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Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of the new active isofetamid in the product KENJA 400 SC FUNGICIDE

APVMA product number 88495

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This publication is available from the APVMA website.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator responsible for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia. Before approving an active constituent and/or registering a product, the APVMA must be satisfied that the statutory criteria, including the safety, efficacy, trade and labelling criteria, have been met. The information and technical data required by the APVMA to assess the statutory criteria 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.

The APVMA has a policy of encouraging transparency in its activities and seeking community involvement in decision making. Part of that process is the publication of public release summaries for products containing new active constituents. 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 advisory agencies, including other Australian Government agencies and State departments of primary industries. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience to encourage public comment.

About this document

This Public Release Summary indicates that the 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 KENJA 400 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 or animal 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 25 August 2020 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. Unless requested by the submitter, the APVMA may release a submission, with any CCI redacted, to the applicant for comment.

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

GPO Box 3262

Sydney NSW 2001

Phone: +61 2 6770 2300

Email: enquiries@apvma.gov.au.

Further information

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

Copies of technical evaluation reports covering chemistry, efficacy and safety, toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request.

Further information on Public Release Summaries can be found on the APVMA website.

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

1 INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of KENJA 400 SC FUNGICIDE. This is the first product registration containing the active constituent, isofetamid (approval number 81806) to be used as a preventative treatment for the control of grey mould (*Botrytis cinerea*) in berries, low growing berries such as strawberries, cane berries including raspberries and bush berries including blueberries in protected and field cropping situations. Isofetamid is a fungicide with the Succinate dehydrogenase inhibitor mode of action. The Fungicide Resistance Action Committee (FRAC), has designated isofetamid as a Group 7 fungicide.

KENJA 400 SC FUNGICIDE is currently registered in the European Union (EU), the United States of America (USA) and Canada for use in berries.

1.1 Applicant

ISHIHARA SANGYO KAISHA, LTD.

1.2 Purpose of application

ISHIHARA SANGYO KAISHA, LTD has applied for registration of a new agricultural chemical product KENJA 400 SC FUNGICIDE containing (400 g/L) of isofetamid as a suspension concentrate. Isofetamid was approved as an active constituent in 2018 and KENJA 400 SC FUNGICIDE is the first product registration for this active constituent.

1.3 Proposed claims and use pattern

The product is to be registered for the control of grey mould (*Botrytis cinerea*) in berries, low growing berries such as strawberries, cane berries including raspberries and bush berries including blueberries, in both field and protected cropping situations.

1.4 Mode of action

Isofetamid has a translaminar character in plant tissues, with a high preventative, curative and anti-sporulant activity, resulting in good rain fastness and providing a long-lasting protection for treated plants.

The Fungicide Resistance Action Committee (FRAC), has designated isofetamid as a Group 7 Fungicide

1.5 Overseas registrations

The product is currently registered in the EU, USA and Canada as KENJA 400 SC FUNGICIDE for control of botrytis bunch rot (*Botrytis cinerea*) in grapes, sclerotinia drop (*Sclerotinia minor, Sclerotinia sclerotiorum*) in lettuce and grey mould (*Botrytis cinerea*) in low growing berries.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

Isofetamid was evaluated in a separate application as a new active constituent and was approved in January 2018 (approval number 81806). Relevant information considered for the active approval is summarised below.

The active constituent isofetamid is manufactured overseas.

Details of the chemical name, structure, and physicochemical properties of isofetamid are listed below (Tables 1–2).

Isofetamid is a solid at room temperature, with low vapour pressure, low water solubility, and high solubility in polar organic solvents and aromatic hydrocarbon solvents. It is slightly corrosive to metals, and has excellent safety properties. The $\log_{10}K_{OW}$ is 2.5. It does not dissociate at environmental pH values (4–10).

Table 1: Nomenclature and structural formula of the active constituent isofetamid

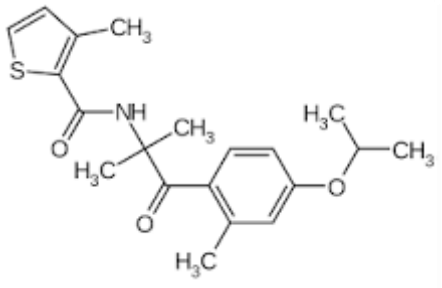
Common name (ISO):	Isofetamid
IUPAC name:	3-Methyl-*N*-{2-methyl-1-[2-methyl-4-(propan-2-yloxy)phenyl]-1-oxopropan-2-yl}thiophene-2-carboxamide
CAS registry number:	875915-78-9
Molecular formula:	$C_{20}H_{25}NO_3S$
Molecular weight:	359.48 $gmol^{-1}$
Structural formula:	

Table 2: Key physicochemical properties of the active constituent isofetamid

Appearance:	White crystalline powder with no discernible odour (pure active ingredient, 99.9% purity); pale brown powder (technical active)	
Melting point:	103.5–105.0°C	
Boiling point:	176.0°C (decomposition without boiling)	
Specific gravity/density/bulk density	1.23 g cm^{-3}	
Stability:	The data are sufficient to support that the product remain within specifications for at least 2 years when stored under normal conditions. Stable when stored at 54°C for 14 days	
Safety properties:	Not expected to self-ignite; not highly flammable	
Solubility in water:	5.33 mg/L at 20°C (99.9% purity)	
Organic solvent solubility (all at 20°C):	n-Heptane	1.2 g/L
	Xylene	61.4 g/L
	n-Octanol	31.7 g/L
	1,2-dichlorethane	>250 g/L
	Acetone	>250 g/L
	Methanol	>250 g/L
	Ethyl acetate	>250 g/L
Dissociation constant (PK_a):	No dissociation constant between pH 4–10 (pure active ingredient)	
pH:	7.3 (1% w/v suspension)	
Octanol/water partition coefficient (Log K_{ow}/K_{OW}):	log Pow = 2.5 (pure active ingredient)	
Vapour pressure:	4.2×10^{-7} at 25°C (Pa)	
Henry's law constant:	1.20×10^{-5} at 25°C (Pa m^3 mol^{-1})	
UV/VIS absorption spectra:	UV absorption maxima (λ_{max} = 261 nm)	

2.2 Formulated product

The product KENJA 400 SC FUNGICIDE will be manufactured overseas. Tables 3 and 4 outline some key aspects of the formulation and physicochemical properties of the product.

KENJA 400 SC FUNGICIDE is a suspension concentrate containing 400 g/L isofetamid and will be available in 1 L, 2 L, 5 L, 10 L and 20 L HDPE (high density polyethylene) containers.

