CONSTITUENT	SPECIFICATION	LEVEL
pyriofenone	pyriofenone	Not less than 965 g/kg

The APVMA has also reviewed the chemistry and manufacturing details provided by the applicant, and on this basis the registration of the product Kusabi 300 SC Fungicide is supported.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological database for pyriofenone, 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 NOEL are used to develop acceptable limits for dietary or other intakes (ie Acceptable Daily Intake (ADI) and Acute Reference Dose (ARfD)) at which no adverse health effects in humans would be expected.

Chemical class

Pyriofenone is a fungicide belonging to the aryl phenyl ketone chemical family and has an unknown mode of fungicidal action.

Toxicokinetics and metabolism

Following a single oral dose of [^{14}C-phenyl]-pyriofenone to rats, absorption of radioactivity was slow (plasma/whole blood T_{max} 6–12 h). The extent of oral absorption from a 5 mg/kg bw dose was high (76–89%). Oral absorption was lower at the higher dose of 200 mg/kg bw (36–53%). The plasma elimination half-life was long (~25 h and ~15 h in males and females respectively). The blood: plasma ratio ranged from 0.64 to 1.38, with higher values observed with repeated dosing, suggesting possible accumulation in blood cells. After repeated dosing with a 5 mg/kg bw daily dose for 14 days, both plasma/whole blood area under the curve (AUC) and C_{max} were higher than that achieved after a single 5 mg/kg bw dose, suggestive of accumulation. Exposure tended to be higher in males than females.

Tissue distribution of radioactivity was wide in rats following a single oral dose of [^{14}C-phenyl]-pyriofenone. The highest levels of radioactivity were seen in organs involved in absorption and excretion (the gastrointestinal tract and contents, liver and kidney). With a few notable exceptions, tissue levels of radioactivity tended to be lower than plasma levels. For the most part, the tissue distribution profile was similar in males and females. The only exceptions were a significant level of radioactivity seen in the adrenal gland of females (200 mg/kg bw only) and there seemed to be some retention of test item-related material in the fat tissue of females. Radioactivity in male reproductive organs was generally fairly low (tissue: plasma ratios 0.15–0.53), while high levels of radioactivity (tissue: plasma ratios of 1.2–1.8) seen in the ovaries of females following a 200 mg/kg bw dose. There appeared to be minimal penetration of the blood-brain barrier (ie brain levels were 2–15% of plasma levels).

Metabolism of pyriofenone in rats largely involved demethylation of a number of the methoxy groups followed by glucuronidation. Unchanged pyriofenone was a major test item-related component in faecal extracts and fat tissue, but was only a minor or negligible test item-related species in plasma, urine and bile.

Following a single oral dose of radiolabelled pyriofenone (5 or 200 mg/kg bw) to rats, excretion of radioactivity was largely in the faeces (73–91%), with the majority of radioactivity eliminated within 48 h. One hundred and twenty hours after a 200 mg/kg bw dose to females, there appeared to be some retention of radioactivity in fat tissue. Following repeat oral dosing with 5 mg/kg bw/d [^{14}C phenyl]-pyriofenone, tissue concentrations of radioactivity tended to be 5–10 fold higher than after a single dose, suggestive of accumulation. Biliary excretion was significant (ie 65–73% or 32–42% of a 5 or 200 mg/kg bw dose respectively). Enterohepatic recirculation was demonstrated.

Dermal absorption

No dermal absorption studies have been conducted with pyriofenone technical grade active constituent. Dermal absorption of pyriofenone in Kusabi 300 SC Fungicide across human skin *in vitro* was 0.17% when it was applied in an undiluted SC formulation (containing 300 g a.i./L). Higher absorption of pyriofenone (6%) was observed when a diluted solution (0.09 g a.i./L) was applied to human skin *in vitro*.

Acute toxicity

Pyriofenone has low acute oral toxicity (LD_{50} >2000 mg/kg bw), low acute dermal toxicity (LD_{50} >2000 mg/kg bw) and low acute inhalational toxicity (4–hour LC_{50} >5180 mg/m^3) in rats. Pyriofenone was not a skin or eye irritant in rabbits, but was a skin sensitiser in Guinea pigs (maximisation test).

Kusabi 300 SC Fungicide has low acute oral toxicity (LD_{50} >2000 mg/kg bw), low acute dermal toxicity (LD_{50} >2000 mg/kg bw) and low acute inhalational toxicity (4–hour LC_{50} >2780 mg/m^3, the maximal achievable concentration) in rats. Kusabi 300 SC Fungicide was not a skin irritant in rabbits or a skin sensitiser in guinea pigs (buehler test), but was a slight eye irritant in rabbits.

Systemic toxicity

Repeat-dose dietary toxicity studies were conducted in rats (4, 13, 52 and 104 weeks), mice (13 and 78 weeks) and dogs (28 days dose range finding, 13 and 52 weeks). The liver and kidney were target organs for toxicity in all three species. Increased absolute and/or relative liver weights were observed in all species and generally correlated with diffuse/centrilobular hepatocyte hypertrophy. Additional hepatic changes included darkened appearance, centrilobular hepatocytic necrosis and hepatocyte fatty change. On occasions there were alterations to serum chemistry parameters (eg aspartate aminotransferase (AST) and alkaline phosphatase (ALP) indicative of these hepatic effects.

Increased absolute and/or relative kidney weights were observed in all species. Kidney histopathological changes included increased calcification of the cortico-medullary junction (rats), increased brown pigment deposition in tubular cells (rats), basophilic change (mice, rats), cortical interstitial inflammatory cell infiltrate (mice), increased incidence/severity of chronic nephropathy (rats), increased incidence of kidneys with a granular appearance (mice) and increased incidence of cortical scarring (mice). No histopathological changes were seen in the kidney of any treated dog. On occasions in rats (but not mice or dogs), changes in

serum chemistry (blood urea nitrogen (BUN), creatinine, bilirubin) and urinalysis parameters (urine colour, volume and ketone level) accompanied the physical changes seen in the kidney.

Other toxicity findings were seen in:

- thyroid (increased weights; rats)
- caecum (increased weights)
- typhilitis, large intestine distension; rats)
- eyes (lenticular degeneration and retinal scar; mice)
- bone marrow (haematopoiesis; rats)
- mesenteric lymph node (increased incidence of sinus dilation; rats)
- skin (hair follicle atrophy/perifollicultitis; rats).

Occasional effects on red blood cell and clotting parameters were observed in rats.

Genotoxicity and carcinogenicity

Pyriofenone was not mutagenic in bacterial and mammalian cells and not clastogenic in mammalian cells, with and without metabolic activation. Pyriofenone did not induce micronuclei *in vivo* in mouse bone marrow following oral administration up to and including the limit dose of 2000 mg/kg bw. Therefore, from the available data, there is no evidence that pyriofenone is an *in vivo* genotoxicant.

The potential carcinogenicity of pyriofenone was assessed in long-term rat (104 week) and mouse (78 week) studies. There was no evidence of carcinogenicity in either species at the highest tested doses (ie ≤254 mg/kg bw/d and ≤716 mg/kg bw/d in rats and mice respectively).

Reproductive and developmental toxicity

There were no treatment-related effects on reproductive performance in a dietary 2–generation rat study up to and including dose levels producing parental toxicity.

Pyriofenone was not teratogenic in rats or rabbits when tested in pregnant animals at sufficiently high doses. Pyriofenone was not considered to be a developmental toxicant in either of these two species.

Neurotoxicity

There was no robust evidence of a neurotoxic potential with pyriofenone based on an acute oral study in rats specifically designed to assess this end point.

3.2 Public health standards

Poisons scheduling

In May 2015, the Chemicals Delegate to the Secretary of the Department of Health on pyriofenone's Scheduling in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) determined to:

- amend pyriofenone's entry in Schedule 6 to create an exception (except when included in Schedule 5); and
- create a new pyriofenone entry in Schedule 5 (PYRIOFENONE in preparations containing 30 per cent or less of pyriofenone).

Following that decision, Kusabi 300 SC Fungicide will be covered under Schedule 5 of the SUSMP. The delegate's decision was published in July 2015, with an implementation date of 1 October 2015:

www.tga.gov.au/book/part-b-final-decisions-matters-not-referred-expert-advisory-committee-5

No Observable Effect level (NOEL)/Acceptable Daily Intake (ADI)

The ADI is that quantity of a 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 pyriofenone was established at 0.09 mg/kg bw/d in 2014 based on:

- NOELs of approximately 9 mg/kg bw/d based on long-term dietary studies with rats:
  - 8.5 mg/kg bw/d in a 1–year dietary study for decreased bilirubin and ALP at 24.9 mg/kg bw/d in males, and
  - 9.1 mg/kg bw/d in a 2–year dietary study for increased chronic nephropathy at 46.5 mg/kg bw/d in females, plus
- application of a default 100–fold safety factor for potential inter- and intra-species differences.

