Australian Government

Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of the new active cyflumetofen in the product Danisaraba Miticide

APVMA product number 89701

December 2021

ISSN 1443-1335 (electronic)

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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 Danisaraba Miticide 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 11 January 2021 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 organisation name (if relevant)
- email or postal address (if available)
- the date you made the submission.

Please note: submissions will be published on the APVMA's website, unless you have asked for the submission to remain confidential, or if the APVMA chooses at its discretion not to publish any submissions received (refer to the public consultation coversheet).

Please lodge your submission using the public consultation coversheet, which provides options for how your submission will be published.

Note that all APVMA documents are subject to the access provisions of the *Freedom of Information Act 1982* and may be required to be released under that Act should a request for access be made.

Unless you request for your submission to remain confidential, the APVMA may release your submission to the applicant for comment.

Written submissions should be addressed to:

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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.

Introduction

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Danisaraba Miticide containing the recently approved active constituent cyflumetofen.

Applicant

BASF Australia Ltd.

Purpose of application

BASF Australia Ltd has applied to the APVMA for registration of the new product Danisaraba Miticide, containing 200 g/L of the active constituent cyflumetofen, as a suspension concentrate formulation.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Danisaraba Miticide. The active constituent was approved in November 2021 under the approval number 89579.

Proposed claims and use pattern

Danisaraba Miticide is a miticide intended for the control of various mite species in pome fruit, almonds, citrus, grapes, fruiting vegetables, strawberries, and ornamentals. This includes protected use in the case of strawberries, tomatoes, and ornamentals. Proposed application rates are 100 mL/100 L water in pome fruit, almonds, citrus, grapes, and ornamentals or 1 L/ha in fruiting vegetables and strawberries. A maximum of 2 sprays per season is recommended for all crops.

Mode of action

Cyflumetofen is a selective miticide with a mode of action that inhibits the mitochondrial complex II, preventing utilization of energy by cells. The Insecticide Resistance Action Committee (IRAC) has designated cyflumetofen as a Group 25A miticide (IRAC 2021).

Overseas registrations

The active constituent cyflumetofen is currently registered as a 200 g/L suspension concentrate in several countries overseas (including the USA, Japan, Canada, and EU) for the control of mites in a wide range of crops. In the USA and Canada, products containing cyflumetofen are currently registered by BASF under the names Nealta Miticide and Sultan Miticide.

Chemistry and manufacture

Active constituent

The active constituent cyflumetofen is manufactured overseas. Details of the chemical name, structure, and physicochemical properties of cyflumetofen are listed below (Tables 1 and 2).

The purified active ingredient is a white solid with no characteristic odour. Cyflumetofen is neither flammable, explosive, nor oxidising. Auto-inflammability is 320˚C. The vapour pressure is less than 5.9× 10^{-6} kPa at 25°C. The water solubility is relatively low at 28 µg/L (purified water). The n-octanol/water partition coefficient (log P_{ow}) is 4.3 at pH 4, indicating cyflumetofen is moderately lipophilic. Cyflumetofen has a melting point range of 77.9 – 81.7°C. The FTIR, NMR and MS spectra are consistent with the molecular structure.

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

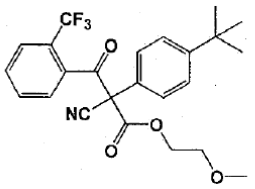
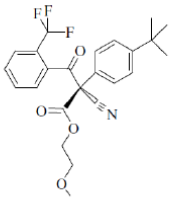
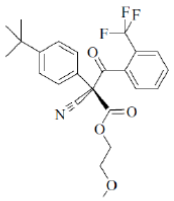
Common name (ISO):	Cyflumetofen
IUPAC name:	2-methoxyethyl (2RS)-2-(4-tert-butylphenyl)-2-cyano-3-oxo-3-[2-(trifluoromethyl)phenyl]propanoate
CAS registry number:	400882-07-7
Molecular formula:	C24H24F3NO4
Molecular weight:	447.45 g/mol
Structural formula:	  *S*-cyflumetofen  *R*-cyflumetofen