Table 3: Key physicochemical properties of the product KENJA 400 SC FUNGICIDE

Distinguishing name:	KENJA 400 SC FUNGICIDE
Formulation type:	Suspension concentrate (SC)
Active constituent concentration:	Isofetamid (400 g/L)
Physical form:	Off-white odourless liquid
pH:	pH 7.3 (1% w/v suspension)
Specific gravity/density:	1.10 g/ml
Pourability:	Residue, 2.39% Rinsed residue, 0.12%
Spontaneity of dispersion:	99% (MT 160)
Suspensibility:	0.13 g a.i./L dilution 100% 2.27 g a.i./L dilution 99%
Safety properties:	Auto-ignition temperature: None below 400°C Explosive properties: Not explosive
Storage stability:	The data are sufficient to support that the product remain within specifications for at least 2 years when stored under normal conditions

2.3 Recommendations

The APVMA has evaluated the chemistry aspects of the active constituent isofetamid and associated product KENJA 400 SC FUNGICIDE, including the physicochemical properties, identification, manufacturing processes, quality control procedures, stability, batch analysis results, analytical methods, and packaging specifications, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least two years when stored under normal conditions.

Based on a review of the chemistry and manufacturing details, the registration of KENJA 400 SC FUNGICIDE is supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

The toxicological assessment considered the proposed use of KENJA 400 SC FUNGICIDE containing the new active constituent isofetamid at 400 g/L. To support the application, toxicological data was provided for isofetamid and several of its metabolites.

3.1 Evaluation of toxicology

The toxicological database for isofetamid, which consists primarily of toxicity studies conducted in rats, mice, rabbits and dogs, is considered sufficient to determine the toxicology profile of isofetamid and characterise the risk to humans.

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 does not necessarily indicate such effects might occur in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless robust 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 takes into account the likely human exposure levels compared with those that 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 Adverse Effect Level (NOAEL) are used to develop acceptable limits for dietary, or other, intakes at which no adverse health effects in humans would be expected.

Chemical class

Isofetamid is a foliar fungicide which acts by inhibiting succinate dehydrogenase (SDH) in complex II of fungal respiration.

Toxicokinetics and metabolism

Isofetamid is well absorbed (more than 93 per cent of the administered dose) following oral administration in rats. Absorption is saturated at the high dose, and clearance from the plasma was slow. Blood:plasma ratios suggest isofetamid or its radiolabelled metabolites are bound to cellular blood constituents. Isofetamid was widely distributed in tissues, with the highest levels being detected in the liver and kidney. There was no evidence of tissue accumulation following repeat dosing. Extensive metabolism occurred, and unchanged isofetamid was not detected in urine. Excretion was rapid, with the majority of administered radioactive isofetamid being eliminated in urine and bile by 48 hours after dosing. The major metabolites were considered to be of no greater toxicological concern than isofetamid. Urinary excretion was predominant in

females compared to males, and, while biliary excretion was a major route of elimination, enterohepatic recirculation resulting in limited amounts being excreted in the faeces.

Dermal absorption was estimated at <10 per cent based on a 28-day dermal toxicity study in rats.

Acute toxicity (active constituent)

Isofetamid had low acute toxicity after oral, dermal and inhalation exposure. Isofetamid was not irritating to the skin of rabbits, and was not a skin sensitiser in mice (local lymph node assay). It caused slight eye irritation in rabbits.

Acute toxicity (product)

KENJA 400 SC FUNGICIDE was of low acute oral, acute dermal and acute inhalational toxicity. It was not a skin or eye irritant nor a skin sensitiser.

Systemic effects

In short- and long-term repeat-dose dietary studies in mice, rats and dogs, treatment-related effects were seen on the liver. In mice, increased liver weight was observed in the absence of histopathology (other than hepatocytes hypertrophy) and clinical chemistry correlates. In contrast, in rats and dogs, increases in liver weight occurred in conjunction with increased plasma levels of gamma glutamyl transpeptidase (GGPT) in both species and alkaline phosphatase (ALP) in dogs. Histopathological changes (ie fatty change, brown pigment deposition and cytoplasmic eosinophilic inclusion bodies), in addition to hepatocellular hypertrophy, were observed and considered to be adverse.

In short- and long-term dietary studies in rats, the thyroid was also a target organ for toxicity with follicular cell hypertrophy being observed at dose levels producing liver toxicity. Increased blood clotting time/potential in the absence of changes in other haematology parameters was also seen in these studies in the presence of liver toxicity. These increases in blood clotting times may indicate a reduction in one or more vitamin K-dependent coagulation factors that was caused by treatment-related hepatic dysfunction. However, from the available data, the adverse effects observed in thromboplastin time (APTT) and prothrombin time (PT), were considered secondary to disturbances in liver function.

The NOAEL of 161 mg/kg bw/day in the 90-day study in mice was based on increased adrenal weight with cortical hypertrophy at the high LOAEL of 1306 mg/kg bw/day. In rats, the NOAEL of 7 mg/kg bw/day in the 90-day study was based on increased liver weight and increased GGPT along with hepatocellular hypertrophy and follicular cell hypertrophy of the thyroid at the LOAEL of 69 mg/kg bw/day. In dogs, the findings in the 90-day and one-year dog studies allowed an overall NOAEL of 5 mg/kg bw/day to be identified, based on decreased albumin, increased ALP, GGPT and liver weight, along with enlarged liver and hepatocellular hypertrophy at 29 mg/kg bw/day.

In a 28-day repeat-dose dermal study in rats, no treatment-related effects were observed, and the NOAEL was 1000 mg/kg bw/day, the highest dose tested.

Chronic toxicity and carcinogenicity

In long-term studies, the NOAEL of 92 mg/kg bw/day in the mouse 78-week study was based on decreased bodyweight gain at 431 mg/kg bw/day.

In rats, liver and thyroid toxicity and prolongation in blood clotting time/potential were seen in the one- and/or two-year studies and were consistent with the target organ toxicity seen in the 90-day study. In the one-year study, the NOAEL of 23 mg/kg bw/day was based on prolongation in APTT and PT, decreased bilirubin, increased GGPT, globulin, total cholesterol, liver and thyroid weight, hepatocellular hypertrophy, fatty change and cytoplasmic eosinophilic inclusion bodies and follicular cell hypertrophy in the thyroid at the next higher dose of 237 mg/kg bw/day. In the two-year study (with no clinical chemistry), the NOAEL of 20 mg/kg bw/day was based on decreased bodyweight gain, increased liver and thyroid weight, darkened liver, hepatocellular hypertrophy, brown pigment deposition and cytoplasmic eosinophilic inclusion bodies in hepatocytes, and follicular cell hypertrophy and cysts in the thyroid at 210 mg/kg bw/day.