Acute Reference Dose (ARfD)

The ARfD 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.

Pyriofenone has low acute toxicity. An ARfD has not been established for pyriofenone.

4 RESIDUES ASSESSMENT

4.1 Introduction

Kusabi 300 SC Fungicide contains the active constituent pyriofenone (see Section 2.1) for use on cucurbits and grapevines. The proposed use is described in Section 1.2.

A harvest withholding period of 'Not required when used as directed' is proposed for cucurbits and 5 weeks for grapes. Kusabi 300 SC Fungicide should not be applied later than EL 31 (ie berries at pea size) when grapes are to be used to make wine for export.

The following restraint is proposed:

- DO NOT graze or feed treated crops to animals.

As part of the residue assessment for registration of pyriofenone, plant and animal metabolism studies, supervised residue trials, analytical methodology, fate in storage and processing data and residues in trade information were considered.

4.2 Metabolism

Studies examining the metabolism of ^{14}C-pyriofenone labelled either on the phenyl or the pyridyl ring in grapes, tomatoes and wheat following foliar application, and in goats and rats following oral ingestion, were considered.

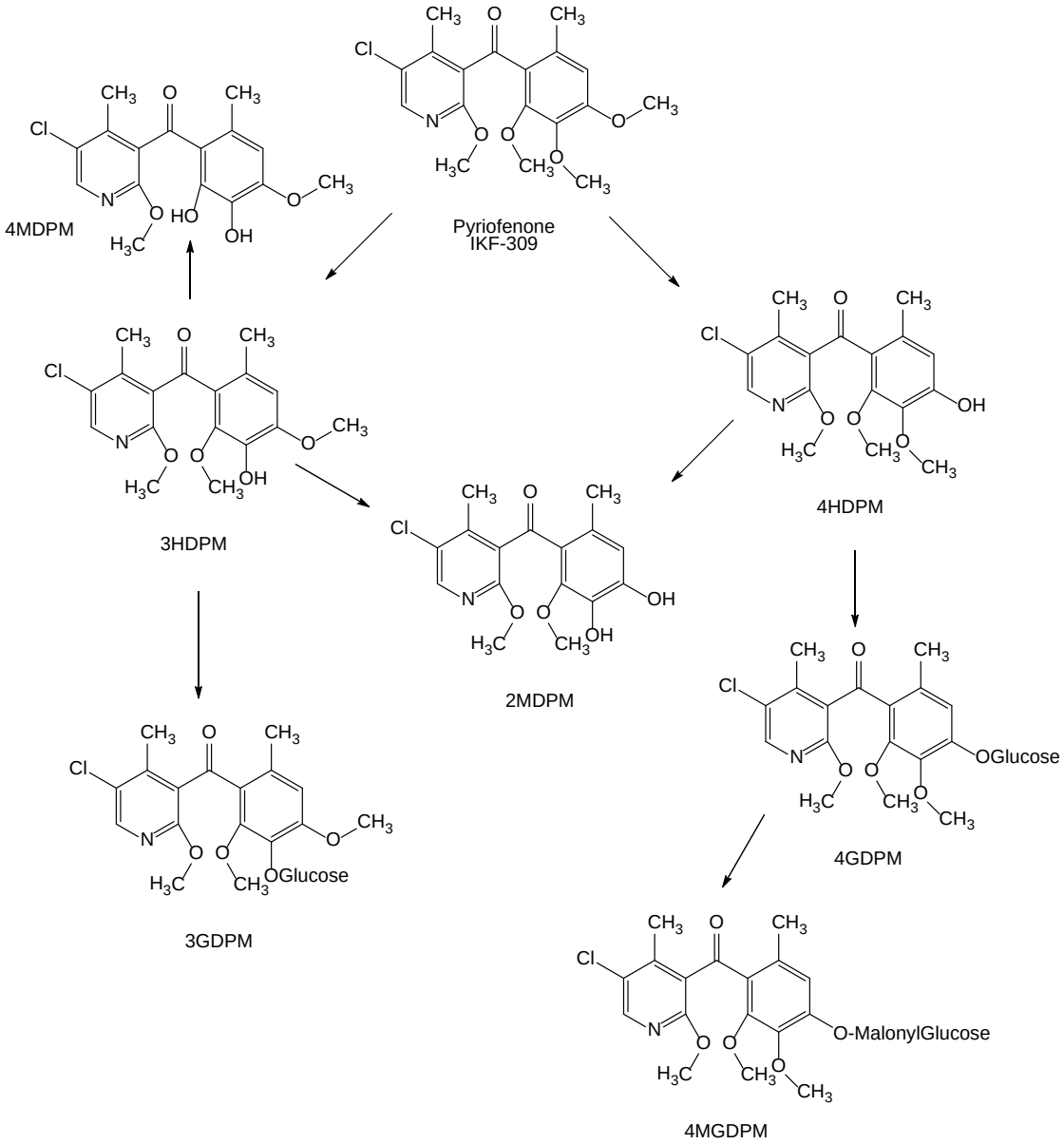
Plants

Plant metabolism studies in grapes, tomatoes and wheat were assessed which involved two or three applications at approximately 100 g a.i./ha.

Parent pyriofenone was the major component of radioactive residues, representing more than 50% Total Radioactive Residue (TRR) in all plant samples collected 7–40 days after the last application, except in wheat grains where it accounted for 13–29% TRR (approximately 0.01 mg/kg) and in wheat straw where it accounted for 35–49% TRR (approximately 0.31–0.61 mg/kg). The remainder of the radioactive residues were composed of a large number of individual fractions, including several hydroxyl metabolites related to pyriofenone, each observed at low level and proportions (mostly <2% TRR). The metabolism was seen to be similar in all plants investigated and proceeds first by demethylation at the positions 3 and/or 4 of the phenyl moiety to give the hydroxy metabolites 3HDPM, 4HDPM and 2MDPM, followed by further glucose conjugations. Additional demethylation of the 3HDPM metabolite at the carbon 2 gives the 4MDPM metabolite.

A similar metabolite pathway was observed in the confined rotational crop study where the radioactive residues were shown to be mainly parent and the 4HDPM glucose and malonylglucose conjugates.

Figure 1: Biotransformation pathway of pyriofenone in plants.



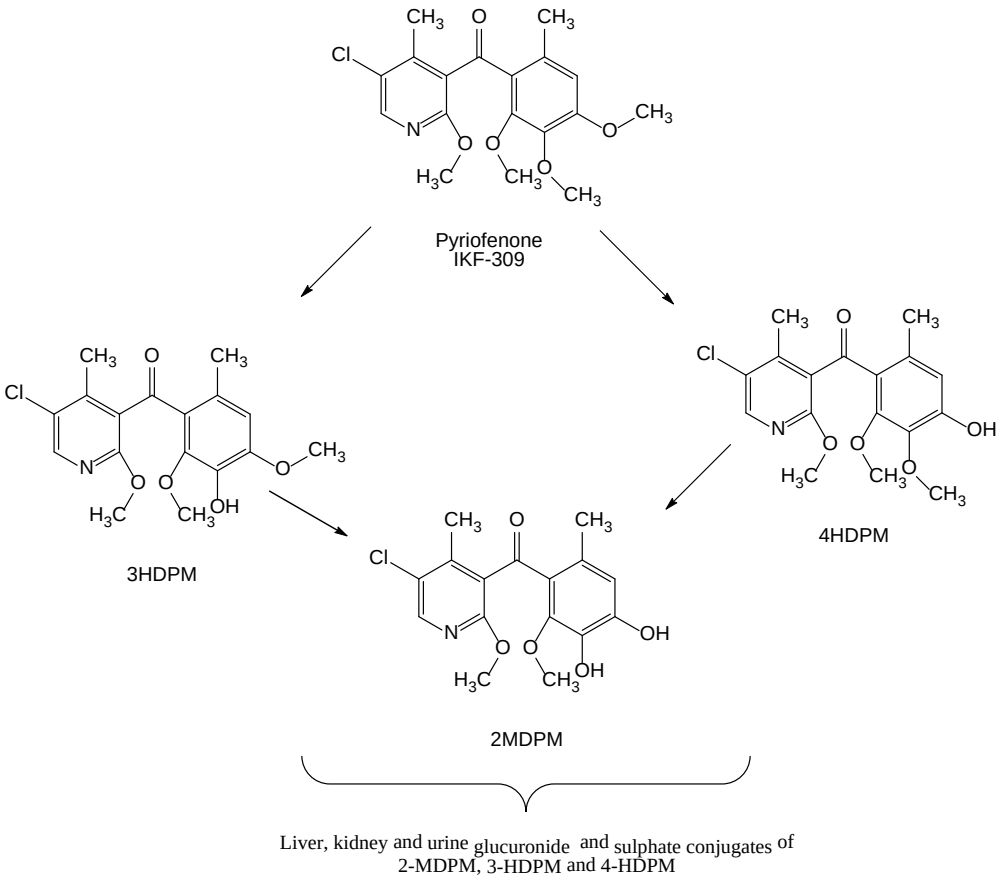
Animals

A goat metabolism study was provided where animals were dosed over five consecutive days with ^{14}C- pyriofenone labelled either on the phenyl or the pyridyl ring at approximately 10 ppm in the diet. Pyriofenone was extensively excreted and less than 2% of the administered radioactivity was recovered in goat matrices. As the TRRs in muscle, fat and milk were less than 0.005 mg/kg, the characterisation of the residues was only investigated in kidney and liver where the total residues were up to 0.05 and 0.16 mg/kg respectively, (table 6) which were composed of:

- parent at 2.8–5.6% TRRs (0.001–0.007 mg eq/kg)
- 2MDPM at 1.0–5.6% TRRs (0.001–0.008 mg eq/kg)
- 3HDPM or 4HDPM at <0.4-4.4% TRRs (<0.001–0.007 mg eq/kg).

Most of the radioactivity in liver and kidney extracts was characterised as the fractions L12, L13/K13 or L14/K14 accounting individually for 8% to 60% TRR (0.01–0.06 mg eq/kg) and identified following various enzymatic or acid/base hydrolysis, as mixtures of glucuronide conjugates of 2MDPM and 3HDPM and/or 4HDPM.

Figure 2: Biotransformation pathway for pyriofenone in ruminants



Metabolism of pyriofenone in rats largely involved demethylation of a number of the methoxy groups followed by glucuronidation. Unchanged pyriofenone was a major component in faecal extracts and fat tissue, but was only a minor or negligible test item-related species in plasma, urine and bile.

4.3 Analytical methods

Residues of pyriofenone were determined in cucurbits, grape and various animal commodities (milk, eggs, liver, kidney, fat, muscle) using LC-MS/MS methods with a limit of quantitation of 0.01 mg/kg.

4.4 Stability of the pesticide in stored analytical samples

A study was submitted which showed that pyriofenone residues in wheat grain, wheat straw and grapes are stable for at least 12 months in frozen storage at -20°C.

4.5 Residue definition

Parent pyriofenone was the major component of radioactive residues observed in primary crops (grapes, tomatoes and wheat) and in the confined rotational crop study.

As parent pyriofenone was shown to be a major component of the radioactive residues in both primary and secondary crops, the proposed residue definition is limited to pyriofenone *per se*.

The OCS assessment of the active constituent pyriofenone states that the ADI has been established at 0.09 mg/kg bw/day, with an ARfD not considered necessary (Section 3.2).

Based on the available animal metabolism data (Section 4.3), the capability of the analytical method and toxicological advice and noting that detectable residues are not expected to occur in animal commodities from the proposed use, it is concluded that a suitable residue definition for commodities of animal origin is parent only. This may be reconsidered in the future if there is an increase to the livestock dietary burden, which would also require the provision of an animal transfer study.

A residue definition of parent compound is therefore considered appropriate for pyriofenone on commodities of plant and animal origin.

4.6 Residue trials

Cucurbits

Trial results were provided and reviewed from the following trials on cucurbit crops:

- Australia—9 trials, from a range of cucurbit growing areas
  - 2011 (4 trials)—New South Wales (NSW) (2 rockmelon), Queensland (2 rockmelon, 2 zucchini and 2 cucumber) and Western Australia (rockmelon)
  - 2012 (5 trials)—South Australia (protected cucumber), Queensland (zucchini and rockmelon), NSW (rockmelon) and Victoria (zucchini).
  - North American—28 trials, from cucurbits growing areas in 2012:
    - USA (26 trials)—cucumbers (8), summer squash (8) and cantaloupe (= rockmelon) (10)
    - Canada (2 trials)—cucumbers (1) and summer squash (1).

The combined dataset suitable for Maximum Residue Level (MRL) estimation is, in ranked order:

- 0.013, 0.018, 0.022, 0.023, 0.026, 0.032, 0.034, 0.035, 0.035, 0.043, 0.044, 0.045, 0.048, 0.049, 0.050, 0.051, 0.057, 0.057, 0.058, 0.067, 0.068, 0.070, 0.070, 0.072, 0.075, 0.081, 0.085, 0.085, 0.097, 0.098, 0.10, 0.10, 0.10, 0.11, 0.11, 0.12, 0.12, 0.14, 0.16, 0.17, 0.22 and 0.39 mg/kg (n=42, with Supervised Trials Median Residue (STMR) = 0.069 mg/kg).

The Organisation of Economic Cooperation and Development (OECD) MRL calculator estimates an MRL of 0.4 mg/kg.

APVMA data guidelines state that residues data for rockmelon, cucumber and zucchini can be extrapolated to the whole fruiting vegetables other than cucurbits group[2]. A pyriofenone MRL of 0.7 mg/kg for VC 0045 Fruiting vegetables, cucurbits is considered appropriate for the proposed use pattern, noting the variation in residue potential within the crop group, in conjunction with a harvest withholding (WHP) period of 'Not required when used as directed'.

[2] apvma.gov.au/node/1028

Grapes

Trial results were provided and reviewed from the following trials on grapes conducted between 2007 and 2013:

- Australia—19 trials, spread across Queensland, South Australia, New South Wales, Western Australia, Tasmania and Victoria
- New Zealand—6 trials
- European Union (EU)—17 trials.

Some of the Australian, New Zealand and EU trials included information on the concentration of residues during processing.

The combined dataset from Australia, New Zealand and the EU suitable for MRL estimation is, in ranked order:

- <0.01, <0.01, 0.011, 0.02, 0.03, 0.032, 0.04, 0.04, 0.043, 0.043, 0.06, 0.065, 0.065, 0.07, 0.07, 0.071, 0.08, 0.080, 0.081, 0.093, 0.11, 0.18, 0.19, 0.20 and 0.30 mg/kg (n = 25, STMR = 0.065 mg/kg).

The OECD MRL calculator estimates an MRL of 0.4 mg/kg.

A MRL of 0.5 mg/kg is recommended for pyriofenone on FB 0269 grapes in conjunction with a WHP of 5 weeks.

The processing trials indicated that pyriofenone residues do not concentrate in wine or juice, so it was not necessary to establish separate MRLs for these commodities.

Residues concentrated on processing to raisins by a median processing factor of 3.0×. Based on the highest residues (HR) in grapes, the highest predicted residue (HR-P) value in raisins is 0.90 mg/kg.

An MRL of 2 mg/kg is recommended for pyriofenone on DF 0269 dried grapes (= currants, raisins and sultanas).

The processing trials indicate that pyriofenone residues do concentrate into pomace. Processing factors for dry pomace were 7.09, 8.33, 9.86 and 12.4×. The median dry pomace processing factor is 9.1×. Based on the HR in grapes (0.30 mg/kg), the HR-P value in raisins is 2.73 mg/kg.

An MRL of 5 mg/kg is recommended for pyriofenone on AB 0269 grape pomace, dry.

4.7 Animal commodity MRLs

Grape pomace is the only commodity originating from the proposed uses that might be used as an animal feed in Australia. Grape pomace may form 20% of the diet for beef and dairy cattle, and 20% of the diet for turkeys[3]. Possible residues in primary feed commodities produced from follow crops, after application of pyriofenone to cucurbits, is also considered.

A 'DO NOT graze or feed treated crops to animals' restraint is proposed and considered to be acceptable.

No animal feeding studies have been submitted. In a lactating goat metabolism study, two goats were administered five consecutive daily doses of either ^{14}C-(phenyl)-IKF-309 or ^{14}C-(pyridyl)-IKF-309 at a nominal dose of 10 ppm in the diet (20 mg/goat/day). Pyriofenone was extensively excreted and less than 1.5% of the administered radioactivity was recovered in goat matrices.

As the TRRs in milk, muscle and fat were less than 0.005 mg/kg, the characterisation of the residues was only investigated in kidney and liver, where the total residues were up to 0.05 and 0.16 mg/kg respectively (table 6).