Table 2: Key physicochemical properties of the active constituent cyflumetofen

Physical form:	Powder
Colour:	White powder (purified active, 98.46% purity) Pale yellow powder (technical active, 98.4% purity)
Odour:	No characteristic odour
Melting point:	77.9 to 81.7°C (purified active)
Temperature of decomposition:	>293°C (purified active)
Density	1.229 g/cm3 at 20°C
Stability:	Stable after storage at 25°C in commercial heat-sealed pouches at 3,6,9 and 12 months with integrity of package
Safety properties:	
Flammability	Not considered highly flammable
Auto ignition	320°C
Explosive properties	Not considered explosive
Oxidising properties	Not oxidizing
Solubility in purified water:	28 µg/L at 20°C (purified active)
Organic solvent solubility at 20 °C (purified active):	n-Hexane 5.16 g/L Toluene >500 g/L Dichloromethane >500 g/L Acetone >500 g/L Methanol 98.7 g/L Ethyl Acetate >500 g/L
Dissociation constant (PKa):	No dissociation expected in a relevant pH range
PH (1% in distilled water):	4.31 at 25°C
Octanol/water partition coefficient (Log Kow/KOW):	log Pow = 4.3 (purified active) at 25°C
Vapour pressure at 25 °C:	<5.9×10-6 Pa (purified active)
Henry's law constant:	<9.4×10-2 Pa·m³/mol at 20°C
UV/VIS absorption spectra:	At 25°C (98.46%): No maximum above 290 nm but significant absorption does occur (>10 L.mol-1.cm-1) at acidic and neutral conditions. Under alkaline conditions, cyflumetofen is insufficiently stable to conclude if absorption is of breakdown products or of cyflumetofen.

Quantum yield of direct Phototransformation:	The quantum yield was calculated to be Φ = 0.15.

Formulated product

The product Danisaraba Miticide will be manufactured both overseas and in Australia. Tables 3 and 4 outline some key aspects of the formulation and physicochemical properties of the product.

Table 3: Key aspects of the formulation of the product Danisaraba Miticide

Distinguishing name:	Danisaraba Miticide
Formulation type:	Suspension concentrate (SC)
Active constituent concentration/s:	200 g/L cyflumetofen

Table 4: Physicochemical properties of the product Danisaraba Miticide

Physical form:	Opaque liquid, milky-white/light yellow colour
PH (typical values):	pH 7.0 to 9.5
Density:	1.06 g/cm3 (at 20°C ± 0.5°C)
Viscosity:	16 to 23 mPa (at 20°C) 14 to 19 mPa (at 40°C)
Pourability:	Residue <1.5%, Residue after rinsing <0.5%
Spontaneity of dispersion:	>90%
Suspensibility:	>90%
Wet Sieve	<0.5% retained
Persistent foam	<10 mL at 1 min (standard water D)
Safety properties:	Not explosive, no oxidizing properties, not classified in terms of its flash point and not classified as Dangerous Goods. Auto ignites at 430°C.
Storage stability:	HDPE bottle with screw top lid. No product bottle interaction.

The formulated product is in the form of a suspension concentrate formulation; an opaque liquid with a milky-white colour and no characteristic odour. It has a typical pH of 7.0 to 9.5 at 20°C. Viscosity of the product is 16 to 23 mPa at 20°C and 14 to 19 mPa at 40°C. Density is 1.06 g/cm3 at 20°C ± 0.5°C. The product has a boiling point of 99°C. Danisaraba miticide is an aqueous-based preparation and is not explosive, oxidising or corrosive. It will be available in 1 L to 1,000 L HDPE (high density polyethylene) containers. The active content and all of the physicochemical properties of formulation remained within the product specifications at

both elevated temperatures, and under cold storage. Based on the available data, the product is expected to remain within specifications for at least 2 years when stored under normal conditions.

Recommendations

The APVMA has evaluated the chemistry of the active constituent cyflumetofen and associated product Danisaraba Miticide including the physicochemical properties, manufacturing process, quality control procedures, identification, stability, batch analysis results, and analytical methods, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least 2 years when stored under normal conditions.

Based on a review of the chemistry and manufacturing details, the registration of Danisaraba Miticide, and approval of the active constituent cyflumetofen, are supported from a chemistry perspective. The active constituent was approved in November 2021 under the approval number 89579.

Toxicological assessment

OAT Agrio Co. Ltd have submitted all the supporting toxicity data for approval of cyflumetofen, along with reports from overseas evaluations that have been prepared by the Canadian Pest Management Regulatory Agency (PMRA, 2014), the United States Environmental Protection Agency (US EPA), the European Food Safety Authority (EFSA, 2012), and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR, 2014). The data submitted were sufficient to assess the toxicity of cyflumetofen.