In long-term studies in mice and rats treated in the diet at doses up to 502 and 210 mg/kg bw/day respectively, there was no evidence that isofetamid was carcinogenic. It was concluded that isofetamid is unlikely to pose a carcinogenic risk to humans.

Reproductive and developmental toxicity

In a dietary two-generation rat study, a slight delay in vaginal opening was seen in F1 females at the top dose level (32.3 days compared to 30.6 days in controls). However, this was considered to be linked to reduced bodyweight gain in pups at this dose, and is not considered to be toxicologically significant. Therefore, the NOAEL for reproductive toxicity was 451 mg/kg bw/day. In parental animals, the NOAEL for parental toxicity was 42 mg/kg bw/day based on decreased bodyweight, increased liver weight in the presence of hypertrophy with cytoplasmic eosinophilic inclusion bodies, and increased thyroid weight in the P0 and F1 generations in the presence of follicular cell hypertrophy at 451 mg/kg bw/day. An external malformation (syndactyly/ectrodactyly of the finger(s) or toe(s)) was seen in 1-3 F2 offspring at 0, 1000 and 10000 ppm. Following further progeny tests it was concluded that the observed malformation was due to the inheritance of an autosomal recessive trait. The NOAEL for offspring toxicity was 107 mg/kg bw/day, based on lower bodyweight at 1047 mg/kg bw/day.

In a study of developmental toxicity in rats, the NOAEL for maternal toxicity was 300 mg/kg bw/day, based on increased relative (bodyweight adjusted) liver weight at 1000 mg/kg bw/day. The NOAEL for embryo/foetal toxicity was 300 mg/kg bw/day, based on a slight increased incidence of brain haemorrhage at 1000 mg/kg bw/day, which was considered to be potentially treatment related.

In a study of developmental toxicity in rabbits, the NOAEL for maternal toxicity was 300 mg/kg bw/day, based on decreased bodyweight gain and food consumption and increased absolute and relative (bodyweight adjusted) liver weight at 1000 mg/kg bw/day. The NOAEL for embryo/foetal toxicity was 1000 mg/kg bw/day, the highest dose tested. It was concluded that isofetamid was not a reproductive toxicant in rats and was not teratogenic in rats and rabbits.

Genotoxicity

Isofetamid was negative for genotoxicity in an adequate range of *in vitro* and *in vivo* assays.

Neurotoxicity/immunotoxicity

Isofetamid was negative for neurotoxicity in rats in both acute studies up to 2000 mg/kg bw, or in three month studies at up to 1049 mg/kg bw. Neurotoxicity was investigated in rats by giving them a single dose of up to 2000 mg/kg bw or doses up to 1049 mg/kg bw/day for three months.

No evidence of immunotoxicity was observed in mice in a four week study at doses up to 1380 mg/kg bw/day.

Toxicity of metabolites and/or impurities

GPTC, a significant plant metabolite, was of low acute oral toxicity and was negative for genotoxicity. It was considered that GPTC was of no greater toxicity than isofetamid.

3.2 Health-based guidance values and poisons scheduling

Poisons standard

Isofetamid is listed in Appendix B of the Standard for the Uniform Scheduling of Medicines and Poisons, as a substance not requiring control by scheduling. On this basis, KENJA 400 SC FUNGICIDE is included in Appendix B of the Poisons Standard and does not require a signal heading on the label.

Health-based guidance values

Acceptable Daily Intake

The Acceptable Daily Intake (ADI) is that quantity of an agricultural or veterinary chemical that can safely be consumed on a daily basis for a lifetime and is based on the lowest observable effect level identified in the most sensitive species. This level is then divided by a safety factor that reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

In repeat-dose toxicity studies with isofetamid, the most sensitive species was found to be dog and a NOAEL of 5 mg/kg bw/day in the dietary 90-day and one-year dog toxicity studies was identified on the basis of decreased albumin, increased ALP, GGPT and absolute and relative (bodyweight adjusted) liver weight with enlarged liver and hepatocellular hypertrophy at 29 mg/kg bw/day. A 100-fold uncertainty factor to incorporate differences in toxicodynamics and toxicokinetics between and within species is considered appropriate.

Applying an uncertainty factor of 100 to NOAEL of 5 mg/kg bw/day, the APVMA proposes the ADI for isofetamid is 0.05 mg/kg bw/day.

Acute Reference Dose

The Acute Reference Dose (ARfD) is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed in a single meal or over a single day as an isolated event. The ARfD for isofetamid is proposed at 3 mg/kg bw, based on a NOAEL of 300 mg/kg bw/day in a developmental rabbit study, based on reduced maternal bodyweight gain at 1000 mg/kg bw/day early in gestation, which might be attributable to a single exposure to isofetamid.

3.3 Recommendations

There are no objections on human health grounds to the registration of the product KENJA 400 SC FUNGICIDE, containing 400g/L of isofetamid, when used in accordance with the directions for use.

4 RESIDUES ASSESSMENT

The residue assessment of KENJA 400 SC FUNGICIDE considered metabolism, analytical methodology, residue trial data, fate in storage and trade aspects for the new active constituent, isofetamid.