TABLE 6: RESIDUES (MG/KG) OF PYRIOFENONE OBSERVED IN A GOAT METABOLISM STUDY AFTER 5 CONSECUTIVE DAILY DOSES OF 10PPM

COMPOUND	MILK	MUSCLE	FAT	KIDNEY		LIVER	
	TRR (mg/kg)			% TRR	mg/kg	% TRR	mg/kg
	0.004	<0.001	0.004				
Pyriofenone				5.6	0.002	5.3	0.007

Table 7 shows the predicted residue contribution from grape pomace or primary feed commodities if they were to be used as feed for livestock.

[3] Guidance Document on Residues in Livestock, Page 48, www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)8&doclanguage=en

TABLE 7: PREDICTED RESIDUE CONTRIBUTION (PPM) OF PYRIOFENONE IN GRAPE POMACE OR PRIMARY FEED COMMODITIES

COMMODITY	RESIDUE[A] (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	MAXIMUM DIET CONTENT (%)	MG/ANIMAL	RESIDUE CONTRIBUTION (ppm)
Grape pomace	0.59	STMR-P	100	0.59	20	2.36	0.118
Primary feed commodities	0.045^	HR	25	0.18	100	3.6	0.18
Total					**20**		**0.18**

[A] Grape pomace residue = STMR× median processing value (0.065 × 9.1) = 0.59 mg/kg
Primary feed commodities residue = HR of 0.045 mg/kg in 31–day aged soil from confined rotational study

The predicted residues of pyriofenone in the milk and tissues of cattle fed with a 0.18 ppm dietary burden are shown in table 8.

TABLE 8: PREDICTED[A] RESIDUES (PPM) OF PYRIOFENONE IN THE TISSUES AND MILK OF BEEF AND DAIRY CATTLE AS A RESULT OF FEEDING AT 0.18 PPM AND THE ASSOCIATED RECOMMENDED MRL

FEEDING LEVEL (PPM)	MILK	MUSCLE	LIVER	KIDNEY	FAT
	PYRIOFENONE RESIDUE (mg/kg)				
10	<0.004	<0.001	0.007	0.002	0.004
0.18–beef and dairy cattle, estimated burden	<0.00007	<0.00002	0.0001	0.00004	0.00007
Recommended MRLs	*0.01	-	*0.01		*0.01

[A] based on predicted maximum livestock burden of: Beef and Dairy Cattle 500 kg bw, 20 kg dry matter (DM)/day

The likelihood of detectable residues occurring in livestock commodities as a result of the proposed use is very low. It is appropriate to establish animal commodity MRLs at the respective Limit of Quantification (LOQ)s for pyriofenone in the analytical methods. The following MRLs are recommended:

- MO 0105 Edible offal (mammalian) *0.01 mg/kg
- MM 0095 Meat (mammalian) *0.01 mg/kg
- ML 0106 Milks *0.01 mg/kg.

The estimated dietary burden for poultry is 0.118 ppm which is slightly higher than the level at which there is a requirement for a feeding study (0.1 mg/kg).

However, if the STMR from residue observations of grape pomace in the Australian grape trials is considered (0.29 mg/kg) then the estimated dietary burden for poultry is 0.058 ppm (table 9) which is below the level at which there is a requirement for a feeding study.

TABLE 9: ESTIMATED[A] DIETARY BURDEN FOR POULTRY

COMMODITY	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	MAXIMUM DIET CONTENT (%)	MG/ANIMAL	RESIDUE CONTRIBUTION (ppm)
Grape pomace	0.29	STMR	100	0.59	20	0.0232	0.058
Total					**20**		**0.058**

[A] based on turkeys with a 10 kg bw and fed with 0.4 kg DM/day[8]

In the livestock metabolism study, feeding at 10 ppm in the diet gave a maximum pyriofenone residue of 0.007 mg/kg in liver (ie a transfer factor of 0.007/10 = 0.0007).

No poultry metabolism or feeding studies have been provided. Noting the very low maximum feeding level, the low transfer of residues observed in the goat metabolism study and as grape pomace is only occasionally consumed, there is no likelihood of quantifiable residues in turkey commodities. The following MRLs are recommended:

PE 0112 Eggs *0.01 mg/kg

PO 0111 Poultry, edible offal of *0.01 mg/kg

PM 0110 Poultry meat *0.01 mg/kg.

4.8 Estimated dietary intake

The chronic dietary exposure is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived primarily from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with World Health Organisation (WHO) Guidelines and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for pyriofenone is equivalent to <5 % of the ADI.

The OCS have not established an ARfD for pyriofenone (Section 3.3).

4.9 Bioaccumulation potential

The log P_{ow} value for pyriofenone is 3.2 indicating that there is the potential for bioaccumulation in fat.

The lactating goat metabolism study found that pyriofenone residues were higher in the fat than in the muscle but lower than that in offal (liver and kidney) (table 6). MRLs for meat 'in the fat' are not recommended at this time.

4.10 Spray drift

The draft label includes a restraint that the product should not be applied by air. The product should also not be applied with smaller than MEDIUM spray droplets according to ASAE S572 definition for standard nozzles.

In the goat metabolism study provided with the application, dosing with pyriofenone at 10 ppm gave highest residues of parent of 0.007 mg/kg in liver (Section 4.3). For residues of parent to be at the LOQ (0.01 mg/kg), the maximum feeding level is 14.3 ppm. Assuming pasture consists of 1500 kg DM/ha this corresponds to a maximum permitted drift of 21.45 g a.i./ha.

For ground application to cucurbits at a maximum rate of 150 g a.i./ha, the standard scenario (ie high ground boom, medium droplet) indicates that a no-spray zone is not required for application to cucurbits for protection of international trade.

For ground application to grapevines at a maximum rate of 90 g a.i./ha (assuming a spray volume of 1000 L/ha), the standard scenario (ie airblast—vineyard) indicates that a no-spray zone is not required for application to grapevines for protection of international trade.

4.11 Residues in rotational crops

A confined rotational study shows that residues of pyriofenone in food commodities may occur. Residues in wheat grain were <0.01 mg/kg TRR at all re-plant intervals. Following application to soil at 284g a.i./ha, residues in leafy crops (lettuce) grown in rotational situations were <0.01 mg/kg TRR at 31 and 122 day re- plant intervals (365 days was not studied). Residues in root crops (carrot) were up to 0.029 mg/kg pyriofenone for early harvest root (122 day replant interval).

To cover the possibility of residues in rotational crops it is recommended that an MRL of 0.05 mg/kg be established for pyriofenone in 'All other foods'.

The confined rotational crop study suggests that residues of pyriofenone may occur in succeeding feed crops. For example, observed residues in wheat forage and wheat straw ranged up to 0.045 mg/kg fresh weight, and in wheat hay up to 0.023 mg/kg in 31 day aged soil. To cover this possibility it is recommended that an MRL be established at 0.5 mg/kg for pyriofenone on Primary feed commodities. Residues in feeds at this level are not expected to result in residues in animal commodities.

4.12 Recommendations

Tables 10–12 list the amendments that are proposed to the APVMA MRL Standard (apvma.gov.au/node/10806) for food commodities (standard table 1), residue definitions (standard table 3) and animal feed commodities (standard table 4).

TABLE 10: PROPOSED AMENDMENTS TO MRL STANDARD TABLE 1—MRLS OF AGRICULTURAL AND VETERINARY CHEMICALS AND ASSOCIATED SUBSTANCES IN FOOD COMMODITIES

COMPOUND		FOOD	MRL (mg/kg)
Pyriofenone			
ADD:			
		All other foods	0.05
DF	0269	Dried grapes (=currants, raisins and sultanas)	2
MO	0105	Edible offal (mammalian)	*0.01
PE	0112	Eggs	*0.01
VC	0045	Fruiting vegetables, cucurbits	0.7
FB	0269	Grapes	0.5
MM	0095	Meat [mammalian]	*0.01
ML	0106	Milks	*0.01
PO	0111	Poultry, edible offal of	*0.01
PM	0110	Poultry meat	*0.01

Table 11: Proposed amendments to MRL Standard table 3-Residue definitions (and marker residues)

COMPOUND	RESIDUE
ADD:	
Pyriofenone	Pyriofenone

Table 12: Proposed amendments to MRL Standard table 4-MRLs for pesticides in animal feed commodities

COMPOUND		ANIMAL FEED COMMODITY	MRL (mg/kg)
Pyriofenone			
ADD:			
AB	0269	Grape pomace, dry	5
		Primary feed commodities	0.5

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported

Grapes (including dried grapes) and wine are considered to be major export commodities[4], as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed with feeds produced from treated grapes. Residues in these commodities resulting from the use of Kusabi 300 SC Fungicide may have the potential to unduly prejudice trade.

Residues are not expected in grain and other major exported commodities as defined in APVMA Data Guidelines for Overseas Trade (Part 5B), from rotational crop use.