Evaluation of toxicology

Chemical class

Cyflumetofen is a bridged diphenyl acaricide from the Insecticide Resistance Action Committee (IRAC) group 25A (IRAC 2021). The insecticidal mode of action for substances from group 25 is inhibition of mitochondrial complex II electron transport, which affects energy metabolism highly selectively in mites. It works on contact with the target species and is effective against all life stages of spider mites.

Pharmacokinetics

Cyflumetofen is a racemic mixture. The specific metabolism or degradation of the individual enantiomers was not investigated, although the in vitro cytotoxic effects of cyflumetofen are isomer-dependent (in order of decreasing potency: (−)-cyflumetofen >rac-cyflumetofen >(+)-cyflumetofen). After administration of a low single oral dose, cyflumetofen was rapidly absorbed, with peak plasma levels observed within one to 4 hours. It was widely distributed to the tissues and extensively metabolized. Saturation of absorption was noted at the high dose and following repeated low dose administration. Cyflumetofen was rapidly and almost completely excreted within 72 hours. The major route of elimination at the low dose was via the urine, with lower amounts excreted in the faeces. At high doses in animals, faecal excretion exceeded urinary excretion. Dermal absorption was investigated in human skin in vitro and in rats in vivo. While the formation of a large skin depot was noted in the studies, dermal absorption remained relatively low. A dermal absorption value of 11% was considered appropriate for occupational risk assessment. Based on the available metabolism data, it is notable that the theoretically possible metabolite methoxyethanol, a potential reproductive toxicant, was not detected.

Acute toxicity (active constituent)

Cyflumetofen was of low acute oral, dermal, and inhalation toxicity. It was not irritating to the skin of rabbits but was slightly irritating to rabbit eyes. It was a potent skin sensitiser in a guinea-pig maximisation assay.

Acute toxicity (product)

Danisaraba Miticide was of low oral, dermal, and inhalational toxicity and was not irritating to the skin or eyes of rabbits. In a mouse lymph node assay, Danisaraba Miticide was not a skin sensitiser; however, noting the 100% skin sensitisation result of cyflumetofen in the guinea pig maximisation assay, the potential for skin sensitisation by the product cannot be ruled out.

Repeat-dose toxicity

In repeat dose toxicity studies conducted in rats, mice, and dogs, the primary target organ was the adrenal gland, with lesions characterized principally by vacuolation of adrenal cortical cells, with the rat the species observed to be most sensitive. Additional target tissues include the liver, with changes in liver weight and hypertrophy of liver cells observed. Vacuolation of interstitial cells was observed in the ovary. Mechanistic investigations revealed that cyflumetofen may interfere with lipid and cholesterol metabolism, as well as steroidogenesis in both males and females (increased estradiol and inhibited testosterone).

The no observed adverse effect level (NOAEL) in mice, at either 4 or 13 weeks, was 1000 ppm in the diet, equating to 134 mg/kg bw/day over 4 weeks or 117 mg/kg bw/day over 13 weeks. In rats, the NOAEL from a 4-week study was 37.6 mg/kg bw/day, and from a 13-week study was 16.5 mg/kg bw/day. In dogs, the NOAEL from a 52-week study was 30 mg/kg bw/day.

In a 28-day dermal toxicity study in rats, no treatment-related effects were observed at the maximum tested dose of 1000 mg/kg bw/day.

Chronic toxicity and carcinogenicity

In chronic toxicity studies in mice and rats, similar effects to those noted in shorter-term studies were observed. The NOAEL from an 18-month study in mice was 144 mg/kg bw/day, based on increased adrenal weight, and increased diffuse vacuolation of adrenocortical cells at the next highest dose. In rats, the NOAEL for systemic toxicity after 12 months was 18.8 mg/kg bw/day, based on a reduction in total cholesterol and triglyceride concentrations, increased liver weight in both sexes, and increased adrenal weight in females at the next highest dose. Histopathological changes in adrenocortical cells were also seen at this dose. After 24 months, the NOAEL for systemic toxicity in rats was 16.5 mg/kg bw/day.