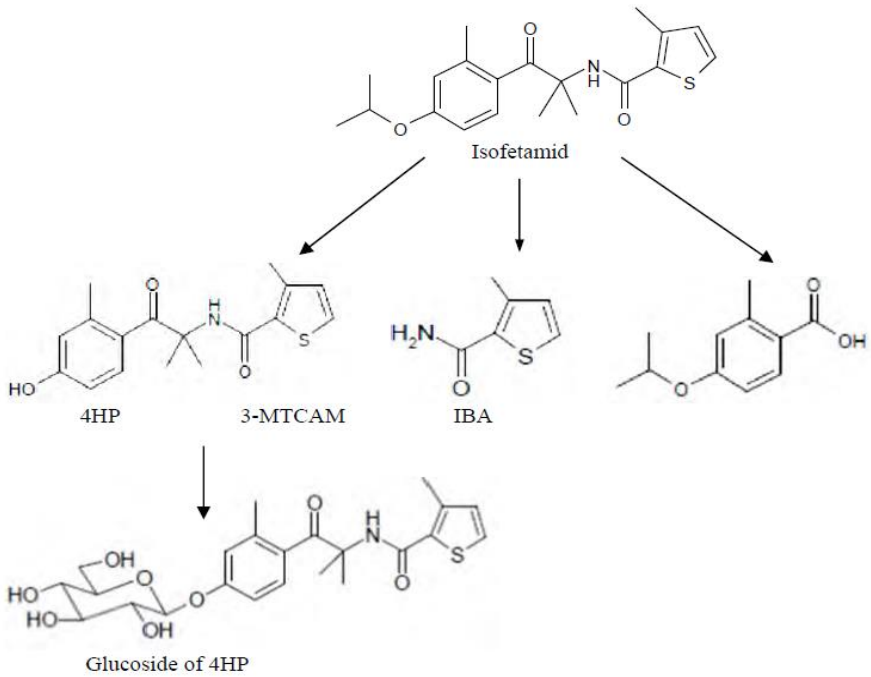
4.1 Metabolism

Plant metabolism studies of isofetamid were provided for grape, lettuce and French bean. Studies have also been conducted on lactating goats and laying hens.

Plants

The parent compound was the major component of the residues observed in grape, lettuce and French beans. The main metabolite observed in grapes, lettuce and French bean was the glucoside of 4HP resulting from O-dealkylation and glucose conjugation of the parent compound. The glucoside of 4HP was found at up to 10 per cent of total radioactive residues (TRR) in grape berries and lettuce head, and up to seven per cent in French beans.

Metabolic pathway of isofetamid in plants (grape, lettuce and French beans)



Livestock

Isofetamid parent compound was the major component in the milk fat fraction and fat in the lactating goat studies. PPA (2-[3-methyl-4-[2-methyl-2- (3-methylthiophene-2-carboxamido)propanoyl]phenoxy]propanoic

acid) was the major metabolite found in the liver and kidney of lactating goat. However, in tissues and eggs of laying hens no significant component was identified.

4.2 Analytical methods and storage stability

Plant commodities

In the methods for determination of isofetamid and the glucoside of 4HP in plant commodities, homogenized samples were extracted with acetonitrile:water, with or without clean up with a solid phase extraction, and residues were determined by High Performance Liquid Chromatography (HPLC) with tandem mass spectrometric detection (MS/MS). The methods of analysis were validated at various fortification levels with a Limit of Quantitation (LOQ) of 0.01 mg/kg for isofetamid and 0.01 mg/kg for the glucoside of 4HP.

Animal commodities

In the methods for determination of isofetamid, 4HP, PPA and 5-HPPA in animal commodities, samples were homogenized with acetonitrile:water, and DisQuE extraction mixture (developed using the QuEChERS method) was added and mixed. An aliquot was diluted in formate buffer. Residues were determined by HPLC with MS/MS detection. The method of analysis was validated with LOQs of 0.01 mg/kg for isofetamid, 4HP, PPA and 5-HPPA.

Storage stability

Storage stability results indicate that isofetamid residue was stable at –20°C for at least 12 months in almonds, rape seeds, grapes, lettuce, potatoes and dry beans.

4.3 Residue definition

Plant commodities

In plant metabolism studies, parent isofetamid was the major component in grape (berries and leaves), lettuce (heads and wrapper leaves) and French beans (forage, immature pods and seeds). Based on the available information, parent isofetamid is considered to be the appropriate residues definition for commodities of plant origin for both enforcement and dietary risk assessment. This is consistent with the residue definition for plant commodities recommended by the 2016 JMPR evaluation of the same metabolism dataset.

Animal commodities

In the lactating goat study, isofetamid was the major component in milk fat and fat. 2-[3-methyl-4-[2-methyl-2-(3-methylthiophene-2-carboxamido) propanoyl]phenoxy]propanoic acid (PPA) was the major component of the residue in goat liver and kidney. For animal commodities the following definition is recommended: Sum of isofetamid and 2-[3-methyl-4-[2-methyl-2-(3-methylthiophene-2- carboxamido) propanoyl]phenoxy]propanoic

acid (PPA), expressed as isofetamid. This is consistent with the JMPR 2016 recommendation that isofetamid and PPA are suitable analytes for establishing a residues definition for animal commodities.

4.4 Residues in food

The proposed use of isofetamid on berries involves up to two foliar applications made at a rate of 200 g ai/ha or 20g ai/100 L with a re-treatment interval of seven to 10 days. A harvest WHP of Not Required When Used as directed is proposed.

A total of two Australian trials each for blueberries and raspberries and a total of 37 strawberry (two Australia, 24 European and 11 North American) were evaluated. All trials included a 0-day Post-Harvest Interval and a subset of the trials addressed protected cropping situations.

If the results of the six Australian trials on blueberries (B), raspberries (R) and strawberries (S) are considered alone, residues in field or protected (P) situations at ~1X the proposed rate were in rank order: 0.26 (S), 0.78 (S), 0.87 (R, P), 0.95 (B), 1.18 (R, P), 2.8 (B, P) mg/kg. The OECD calculator recommends an MRL of 5 mg/kg (Supervised Trials Median Residue (STMR) = 0.91 mg/kg).

The residues observed in overseas trials conducted on field or protected grown strawberries, when scaled to the proposed maximum application rate were between 0.05 and 1.35 mg/kg.

Based on the available residues data, an MRL of 5 mg/kg for Berries and other small fruits {except grapes} is considered appropriate for the proposed use in low growing berries, bush berries and cane berries (field and protected) in conjunction with a “Nil” harvest WHP.

4.5 Residues in animal commodities

Isofetamid and PPA residues are not expected in edible tissues and milk of livestock and poultry as the proposed use does not involve treatment on animal feed commodities. However, for enforcement purposes, it is recommended that MRLs of *0.02 mg/kg for animal commodities based on the validated analytical method for parent isofetamid and PPA (LOQ is *0.01 mg/kg for each analyte) be established.

4.6 Spray drift

The regulatory Acceptable Level (RAL) for livestock areas is the level of residue in animal that should not result in residues in animal commodities above the LOQ. Based on the results of the lactating goat metabolism study, the RAL for isofetamid has been determined to be 2 ppm. The spray drift tool developed by the APVMA, recommends a no spray zone of up to 20 metres for the protection of international trade for the proposed use.

4.7 Dietary risk assessment

The chronic dietary exposure to isofetamid 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 2011–12 National Nutritional and Physical Activity Survey. The NEDI calculation is made in accordance with WHO Guidelines and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for isofetamid is equivalent to <15 per cent of the ADI. It is concluded that the chronic dietary exposure to isofetamid is acceptable.