5.2 Destination of exports

Grapes are a significant export, particularly as wine, although table grapes and dried fruit are also exported. Australia exports wine to the USA, EU and Canada, amongst others (table 13), which accounts for $2 billion of the $3 billion exported each year. The much smaller table grape market ($197.3 million) is predominantly Asia-bound and dried grapes are exported worldwide. The majority (75%) of exported table grapes are sent to Hong Kong, Indonesia, Malaysia, Singapore and Thailand.

In 2013–14, Australia produced 1557.4 kt of grapes comprised of 1438.0 kt for wine making and 119.4 kt for drying and table grapes.[5]

In 2014–15, Australia produced 1,608.2 kt of wine grapes, with exports of 744.9 ML of wine worth $1982.7 million.[5] In the same season, Australia exported 2.5 kt of dried vine fruit worth $10.3 million.[5]

Table 13: Major destinations for Australian wine[5]

CROP	MAJOR DESTINATIONS
Wine	United States, United Kingdom, China, Canada, Hong Kong, New Zealand, Netherlands, Singapore, Japan and Malaysia

The significant export markets for Australian beef, sheep, pig meat and offals are listed in the APVMA regulatory guidelines—data guidelines: agricultural—overseas trade (part 5B).

[4] APVMA regulatory guidelines—data guidelines: agricultural—overseas trade (part 5B) apvma.gov.au/node/1017

[5] Australian Bureau of Agricultural and Resource Economic Sciences (ABARES), Agricultural Commodity Statistics, December 2015: data.daff.gov.au/data/warehouse/agcstd9abcc002/agcstd9abcc0022015/ACS_2015_1.0.0.pdf

5.3 Proposed use pattern

Kusabi 300 SC Fungicide (300 g/L pyriofenone)

DIRECTIONS FOR USE			
Crop	Pest	Rate	Critical comments
Cucurbits	Powdery mildew (*podosphaera xanthii*)	300–500 mL/ha (≡ 90-150 g a.i./ha)	When conditions favour disease development apply Kusabi 300 SC in a spray program at 7 to 10 day intervals. DO NOT wait for disease to appear. Ensure thorough coverage of plants using a volume of 250 to 800 mL per hectare. Do not use more than 3 applications of Kusabi 300 SC applications per crop.
Grapevines	Powdery mildew (*erysiphe necator*)	Dilute spray: 30 mL/100L (≡ 9 g a.i./100L) Concentrate spray: Refer to the application section	When conditions favour disease development apply consecutive sprays of Kusabi 300 SC at 7 to 10 day intervals. DO NOT wait for disease to appear. Use the shorter interval when infection pressure is high. Ensure thorough coverage of plants using a water volume appropriate to canopy size. Do not use more than 2 applications of Kusabi 300 SC applications per crop. Kusabi 300 SC Fungicide should not be applied later than E-L 31 (berries pea size) when grapes are to be used to make wine for export.

RESTRAINTS

WITHHOLDING PERIODS
Harvest
Cucurbits: Not required when used as directed.
Grapevines: DO NOT harvest for 5 weeks after application.

Grazing
DO NOT graze or feed treated crops to animals

Application restraints
DO NOT apply with aircraft
DO NOT apply through any type of irrigation equipment

GENERAL INSTRUCTIONS

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a MEDIUM spray droplet size category according to nozzle manufacturer specifications that refer to the ASAE S572 Standard on the BCPC Guideline.
DO NOT apply when wind speed is less than 3 or more than 20 kilometres per hour as measured at the application site
DO NOT apply during surface inversion conditions at the application site

Mandatory No-spray Zones:
Not required when used as directed

5.4 Overseas registration and approved label instructions

Refer to Section 1.3.

5.5 Comparison of Australian MRLs with Codex and International MRLs

Table 14 lists the relevant international MRLs that have been established for pyriofenone together with those proposed for Australia.

Table 14: Current and proposed Australian and overseas MRLs/tolerances for pyriofenone

COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF PYRIOFENONE (mg/kg)				
	AUSTRALIA	EU	JAPAN	KOREA	USA
Residue Definition	Pyriofenone (proposed)	Pyriofenone	Pyriofenone	Pyriofenone	Pyriofenone
Fruiting vegetables, cucurbits	0.7 (proposed)				
Cucumber (including gherkin)			1	0.7	
Melon				0.5	
Watermelon				0.1	
Korean melon				2.0	
Squash				0.5	
Grape	0.5 (proposed)	0.9 (Table grapes) 0.2 (Wine grapes)			0.30
Dried grapes (= currants, raisins and sultanas)	2 (proposed)				
Grape, raisin					0.50

5.6 Potential risk to trade

Export of treated produce containing finite (measurable) residues of pyriofenone may pose a risk to Australian trade in situations where:

a) no residue tolerance (import tolerance) is established in the importing country, or

b) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

The applicant has proposed the following risk mitigation statement which is considered appropriate and acceptable:

- Export of treated produce

  Growers should note that suitable MRLs or import tolerances do not exist in all markets for produce treated with Kusabi 300 SC Fungicide. In some situations export requirements may be met by limiting application number and/or imposing a longer withholding period than specified above. If you are growing produce for export, please check with ISK Biosciences Oceania Pty Ltd, your industry body or the Australian Wine Research Institute (AWRI) www.awri.com.au/ for the latest information on MRLs and import tolerances and any potential trade issues and their management before using Kusabi 300 SC Fungicide.
  Kusabi 300 SC Fungicide should not be applied later than EL 31 (berries pea size) when grapes are to be used to make wine for export. Contact your winery or AWRI for the updated information on MRLs and overseas tolerances BEFORE using Kusabi 300 SC Fungicide.

Grapes and dried grapes

A finite MRL is proposed for grapes (0.5 mg/kg). The proposed grape MRL is lower than the European table grape MRL (0.9 mg/kg) and higher than the grape MRL for the USA (0.30 mg/kg) (table 16).

A combined residues dataset from field trials conducted on grapes in Australia, New Zealand and Europe using Good Agricultural Practice (GAP) was listed in section 4.6 (grapes). On this basis, low finite residues of pyriofenone may be expected in exported grapes. Although residues will be below and not exceeding the MRLs in established in the EU and USA respectively, there is a potential risk to trade as not all the export markets for fresh grapes have established MRLs.

As processing to raisins concentrated residues by a median processing factor of 3.0× there will be a similar risk to trade in dried grapes.

Wine

The draft label contains the following statement:

- Kusabi 300 SC Fungicide should not be applied later than EL 31 (berries pea size) when grapes are to be used to make wine for export. Contact your winery or AWRI for the updated information on MRLs and overseas tolerances BEFORE using Kusabi 300 SC Fungicide.

In the Australian residue trials provided in support of this application, quantifiable residues did not occur in wine when the last application was made at or near growth stage EL 31 (ie developing fruit (berries) at pea size) and up to 2× the proposed concentration. Quantifiable residues of pyriofenone are therefore not expected in wine for export.

The risk to trade in Australian wine is considered to be low.

Rotational crops

Residues are not expected to occur in major export commodities from the use of Kusabi 300 SC Fungicide on rotational crops.

Animal commodities

As quantifiable residues of pyriofenone are not expected to occur in animal commodities the overall risk to trade is considered to be low.

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Pyriofenone (CAS: 688046-61-9) is currently listed on the Safe Work Australia (SWA) Hazardous Substances Information System (HSIS) Database (SWA, 2015). With the available toxicology information (Section 3.2), OCS classified pyriofenone as a hazardous substance according to the National Occupational Health and Safety Committee (NOHSC) *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004). Based on the product toxicology information and concentrations of pyriofenone (30%) and other ingredients in the product, Kusabi 300 SC Fungicide, is not classified as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

6.2 Formulation, packaging, transport, storage and retailing

The active ingredient, pyriofenone, and the product Kusabi 300 SC Fungicide will be manufactured overseas and imported into Australia in HDPE plastic bottles. It will be available in the following pack sizes: 200, 250, 500 ml and 1, 2, 5 and 10 L.

6.3 Use pattern

Kusabi 300 SC Fungicide is intended as a fungicide for the control of powdery mildew in grapevines and cucurbits.

The maximum amount of product to be used is 600 mL *per* hectare (180 g *per* hectare pyriofenone) on grapevines and 500 mL *per* hectare (150 g *per* hectare pyriofenone) on cucurbits. Kusabi 300 SC Fungicide is expected to be applied with airblast, handwand or knapsack applicators when treating grapevines; and with groundboom, handwand or knapsack applicators when treating cucurbits.

Kusabi 300 SC Fungicide is to be applied at 7 to 10 day intervals as part of a protectant spray management program in conjunction with other fungicides. A maximum of two and three applications *per* crop is recommended for grapevines and cucurbits, respectively. Where grapes are being grown for to make wine for export, Kusabi 300 SC Fungicide should not be applied later than EL31 (berries are pea size).

6.4 Exposure during use

Farmers and their employees will be the main users of the product. Workers may be exposed to the product when opening containers, mixing/loading, during application and cleaning up spills and equipment. The main route of exposure to the product and diluted spray will be dermal and inhalational, although ocular exposure is also possible.

In the absence of exposure data for the proposed mode of application, the PHED Surrogate Exposure Guide (1998) was used to estimate potential worker exposure. The toxic endpoint of concern and identified NOEL is derived from a repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account potential interspecies and intraspecies variation and the seriousness of the critical health effect of concern.

The MOE values associated with repeated use of the product when mixing and loading and for application using ground boom, airblast sprayer or hand wand (low or high pressure) are acceptable (*ie* >100) without the use of personal protective equipment. The MOE value for application using equipment carried on the back of the user was acceptable when cotton overalls, over normal clothing, buttoned to the neck and wrist and elbow-length chemical resistant gloves were worn during application.

6.5 Exposure during re-entry

Occupational post application exposure is likely to occur through activities carried on sprayed areas upon re- entry. The most likely route of exposure upon re-entry is considered to be dermal. Activities requiring re- entry in vineyards include propagating, scouting, trying/training, pruning, irrigation, disease/pest management, leaf pulling, trellis repair, pruning, and harvesting. Activities requiring re-entry in cucurbits fields include transplanting, scouting, irrigation, disease/pest management, pruning, fruit thinning, training and harvesting.

In the absence of re-entry work exposure data, the OCS estimated post application dermal exposure for workers undertaking crop management activities, using the US Occupational Post-Application Risk Assessment Calculator (US EPA, 2013) actualised for Australian values.

The MOE estimates for workers re-entering treated areas to conduct high exposure activities is considered acceptable on day zero after treatment (ie MOE>100) for both cucurbits and grapes. As the re-entry risks associated with Kusabi 300 SC Fungicide are considered to be low, a re-entry statement was not considered to be necessary.

6.6 Recommendations for safe use

Taking into consideration the potential toxicological hazard, use pattern and likelihood of handler exposure, OCS considered the following First Aid and Safety Directions as appropriate.

First Aid Instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 0800 764 766.

Safety Directions

May irritate the eyes. Avoid contact with eyes. If applying by spraying equipment carried on the back of the user wear cotton overalls, over normal clothing, buttoned to the neck and wrist and elbow-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

6.7 Conclusion

The registration of Kusabi 300 SC Fungicide, containing 300 g/L pyriofenone for the control of powdery mildew in grapevines and cucurbit vegetables, is supported.

Kusabi 300 SC Fungicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available on the product Safety Data Sheet (SDS).

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

It is proposed to register Kusabi 300 SC Fungicide for the control of powdery mildew in cucurbits and grapes. Section 1.2 describes the proposed use in greater detail.

7.2 Environmental fate and behaviour

Hydrolysis

Pyriofenone is expected to be hydrolytically stable under normal environmental conditions.

Photolysis/photodegradation

Photolysis on soils is unlikely to be a major degradation route (ie with a disappearance time (DT_{50}) of 98 d), but pyriofenone may photodegrade slightly quicker in water (DT_{50} values of 33 and 54 d for natural and purified water respectively).

Fate and behaviour in soil

Photolysis on soils is unlikely to be a major degradation route (DT_{50}= 98 d).

In aerobic soils, pyriofenone had a geometric mean half-life (n = 4) of 89 days at 20^{o}C, with no major metabolites (>10) formed. Pyriofenone degraded rapidly under anaerobic conditions with a geometric mean half-life (n = 5) of 27 days. The major soil metabolites under anaerobic conditions identified were 2DMPM (23%) and 3HDPM (32%) which were not persistent with half-lives of 36 days or less.

Despite individual laboratory soil half-lives up to 170 days, in field dissipation trials (n = 4 sites), pyriofenone dissipated rapidly with half-lives of 32 days or less. Residues were primarily restricted to the top 10 cm of soil.

Fate and behaviour in water

In water, pyriofenone is hydrolytically stable in the environmental pH range (ie pH 4–9).

In two aerobic water/sediment systems, with application to the water column, pyriofenone partitioned to the sediment with water column dissipation half-lives of up to 9.6 days. Degradation in the sediment from these systems was fast, with whole system half-lives ranging from 4.7–12 days.

In two anaerobic water/sediment systems, whole system half-lives ranged from 37.4–56.3 days. In all cases the radioactivity consisted largely of the parent compound. The amounts of radioactivity converted to non-extractable sediment residues rose to up 90% of the applied radioactivity in one water sediment system. The amount of radioactivity detected as volatiles was low (< 5% of the applied dose) by day 30 in both systems and for both labels.

Mobility

In standard batch equilibrium studies in five soils originating from England with organic carbon levels ranging from 0.5–4.3%, Koc values were all between 705–2720 L/kg. While this suggests a low to slight mobility in soil, field dissipation data indicate limited mobility with residues restricted to the top 10 cm soil. There was evidence %OC dependence (r^2= 0.92).

Bioaccumulation

Pyriofenone is not expected to bioconcentrate in organisms. The steady-state bioconcentration factors based on the measured pyriofenone concentrations were 160 and 142 at the higher (0.01 mg/L) and lower (0.001 mg/L) pyriofenone technical concentrations, respectively for whole fish.

7.3 Environmental effects

Terrestrial organisms

The toxicity of pyriofenone to a number of terrestrial organisms based on the results (table 15) from submitted studies, can be summarised as:

- practically non-toxic to birds
- not toxic to bees
- no reproductive effects observed on two standard non-target arthropod species (ie *aphidius rhopalosiphi,* and *typhlodromus pyri*) with an LR_{50} greater than the highest rate tested (1000 g ac/ha)
- non-toxic to earthworms in soil, with no effects on body weight or reproductive capacity at up to 32.0 mg/kg.

Soil micro-organisms

Exposure of pyriofenone to soil microorganisms showed no significant adverse effects on the soil nitrogen cycle or soil respiration at levels up to 1 kg ac/kg dw soil, the highest tested rate.

Aquatic organisms

Effects on fish

Pyriofenone is categorised as slightly toxic to fish based on acute toxicity and chronic exposure studies (table 15). The major metabolites were shown to be at worst slightly, to practically non-toxic to fish.

Effects on aquatic invertebrates

Pyriofenone is classified as slightly toxic, based on acute toxicity studies with *daphnia magna* (table 15).

Exposure of sediment organisms (c*hironomus riparius*) to spiked water showed that pyriofenone is slightly toxic to these organisms (table 15).

Effects on algae and aquatic plants

Tests were provided for four algal and one vascular aquatic plant species (*lemna gibba*). The growth rate EC_{50}s for three algal species indicated pyriofenone was moderately toxic to algae. Growth rate EC_{50} values for the aquatic plant *L. gibba* could not be calculated as 50% inhibition did not occur at the highest rate tested (table 17). The major metabolites were shown to be less toxic to algae than the parent compound.

TABLE 15: TOXICITY OF ACTIVE CONSTITUENT PYRIOFENONE AND THE PRODUCT KUSABI 300 SC FUNGICIDE FOR VARIOUS ORGANISMS

ORGANISM		MEASURE OF TOXICITY OR EFFECT	PARAMETER (TEST PERIOD)	TOXICITY (UNIT)
Terrestrial species				
Bird	Bobwhite quail	Acute toxicity (oral)	LD50	>2250 mg ac/kg bw
	Bobwhite quail, mallard duck	Short term dietary exposure	LC50 (5 d)	>5620 ppm
	Bobwhite quail	Reproduction	NOEC	91.1 mg ac/kg bw/d
	Honeybee (apis mellifera)	Oral and contact toxicity	LD50	>100 µg/bee
Non-target arthropods	parasitoid (aphidius rhopalosiphi)	Tier 1 dose/response	LR50	>1000 g ac/ha
	predatory mite (typhlodromus pyri)			
	Earthworm	Acute toxicity	LC50	>1000 mg/kg
		Reproduction	NOEC	32.0 mg/kg
Plants	Sugarbeet	Seedling emergence test	NOEC	12.35 g ac/kg (= 18 kg ac/ha
Aquatic species				
Fish	Rainbow trout	Acute toxicity	LD50 (96 h)	13.7 mg ac/L
	Fathead minnow	Early life stage toxicity	NOEC (28 d)	0.435 mg ac/L
Aquatic invertebrate	Daphnia magna	Acute toxicity	EC50	31.4 mg ac/L
	Daphnia magna	Reproduction	NOEC (21 d)	0.0899 mg ac/L
	Chironomus riparius	Chronic exposure	NOEC (28 d)	1.6 mg/L
Aquatic plants	Lemna gibba	Growth inhibition	EC50	Not achieved at 1.574 mg ac/L
Algae	Pseudokirchneriella subcapitata	Growth inhibition	ErC50	1.77 mg/L
	Skeletonema costatum (marine species)			>1.349 mg/L
	Anabaena flos-aquae			>1.413 mg/L

Terrestrial plants

The effects of pyriofenone on terrestrial plants was determined by dose/response testing for seedling emergence using 6 standard test plant species, and tier 2 vegetative vigour studies for 10 test plant species. The highest application rate was 1000 mg ac/kg for plant growth test seedling emergence and 360 g ac/ha for vegetative vigour.