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 with 97.5th percentile food consumption data derived primarily from the 2011–12 National Nutritional and Physical Activity Survey. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. The NESTI for isofetamid is equivalent to <5 per cent of the ARfD. It is concluded that the acute dietary exposure for isofetamid is acceptable.

4.8 Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 5).

Table 4: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
ADD:			
Isofetamid			
FB	0018	Berries and other small fruits {except grapes}	5
PE	0112	Poultry eggs	*0.02
MO	0105	Edible offal (mammalian)	*0.02
MM	0095	Meat (mammalian) [in the fat]	*0.02
ML	0106	Milks	*0.02
ML		Milks fats	*0.02
PO	0111	Poultry, edible offal of	*0.02
PM	0110	Poultry meat [in the fat]	*0.02

Amendments to Table 3	
Compound	**Residue**
ADD:	
Isofetamid	Commodities of plant origin: Isofetamid
	Commodities of animal origin: Sum of isofetamid and 2-[3-methyl-4-[2-methyl-2-(3-methylthiophene-2- carboxamido) propanoyl]phenoxy]propanoic acid (PPA), expressed as isofetamid

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Berries (low growing berries, bush berries and cane berries) are not considered to be major export commodities[2]. The proposed use does not involve treatment of major trade commodities and significant residues are not expected to arise in livestock feeds as a result of the proposed use.

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Isofetamid has been considered by Codex. The following relevant international MRLs have been established for isofetamid in overseas markets (Table 6).

[2] apvma.gov.au/node/1017#major_export_food_commodity_groups

Table 5: Proposed Australian and current international MRLs for isofetamid

Commodity	Tolerance for residues arising from the use of isofetamid (mg/kg)						
	Australia	Canada[3,4]	EU[5]	US[6,7]	Korea[8]	Codex[9]	Japan[10]
Residue definition (compliance)	Isofetamid	Isofetamid	Isofetamid	Isofetamid	-	Isofetamid	Isofetamid
Berries and other small fruits (except grapes)	5 (proposed)						
Low growing berries				4		4	
Strawberries		4	4		4		4
Cane berries				4	3	3	
Raspberries		4	*0.01		-	-	4
Bushberries				5			
Blueberries		5	*0.01		3	-	4

Isofetamid MRLs have been established by Codex at 3 mg/kg for cane berries and 4 mg/kg for low growing berries. While the proposed Australian MRL is 5 mg/kg, the high residue detected in trials was 2.8 mg/kg, lower than the Codex MRLs. It is concluded that the risk to trade associated with the proposed use is considered to be low.

[3] pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php

[4] canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/pesticides-food/residue-definitions-chemicals-maximum-residue-limits-regulated-under-pest-control-products-act.html

[5] ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.CurrentMRL&language=EN&pestResidueId=2463

[6] ecfr.gov/cgi-bin/text-idx?SID=013ab7d96d7f5950a7b2dac6211a40a4&mc=true&node=se40.26.180_1681&rgn=div8

[7] govinfo.gov/content/pkg/CFR-2017-title40-vol26/xml/CFR-2017-title40-vol26-sec180-41.xml

[8] foodsafetykorea.go.kr/residue/prd/mrls/list.do?currentPageNo=1&searchCode=P01802&searchFoodCode=&menuKey=1&subMenuKey=161&subChildMenuKey=&searchConsonantFlag=&searchConsonantFlag2=&searchValue2=&searchFlag=prd&searchClassLCode=&searchClassMCode=&searchClassScode=&searchValue=

[9] fao.org/fao-who-codexalimentarius/codex-texts/dbs/pestres/pesticide-detail/en/?p_id=290

[10] db.ffcr.or.jp/front/pesticide_detail?id=6980

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

KENJA 400 SC FUNGICIDE has low acute oral, acute dermal and acute inhalational toxicity. It is not a skin or eye irritant nor a skin sensitiser.

6.2 Occupational exposure

Exposure during use

KENJA 400 SC FUNGICIDE is to be used for the control of grey mould in berries, including low growing berries, cane berries and bush berries in both field and protected cropping situations, with application by groundboom, tractor drawn airblast sprayers and hand held spraying equipment. Based on the proposed label rate, and maximum work rate for groundboom/airblast, it is anticipated that workers will be handling up to 3 kg isofetamid per day for groundboom/airblast use, and 0.12 kg isofetamid per day for handheld equipment. A NOAEL of 5.0 mg/kg bw/day from a long term dog study was selected for workers involved in using KENJA 400 SC FUNGICIDE, with dermal absorption factors based on assessed studies. Risks were acceptable for mixing, loading and application by all methods with a single layer of clothing and no gloves. The applicant's proposal to include the use of gloves for these activities was accepted on the basis of it being good hygiene practice in the workplace.

Exposure during re-entry or rehandling

Workers performing post-application activities in berry crops may be exposed to isofetamid residues from dermal contact with fruit and foliage. A NOAEL of 1000 mg/kg bw/day from a four week dermal study was considered appropriate for the risk assessment. Based on the calculation of exposure for relevant maintenance activities in representative crops, exposure was acceptable on the day of product application without the use of PPE.

6.3 Public exposure

The product is intended for professional use only, and risks from product use are not relevant to the general public. Risks from spraying activities were calculated, and no buffer zones for bystander protection are required for mechanical ground spraying.

6.4 Recommendations

The following first aid instructions, safety directions and precautionary (warning) statements are recommended for the product label.

First aid instructions

First aid is not generally required. If in doubt, contact a Poisons Information Centre (phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.

Safety directions

When opening the container, preparing spray and using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and gauntlet-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

Precautionary (warning) statements

DO NOT allow bystanders to come into contact with the spray cloud.

7 ENVIRONMENTAL ASSESSMENT

7.1 Fate and behaviour in the environment

Soil

The main degradation pathway of isofetamid under aerobic soil conditions is microbial degradation with up to 31 per cent mineralisation and 54 per cent bound residues after 120 days. The principle metabolite detected in soils was 4HP[11] (formed from the separation of the isopropyl side chain) reaching a maximum of 9.2 per cent of applied radioactivity after 30 days.

Photolysis was determined not to be an important degradation pathway.

Under laboratory conditions at 20°C, isofetamid was moderately persistent in four aerobic soils (DT_{50} 39–55 days, geomean 37 days) and persistent in anaerobic soil (DT_{50} 572 days). The soil metabolite 4HP was not persistent in three aerobic soils (DT_{50} 1.8–2.8 days, geomean 2.2 days).

Based on batch equilibrium studies in five soils, isofetamid is considered to be moderately mobile with the Freundlich organic carbon absorption coefficient (K_{foc}) 274–597 mL/g (mean 489 mL/g, 1/n 0.94). Absorption and desorption of isofetamid is correlated to concentration, with sorption decreasing slightly with increasing isofetamid concentration. Soil sorption of isofetamid is not pH dependent. The soil metabolite 4HP is slightly more mobile with K_{foc} 110–305 mL/g (mean 196 mL/g, 1/n 0.89).

Field dissipation studies were conducted in seven bare soil sites and two turfed sites across Europe and North America. Isofetamid was moderately persistent when applied to bare soil (DT_{50} 7.0–52 days) or turfed soil (DT_{50} 39–80 days). Isofetamid was very persistent in Saskatchewan, Canada (DT_{50} 247 days); however, this site was not considered to be relevant to Australia. The metabolite 4HP was the only metabolite detected in field soils (maximum mean 24 ng/g). Isofetamid and 4HP generally remained in the upper soil horizon (0–10cm depth). Based on results for field dissipation and soil sorption, isofetamid and 4HP are not expected to readily leach into ground water.

Water and sediment

Isofetamid is stable to hydrolysis, but is highly susceptible to aqueous photolysis (DT_{50} 1.4 and 1.8 days in natural water and pH 7 buffer, respectively). The major photoproducts were IBA[12] (up to 80 per cent) and 3–MTCAM[13] (up to 36 per cent).

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[11] N-[1,1-dimethyl-2-(4-hydroxy-2- methylphenyl)-2-oxoethyl]-3-methyl-2- thiophenecarboxamide

[12] 2-methyl-4-(propan-2-yloxy)benzoic acid

[13] 3-methyl-2-thiophenecarboxamide

In two aerobic water/sediment systems under laboratory conditions, isofetamid partitioned quickly to the sediment (water phase DT_{50} 12-27 days, geomean 18 days), but was persistent in the whole system (DT_{50} 114–175 days, geomean 141 days). PPA[14] was the only major metabolite reaching 11 per cent in the whole system (7.5 per cent in water and 3.4 per cent in sediment). Under anaerobic conditions, isofetamid also partitioned moderately quickly to the sediment (water phase DT_{50} 40–87 days) where it was stable (DT_{50} >1000 days). Mineralisation and bound residues were low in all systems reaching no more than 2.7 per cent and 12 per cent, respectively.

Air

Based on its low vapour pressure and low water solubility, isofetamid is not expected to volatilise from soil or water surfaces. Based on the predicted rapid rate of photochemical oxidative degradation (DT_{50} 0.058 days), isofetamid is not expected to be found in any significant concentration in the air or be subject to long range transport.

7.2 Effects and associated risks to non-target species

Terrestrial vertebrates

Isofetamid has low toxicity to mammals (LD_{50} > 2000 mg ac/kg bw/d, *Rattus norvegicus*) and birds (LD_{50} >2000 mg ac/kg bw/day, two species tested). The major plant metabolite GPTC[15] also has low toxicity to mammals (LD_{50} >2000 mg/kg bw/day, *Rattus norvegicus*). In reproductive toxicity testing, the most sensitive ecologically relevant effects were reduced F1 and F2 pup weights in mammals at doses as low as 451 mg ac/kg bw/day (NOAEL 57 mg ac/kg bw/day*, Rattus norvegicus*) and reduced eggshell thickness in birds at doses as low as 130 mg ac/kg bw/day (NOEL 25 mg ac/kg bw/day, two species tested). Acceptable risks could be concluded assuming dietary exposure to food items (eg vegetation and invertebrates) directly contaminated from spray application of the product within the treatment area. Therefore, no protection measures are required for terrestrial vertebrates.

Aquatic species

Isofetamid has moderate toxicity to fish (lowest LC_{50} 2.3 mg ac/L, *Oncorhynchus mykiss*), high toxicity to aquatic invertebrates (lowest EC_{50} 0.44 mg ac/L, *Crassostrea virginica*), and low toxicity to algae and aquatic plants at the limit of water solubility (EC_{50} >4.1 mg ac/L, four species tested). The formulation does not enhance the toxicity to aquatic species and major metabolites (PPA, IBA, and 3-MTCAM) have low toxicity to all aquatic taxa. Following long-term exposure to isofetamid, a biologically relevant reduction of larval growth in fish was observed at concentrations as low as 0.35 mg ac/L (NOEC 0.81 mg ac/L, *Pimephales promelas*), a biologically relevant reduction in growth and reproduction was observed in aquatic invertebrates at concentrations as low as 1.7 mg ac/L (NOEC 0.81 mg ac/L, *Daphnia magna*) and decreased emergence of

14 2-[3-methyl-4-[2-methyl-2-(3-methylthiophene-2-carboxamido)propanoyl]phenoxy]propanoic acid

15 N-{1-[4-(b-D-glucopyranosyloxy)-2-methylphenyl]-2-methyl-1-oxopropan-2-yl}-3-methylthiophene-2-carboxamide

sediment dwellers at concentrations as low as 993 mg ac/kg dry sediment (NOEC 483 mg ac/kg dry sediment, *Chironomus riparius*).

Due to the toxicity of isofetamid to fish and aquatic invertebrates a protection statement is required on the label. Spray drift risks to aquatic species were determined to be acceptable provided buffer zones of 10 metres for boom sprayers or five metres for vertical sprayers are observed under certain conditions. Runoff risks were also acceptable provided the product is not applied when a runoff event can be expected soon after application (ie due to storms or irrigation). Standard runoff restraints are advised to mitigate this risk.

Bees and other non-target arthropods

Isofetamid has low toxicity to bees by contact exposure (LD_{50} >100 µg ac/bee, *Apis mellifera*) and oral exposure (LD_{50} >100 µg ac/bee, *Apis mellifera*). The formulation does not enhance the toxicity to bees. No adverse effects on mortality rates or behaviour were observed at the limit doses tested (lowest NOEL 30 µg ac/bee, *Apis mellifera*). Spray application is to be directed at foliage, flowers and fruit; therefore, it is considered possible for bees and other insect pollinators to be exposed to isofetamid residues when foraging for pollen and nectar in over-sprayed blooming plants in the treatment area. Risks were determined to be acceptable assuming bees foraged on oversprayed blooming plants at the maximum rate of application. Therefore, no protection measures are required for bees.