The most sensitive plant in the seedling emergence test was the sugarbeet with dry weight significantly reduced at concentrations from 37.04 mg ac/kg and a 21% reduction at the highest concentration tested. The study NOEC was equivalent to 18 kg ac/ha. Otherwise, no inhibitory effects (ie on mortality, germination or dry weight reduction) exceeding 10% were found.

In the vegetative vigour test, there were no statistically significant effects on height, dry weight reduction or mortality up to the highest test rate, and the study NOEC was 360 g ac/ha.

7.4 Risk assessment

Pyriofenone has been assessed for maximum application rates of 310.5 g ac/ha (ie on grapevines, using up to 3 sprays applied 7 days apart), and 150 g ac/ha (ie on cucurbits using 3 sprays applied 7 days apart). The risk assessment, performed using standard methodology, showed an acceptable risk to all of the environmental organisms considered, for both the parent and major metabolites.

A spray drift risk assessment was undertaken as per APVMA's spray drift policy and demonstrated that the risk to aquatic organisms and terrestrial plants is acceptable, provided that appropriate downwind aquatic buffer zones are included. There is not a requirement for terrestrial downwind buffer zones. The runoff risk assessment to aquatic organisms was undertaken using the DoE screening model, after refinement of the model parameters. This assessment demonstrated that risk to aquatic organisms from runoff of both the active constituent and major metabolites was acceptable.

7.5 Conclusions

The APVMA is satisfied that the proposed use of this product is unlikely to have an unintended effect that is harmful to animals, plants or things or the environment.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

The proposed use of Kusabi 300 SC Fungicide is for the control of powdery mildew species on cucurbits and grapes. More details on the proposed use are provided in Section 1.2.

8.2 Summary of evaluation of efficacy and crop safety

Efficacy

The applicant presented results from twenty Australian field trials (2011–14) on the efficacy and safety of Kusabi 300 SC Fungicide on grapevines or cucurbits. The Australian trials tested the product at the proposed label rate of 30 mL/100 L (and other rates ranging from 7.5 to 100 mL/100L) on grapevines and at the proposed label rate of 300–500 mL/ha (as well as rates of 75 to 1,000 mL/ha) on cucurbits with multiple spray applications at 7–10 day intervals.

The trials were replicated and conducted in commercial vineyards and farms and in one greenhouse trial in South Australia, Western Australia, Queensland, New South Wales, Victoria and Tasmania under natural disease pressures on common grape and cucurbit varieties. Disease pressure varied during the trials from high to low levels.

The trials on grapes demonstrated that Kusabi 300 SC Fungicide was effective against powdery mildew infections reducing incidence and severity of disease on leaves and bunches in a number of Australian grapevine cultivars. The product was as effective as the industry standards tested, and was also effective when pre-mixed with azoxystrobin or tebuconazole fungicides.

The trials on cucurbits demonstrated that Kusabi 300 SC Fungicide was effective against powdery mildew infections reducing the incidence and severity of disease on the upper and lower leaves of a number of different cucurbit species including rock melon, honeydew melon, zucchini, cucumber and pumpkin. Control lasted up to 14 days after the third spray.

The trial data supports the application for registration of Kusabi 300 SC Fungicide for control of powdery mildews in grapevines and cucurbits and that the efficacy claims are acceptable.

Crop safety

The field data evaluated demonstrated that Kusabi 300 SC Fungicide is safe to use at rates up to 100 ml/100 L (x3 application label rate) on grapevines and 1000 mL/ha (x2 maximum label rate) on cucurbits with spray applications at 7–10 day intervals.

Resistance management

The Fungicide Resistance Action Committee (a specialist technical group of Crop Life International) has designated pyriofenone as a group U8 fungicide. Whilst the exact mode of action for pyriofenone (the mode of action proposed by FRAC being actin disruption) is unknown, it has preventative and curative action against fungi in powdery mildew groups. Kusabi 300 SC Fungicide is to be used as part of a protectant spray management program in conjunction with other fungicides. The maximum number of applications of Kusabi SC Fungicide per crop is three on cucurbits and two on grapevines.

8.3 Conclusions

The claims on the proposed label that Kusabi 300 SC Fungicide provides acceptable control of powdery mildew on grapevines and cucurbits when used as directed are supported by the results from the Australian trials.

Acceptable crop safety is expected when the product is used as directed. The directions for use are appropriate and consistent with fungicide use in commercial agriculture in Australia.

The application for the registration of Kusabi 300 SC Fungicide is supported on efficacy and crop safety grounds when used in accordance with label instructions.

9 LABELLING REQUIREMENTS

CAUTION

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

Kusabi®

300 SC Fungicide

ACTIVE CONSTITUENT: 300 g/L PYRIOFENONE

GROUP	U8	FUNGICIDE

For the control of powdery mildew in cucurbits and grapes as specified in the DIRECTIONS FOR USE table

CONTENTS: (1 L, 2 L, 5 L, 10 L)

ISK Biosciences Oceania Pty Ltd

Distributed in Australia by:
AgNova Technologies Pty Ltd
ABN 70 097 705 158
Suite 3 935 Station Street
Box Hill North, Vic. 3129 Australia
Phone (03) 9899 8100
agnova.com.au

® **Registered trademark of Ishihara Sangyo Kaisha, Ltd**

Ancillary panel

DIRECTIONS FOR USE
RESTRAINTS
DO NOT apply with aircraft.
DO NOT apply through any type of irrigation equipment.

SPRAY DRIFT RESTRAINTS:
Except when applying with orchard/vineyard airblast equipment, DO NOT apply with spray droplets smaller than a MEDIUM spray droplet size category according to nozzle manufacturer specifications that refer to the ASAE S572 Standard or the British Crop Production Council Guideline.
DO NOT apply when wind speed is less than 3 or more than 20 kilometres per hour as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.

Users of this product **MUST make an accurate written record** of the details of each spray application within 24 hours following application, and must KEEP this record for at least 2 years.
The spray application details that must be recorded are:

1. Date with start and finish times of application;
2. Location address and paddock(s) sprayed;
3. Full name of this product;
4. Amount of product used per hectare and number of hectares applied to;
5. Crop or situation and weed or pest;
6. Wind speed and direction during application;
7. Air temperature and relative humidity during application;
8. Nozzle brand, type, spray angle, nozzle capacity and spray system pressure measured during application;
9. Name and address of person applying this product.

(Additional record details may be required by the state or territory where this product is used.)
MANDATORY NO-SPRAY ZONES: Not required when used as directed.

Ancillary panel continued

Cucurbits

Crop	Disease	Rate	WHP	Critical Comments
Cucurbits	Powdery mildew (*Podosphaera xanthii)*	300–500 mL/ha	-	When conditions favour disease development apply Kusabi 300 SC Fungicide in a spray program with other fungicides at 7 to 10 day intervals. DO NOT wait for disease to appear. Ensure thorough coverage of plants using a volume of 250 to 800 L of water per hectare. Do not use more than 3 applications of Kusabi 300 SC Fungicide per crop.

Grapevines

RATE: In the following table rates are given for dilute spraying. For concentrate spraying refer to the Application Section.				**CRITICAL COMMENTS:** For uses in this table: Apply by dilute or concentration spraying equipment. **Apply the same amount of product to the target crop whether applying this product by dilute or concentrate spraying methods.**
Crop	**Disease**	**Rate**	**WHP**	**Critical Comments**
Grapevines	Powdery mildew *(Erysiphe necator)*	**Dilute Spray:** 30 mL/100 L **Concentrate spray:** Refer to the application section	5 weeks	When conditions favour disease development apply Kusabi 300 SC Fungicide at 7 to 10 day intervals as part of a protectant disease management program. DO NOT wait for disease to appear. Use the shorter interval when infection pressure is high. Ensure thorough coverage of plants using a water volume appropriate to canopy size. Do not use more than 2 applications of Kusabi 300 SC per crop. Kusabi 300 SC Fungicide should not be applied later than EL31 (berries pea size) when grapes are to be used to make wine for export.