A representative SC formulation of isofetamid was not toxic to the indicator species for predatory arthropods (LR_{50} >1000 g ac/ha, *Typhlodromus pyri*) and parasitic arthropods (LR_{50} >1000 g ac/ha, *Aphidius rhopalosiphi*) in Tier 1 (glass plate) laboratory toxicity tests. Acceptable risks were concluded assuming the non-target arthropods are exposed to fresh-dried residues within the treatment area immediately after application. Therefore, the product is considered compatible with integrated pest management (IPM) programs utilising beneficial arthropods.

Soil organisms

Isofetamid has low toxicity to soil macro-organisms such as earthworms (LC_{50corr} >500 mg ac/kg dry soil, *Eisenia foetida*), and the formulation does not enhance its toxicity. Following long-term exposure to isofetamid, inhibited reproduction of soil macro-organisms was observed in a dose-dependent manner (lowest EC_{10corr} 10 mg ac/kg dry soil, *Eisenia foetida*). Isofetamid does not adversely affect soil microbial processes such as nitrogen transformation or carbon transformation at exaggerated soil concentrations (NOEC 9.1 mg ac/kg dry soil). Acceptable risks were concluded assuming direct overspray of soil without interception. Therefore, no protection measures are required for soil organisms.

Non-target terrestrial plants

A representative SC formulation of isofetamid had low toxicity to non-target terrestrial plants by both pre-emergent exposure (seedling emergence test) and post-emergent exposure (vegetative vigour test). The most sensitive species was tomato following pre-emergent exposure (ER_{25} 12,000 g ac/ha, ER_{50} 184,500 g ac/ha, *Lycopersicon esculentum*) and corn following post-emergent exposure (ER_{25} 1365 g ac/ha, ER_{50} 1711 g ac/ha, *Zea mays*). A spray drift assessment indicated that buffer zones are not required for the protection of non-target terrestrial plants.

7.3 Recommendations

Based on assessment of the environmental data, the proposed use of KENJA 400 SC FUNGICIDE is not, or would not be, likely to have an unintended effect that is harmful to animals, plants or things or to the environment following use in accordance with label instructions. Buffer zones of 10 metres for boom sprayers or five metres for vertical sprayers are advised for the protection of natural aquatic areas under certain conditions. Standard runoff restraints are advised to avoid a runoff event occurring soon after application (ie due to storms or irrigation).

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

The product is to be registered for the control of grey mould (*Botrytis cinerea*) in all berries, including low growing berries such as strawberries, cane berries including raspberries and bush berries including blueberries, in both field and protected cropping situations. The product may be applied up to twice per crop at 500 mL/ha (at spray volumes less than 1000 L/ha) or at 50 mL/100 L where the spray volume is between 1000 L/ha and 1,500 L/ha.

8.2 Efficacy and target crop/animal safety

A total of 14 efficacy trials (including crop safety assessments in each of the trials) were provided for KENJA 400 SC FUNGICIDE where efficacy was evaluated in comparison to several industry standards.

The trials used appropriate trial design, scientific methodology, and assessment parameters, with multiple replicates, industry standards, and untreated controls. Results were analysed using standard statistical procedures (ANOVA and LSD).

Efficacy

Efficacy was evaluated against grey mould (*Botrytis cinerea*) in strawberries, blueberries, raspberries and blackberries at rates ranging from 31.25 mL/100 L up to 375 mL/100 L totalling a maximum of 3,750 mL//ha. The proposed label rate is 500 mL/ha (at spray volumes less than 1000 L/ha.) or at 50 mL/100 L where the spray volume is between 1000 L/ha and 1,500 L/ha up to a maximum of 750 mL/ha.

In nine efficacy trials conducted in strawberries (seven), raspberries (protected) (one) and blueberries (protected) (one) in Australia, KENJA 400 SC FUNGICIDE at the label rate (500 mL/ha. or 50 mL/100L for spray volumes greater than 1000 L/ha.) or at rates similar to the label rate (up to a maximum 1.25X label rate) resulted in a statistically significant reduction in grey mould in both disease incidence and disease severity. In all but one of those trials, the level of control achieved by KENJA 400 SC FUNGICIDE was also statistically equivalent or superior to a registered industry standard.

While the number of applications in the trials often exceeded the maximum of two stipulated in the directions on the proposed label, it is recognised that the proposed product would be employed as a preventative, rather than a curative treatment as part of a program of treatments from a range of different mode of action groups to control grey mould in berries as proposed on the product label.

Crop safety

Application of KENJA 400 SC FUNGICIDE at up to ~5X label rate (3,750 mL/ha.) in strawberries for up to four applications per season (greater than the maximum two applications proposed on the draft label) did not result in any adverse effects to the leaves, flowers, fruit or harvest yield. In protected cropping trials in blueberries and raspberries, KENJA 400 SC FUNGICIDE was applied to 3X label rate (150 mL/100 L) (four to eight applications) was found not to be phytotoxic.

No phytotoxicity was reported in trials conducted in the USA in blueberries, raspberries and blackberries, at rates up to ~2X the proposed label rate (1,132 mL/ha.) after six or more applications per season.

Resistance management

Isofetamid is a succinate dehydrogenase inhibitor mode of action fungicide. The fungicide resistance action committee (FRAC) has designated isofetamid as a Group 7 fungicide.

There is currently a resistance management strategy in place for Group 7 fungicides for treatment of grey mould in strawberries according to CropLife Australia.

8.3 Recommendations

KENJA 400 SC FUNGICIDE provided effective control of grey mould in strawberries, blueberries and raspberries in field and protected cropping situations at the proposed label rates and timings; providing similar or superior control to other registered fungicides. Trial data confirmed crop safety of KENJA 400 SC FUNGICIDE when applied to strawberries, blueberries, raspberries and blackberries at the proposed label rate.

9 LABELLING REQUIREMENTS

Company Name:	ISHIHARA SANGYO KAISHA, LTD
Product Name:	Kenja 400 SC Fungicide
eLabel Application No:	DC10-11891496E5
APVMA Approval No:	88495/121499

Label Name:	Kenja 400 SC Fungicide
Signal Headings:	READ SAFETY DIRECTIONS BEFORE OPENING OR USING
Constituent Statements:	400 g/L ISOFETAMID
Mode of Action:	GROUP 7 FUNGICIDE
Statement of Claims:	For the control of grey mould in berries as specified in the DIRECTIONS FOR USE table
Net Contents:	1 L, 2 L, 5 L, 10 L, 20 L
Restraints:	RESTRAINTS FOR PROFESSIONAL USE ONLY DO NOT apply with aircraft. DO NOT apply through any type of irrigation equipment. DO NOT graze treated areas DO NOT apply if heavy rains or storms are forecast within 3 days. DO NOT irrigate to the point of runoff for at least 3 days after application. SPRAY DRIFT RESTRAINTS: See attachment

Withholding Periods:	BERRIES: NIL

Trade Advice:	

General Instructions:	Mixing Fill minimum 50% of the required water into the spray tank, and agitate when adding the required amount of Kenja 400 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. Crop Safety Not all berry crops, varieties, or cultivars have been individually tested for crop safety. To test for crop safety, apply the product in accordance with the label instructions to a small area of the target crop to ensure that a phytotoxic response will not occur, especially where the application is a new use of the product by the applicator.

Resistance Warning:	Fungicide Resistance Warning GROUP 7 FUNGICIDE Kenja 400 SC Fungicide is a member of the inhibition of succinate dehydrogenase mode of action group. For fungicide resistance management Kenja 400 SC Fungicide is a group 7 fungicide. Some naturally occurring individual fungi resistant to the product and other group 7 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 7 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 and AgNova Technologies Pty Ltd accept no liability for any losses that may result from the failure of this product to control resistant fungi.

Precautions:	RE-ENTRY PERIOD 0 days when used as directed

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

Storage and Disposal:	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:	SAFETY DIRECTIONS When opening the container, preparing spray and using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and gauntlet-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

First Aid Instructions:	FIRST AID First aid is not generally required. If in doubt, contact a Poisons Information Centre (phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.

First Aid Warnings:	

SPRAY DRIFT RESTRAINTS

Specific definitions for terms used in this section of the label can be found at apvma.gov.au/spraydrift

DO NOT allow bystanders to come into contact with the spray cloud.

DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The advisory buffer zones in the relevant buffer zone tables below provide guidance but may not be sufficient in all situations. Wherever possible, correctly use application equipment designed to reduce spray drift and apply when the wind direction is away from these sensitive areas.

DO NOT apply unless the wind speed is between 3 and 20 kilometres per hour at the application site during the time of application.

DO NOT apply if there are hazardous surface temperature inversion conditions present at the application site during the time of application. These conditions exist most evenings one to two hours before sunset and persist until one to two hours after sunrise.

DO NOT apply by a boom sprayer unless the following requirements are met:

- spray droplets are not smaller than a MEDIUM spray droplet size category
- minimum distances between the application site and downwind sensitive areas (see the following table titled 'Buffer zones for boom sprayers') are observed.

Buffer zones for boom sprayers			
Application rate	**Boom height above the target canopy**	**Natural aquatic areas**	**Livestock areas**
Up to 750 mL/ha	0.5 m or lower	0 metres	0 metres
	1.0 m or lower	10 metres	20 metres
500 mL/ha	0.5 m or lower	0 metres	0 metres
	1.0 m or lower	0 metres	10 metres

DO NOT apply by a vertical sprayer unless the following requirements are met:

- spray is not directed above the target canopy
- the outside of the sprayer is turned off when turning at the end of rows and when spraying the outer row on each side of the application site
- for dilute water rates up to the maximum listed for each type of canopy specified, minimum distances between the application site and downwind sensitive areas (see the following table titled 'Buffer zones for vertical sprayers') are observed

Buffer zones for vertical sprayers		
Type of target canopy	**Natural aquatic areas**	**Livestock areas**
2 metres tall and shorter, maximum dilute water rate of 1500 L/ha	0 metres	0 metres
taller than 2 metres (not fully-foliated), maximum dilute water rate of 1500 L/ha	5 metres	10 metres
taller than 2 metres (fully-foliated), maximum dilute water rate of 1500 L/ha	0 metres	0 metres

DIRECTIONS FOR USE

Crop	Disease	Rate	Critical Comments
Berries Low growing berries including strawberries Cane berries including raspberries Bush berries including blueberries (field and protected cropping)	Grey Mould (*Botrytis cinerea*)	Dilute spraying: 50 mL/100 L Use when spray volume is 1000 to 1500 L/ha OR 500 mL/ha Use when spray volume is less than 1000 L/ha Do not apply volumes less than 500 L/ha	Reduce background levels of disease by removing infected plant debris and/or rotted fruit throughout the season. Apply a program of protectant fungicides from flowering. Apply KENJA 400 SC FUNGICIDE before first sign of disease or when conditions are conducive to disease development as part of a disease management program. Apply sprays at 7 to 10 day intervals. Use the shorter interval under conditions favouring disease infection. To ensure thorough spray coverage of the crop, apply to the point of run-off targeting foliage, flowers and fruit. The required dilute spray volume will change and the sprayer setup and operation may also need to be changed, as the crop grows. Do not apply more than 2 sprays of KENJA 400 SC FUNGICIDE per crop, and follow the CropLife Australia resistance management guidelines. If conditions are conducive to further disease infection, additional application of fungicides from other mode of action groups may be required.

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

ABBREVIATIONS

ACCS/ACMS	Advisory Committee for Chemicals Scheduling/Advisory Committee for Medicines Scheduling
ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ALP	Alkaline Phosphatase
APTT	activated partial thromboplastin time
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50 per cent of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50 per cent of the test population is impacted
EC_{50}	concentration at which 50 per cent of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50 per cent of the test population is impacted
EI	Export Interval
EGI	Export Grazing Interval
ESI	Export Slaughter Interval
EUP	End Use Product
F_0	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice

GGPT	gamma glutamyl transpeptidase
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hb	Haemoglobin
HPLC	High Pressure Liquid Chromatography or High Performance Liquid Chromatography
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
kg	kilogram
K_{FOC}	Freundlich organic carbon absorption coefficient
K_{OC}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50 per cent of the test population of organisms
LD_{50}	dosage of chemical that kills 50 per cent of the test population of organisms
LOD	Limit of Detection—level at which residues can be detected
Log K_{OW}	Log to base 10 of octanol water partitioning co-efficient, synonym POW
LOQ	Limit of Quantitation—level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit

MSDS	Material Safety Data Sheet
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
NOAEL	No Observed Adverse Effect Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
PT	Prothrombin Time
Q-value	Quotient-value
RBC	Red Blood Cell Count
REI	Re-Entry Interval
s	second
sc	subcutaneous
SC	Suspension Concentrate
STMR	Supervised Trials Median Residue
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
TRR	Total radioactive residues
µg	microgram
vmd	volume median diameter

WG	Water Dispersible Granule
WHP	Withholding Period

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 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
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