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

WITHHOLDING PERIODS:
Cucurbits: NOT REQUIRED WHEN USED AS DIRECTED
Grapevines: DO NOT HARVEST FOR 5 WEEKS AFTER APPLICATION
Grazing: DO NOT GRAZE OR FEED TREATED CROPS TO ANIMALS

Ancillary panel label continued

GENERAL INSTRUCTIONS

Fungicide Resistance Warning

GROUP	U8	FUNGICIDE

Kusabi 300 SC Fungicide is a member of the unspecified group of fungicides. For fungicide resistance management Kusabi 300 SC Fungicide is a group U8 fungicide. Some naturally occurring individual fungi resistant to the product and other group U8 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 the product or other Group U8 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, ISK Biosciences Oceania Pty Ltd accepts no liability for any losses that may results from the failure of this product to control resistant fungi.

Mixing
Fill minimum 50% of the required water into the spray tank, and agitate when adding the required amount of Kusabi 300 SC Fungicide. Finally add the rest of the required water volume. Keep the spray solution agitated until all product is applied. Never prepare more spray solution than required.
Triple rinse empty product container and add the rinsings to the spray solution.

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

Ancillary panel continued

Concentrate Spraying (Grapevines Only)
Use a sprayer designed and set up for concentrate spray (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 spray above) for the crop canopy.
This is needed to calculate the concentrate mixing rate.
The mixing rate for concentrate spraying can then be calculated in the following way:

Example only

1. Dilute spray volume as determined above: for example 1500 L/ha
2. Your chosen concentrate spray volume: for example 500 L/ha
3. The concentrate factor in this example is 3X (ie. 1500 L ÷ 500 L = 3)
4. If the dilute label rate is 30 mL/100 L, then the concentrate rate becomes 3 x 30, which is 90 mL product per 100 L of concentrate spray.

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

Compatibility
For information on the compatibility of Kusabi 300 SC Fungicide with other products, contact your local ISK Biosciences Oceania Pty Ltd representative.

Export of treated produce
Growers should note that suitable MRLs or import tolerances do not exist in all markets for produce treated with Kusabi 300 SC Fungicide. In some situations export requirements may be met by limiting application number and/or imposing a longer withholding period than specified above. If you are growing produce for export, please check with ISK Biosciences Oceania Pty Ltd, your industry body or the Australian Wine Research Institute (AWRI) www.awri.com.au for the latest information on MRLs and import tolerances and any potential trade issues and their management before using Kusabi 300 SC Fungicide.
Kusabi 300 SC Fungicide should not be applied later than EL31 (berries pea size) when grapes are to be used to make wine for export. Contact your winery or AWRI for the updated information on MRLs and overseas tolerances BEFORE using Kusabi 300 SC Fungicide.

Ancillary panel continued

PROTECTION OF LIVESTOCK
DO NOT graze or feed treated crops to animals.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Toxic to aquatic life, DO NOT contaminate wetlands or watercourses with this product or used containers.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
DO NOT apply under weather conditions, or from spaying equipment that may cause drift onto nearby plants/crops, cropping lands or pastures.

STORAGE AND DISPOSAL
Store in the closed, original container in a cool, well-ventilated area. Do NOT store for prolonged periods in direct sunlight. Triple rinse containers before disposal. Add rinsings to the 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 deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots in compliance with relevant Local, State or Territory government regulations. Do not burn empty containers or product.

SAFETY DIRECTIONS
May irritate the eyes. Avoid contact with eyes. If applying by spraying equipment carried on the back of the user wear cotton overalls, over normal clothing, buttoned to the neck and wrist and elbow-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre. Phone Australia 131 126; New Zealand 0800 764 766.

SAFETY DATA SHEET
Additional information is listed in the Material Safety Data Sheet which can be obtained from the supplier representative.

Ancillary panel continued

CONDITIONS OF SALE

ISK Biosciences Oceania Pty Ltd and AgNova Technologies Pty Ltd shall not be liable for any consequential or other loss or damage relating to the supply or subsequent handling or use of this product, unless such liability by law cannot be lawfully excluded or limited. All warranties, conditions or rights implied by statute or other law which may be lawfully excluded are so excluded. Where the liability of Ishihara Sangyo Kaisha, Ltd and AgNova Technologies Pty Ltd for breach of any such statutory warranties and conditions cannot be lawfully excluded but may be limited to it re-supplying the product or an equivalent product or the cost of a product or an equivalent product, then the liability of AgNova Technologies Pty Ltd for any breach of such statutory warranty or condition is so limited.

APVMA Approval Number: 68898/59333 Bar code, label code to be inserted
BN DOM

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
ALP	alkaline phosphatase
ARfD	Acute Reference Dose
ASAE	Australian Standards on Assurance Engagements
AST	aspartate aminotransferase
AUC	Area Under Curve
AWRI	Australian Wine Research Institute
BCPC	British Crop Production Council
bw	bodyweight
CAS	Chemistry Abstracts Service
C_{max}	maximum (or peak) serum concentration
d	day
DAT	Days After Treatment
DM/ha	Dry matter per hectare
DT_{50}	Disappearance Time, time taken for 50% of the concentration to dissipate
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
EI	Export Interval
E-L (or EL)	Eichhorn Lorenz scale for rating berry size of fruit on grapevines
eq	equivalent
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EU	European Union
g	gram
GAP	Good Agricultural Practice

GLP	Good Laboratory Practice
h	hour
ha	hectare
HDPE	High density polyethylene
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
HR	Highest residue
HR-P	Highest residue - predicted
HSIS	Hazardous Substances Information System (Safe Work Australia)
IPM	Integrated Pest Management
ISO	International Organisation for Standardization
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
K_{ow}	Octanol-water partition coefficient
kt	Kilo tonne
L	Litre
LC-MS	Liquid chromatography- mass spectrophotometry
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
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
LR_{50}	Lethal body residues required for 50% mortality
mg	milligram
mL	millilitre

mN/m	milliNewton per metre
MOE	Margin of exposure
mPa.s	milliPascal per second
MRL	Maximum Residue Limit
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
NOHSC	National Occupational Health and Safety Commission
OCS	Office of Chemical Safety
OECD	Organisation of Economic Cooperation and Development
OM	Organic Matter
PHED	Pesticide Handler Exposure Database
P_{ow}	Octanol-water partition coefficient
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
s	second
SC	Suspension Concentrate
SDS	Safety Data Sheet
STMR	Supervised trials median residue
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
SWA	Safe Work Australia
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent

T_{max}	Time to achieve maximum concentration
TRR	Total Radioactive Residue
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
WHO	World Health Organisation
WHP	Withholding Period
w/v	Weight/volume

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.
Buehler Guinea Pig test	An in vivo test to screen for the skin sensitisation potential of substances
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through 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	repels water
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
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

Australian Bureau of Statistics (1999). National Nutrition Survey: Foods eaten, Australia, 1995. Available at: abs.gov.au/AUSSTATS/abs@.nsf/0/9A125034802F94CECA2568A9001393CE

Australian Pesticides and Veterinary Medicines Authority (2015). *Registration and Permits, Data Guidelines (2015),* Available at: apvma.gov.au/registrations-and-permits/data-guidelines.

Bond, E.J. (1984). *Manual of Fumigation for Insect Control.* FAO. 1984.

Howard, P.H. (1989). *Handbook of Environmental Fate and Exposure Data for Organic Chemicals. Volume 1: Large Production and Priority Pollutants.* Lewis Publishers, INC, Michigan.

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

National Occupational Health and Safety Commission (2004). *NOHSC Approved Criteria for Classifying Hazardous Substances*.

SWA (2015). Safe Work Australia (SWA), *Hazardous Substances Information System (HSIS) Database*, SWA, Canberra, 2015. Available at: hsis:safeworkaustralia.gov.au/

US EPA (1998). United States Environmental Protection Agency (US EPA). *The Pesticide Handlers Exposure Database (PHED), version 1.1-PHED Surrogate Exposure Guide, Estimates of Worker Exposure.* US EPA, Washington DC, United States, 1998.

US EPA (2003). *US EPA ECOTOX Database.* Available at: epa.gov/ecotox/

WHO (1997). *Joint FAO/WHO Codex Alimentarius Commission. Guidelines for predicting dietary intake of pesticide residues.* 1997. Available at: who.int/foodsafety/publications/pesticides/en/