In mice, there was no increase seen in tumour incidence at any dose. In rats, an increased incidence of Leydig cell adenoma was seen at 220 mg/kg bw/day, with the NOAEL for carcinogenicity established at 49.5 mg/kg bw/day.

Reproductive and developmental toxicity

In a 2-generation reproductive toxicity study in rats, the NOAEL for parental toxicity and offspring toxicity was 10.4 mg/kg bw/day, based on effects on the adrenal gland at the next highest dose. Delayed vaginal opening and increased follicle stimulating hormone and progesterone concentrations were also observed. There were no adverse effects on reproductive outcomes at 100.3 mg/kg bw/day, the highest dose tested.

In a development toxicity study in rats, an NOAEL of 50 mg/kg bw/day was established based on developmental effects including an increased incidence of incompletely ossified sternal centra observed at maternotoxic doses. In rabbits, delayed development was seen at maternotoxic doses, resulting in an NOAEL of 50 mg/kg bw/day.

Genotoxicity

Cyflumetofen was positive in a mouse lymphoma gene mutation assay at a concentration close to that where precipitation occurred. Cyflumetofen was not positive in an Ames test or in an in vitro chromosomal aberration assay. There was no evidence of genotoxicity in an in vivo micronucleus assay or in an in vivo unscheduled DNA synthesis assay in rat liver. Overall, it was concluded that cyflumetofen is unlikely to be genotoxic.

Neurotoxicity/immunotoxicity

No signs of treatment related neurotoxicity were seen in rats in an acute or a 13-week neurotoxicity study, with NOAELs of 2000 mg/kg bw/day or 293 mg/kg bw/day respectively.

No signs of immunotoxicity were observed in a 4-week immunotoxicity study in mice at doses up to 349 mg/kg bw/day.

Mode of action (toxicology)

A number of mechanistic studies were conducted to investigate the possible mode of action for the Leydig cell adenomas. Cyflumetofen was not a significant aromatase inhibitor in a human recombinant cell system. It did not significantly interact with androgen or estrogen receptor binding using rat prostate or uterine cytosol protein preparations. It was not an agonist in a human estrogen receptor transcriptional activation system. In a steroidogenesis assay, cyflumetofen induced estrogen production at and above 5 µmol/L (maximally 1.64-fold) and inhibited testosterone production at and above 1 µmol/L (maximally 0.63-fold) in human adenocarcinoma cells.

In view of the lack of genotoxicity, the absence of carcinogenicity in mice, and the fact that only Leydig cell adenomas were observed in a particularly sensitive strain of rat at the highest dose tested, cyflumetofen is unlikely to pose a carcinogenic risk to humans.

Toxicity of metabolites and/or impurities

Acute toxicity and genotoxicity studies were conducted with the impurity AB-13 present in the TGAC at up to 20 g/L. AB-13 was of low acute oral toxicity and was negative in a battery of in vitro and in vivo genotoxicity studies.

Acute toxicity and genotoxicity studies were performed for B-1, a goat and plant metabolite and food processing hydrolysis product. B-1 is also a major metabolite in the rat (occurring at up to 28% of the applied dose). B-1 was of low acute oral toxicity (LD50 >2000 mg/kg bw/d).

The potential genotoxicity of B-1 was tested in an adequate range of in vitro and in vivo assays. A mouse lymphoma gene mutation assay was positive at 1000 µg/mL without liver enzyme activation, and in one of 2 experiments at 333 µg/mL with enzyme activation. B-1 was not mutagenic in an Ames test and was not genotoxic in an in vitro chromosomal aberration assay. There was no evidence of genotoxicity in an in vivo unscheduled DNA synthesis assay in rat liver. Overall, it is concluded that metabolite B-1 is unlikely to be genotoxic in vivo.

Health-based guidance values and poisons scheduling

Poisons Standard

Cyflumetofen is listed in Schedule 5 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), effective 1 October 2021.

Health-based guidance values

Acceptable daily intake

The acceptable daily intake (ADI) for cyflumetofen is proposed to be established at 0.2 mg/kg bw/d. The NOAEL of 16.5 mg/kg bw/d was determined in 2 co-critical studies: the 90-day and 2-year studies in rats, based on adverse effects on the adrenal gland including increased organ weight and vacuolation of adrenal cortical cells.

Acute reference dose

No acute reference dose (ARfD) is proposed for cyflumetofen. An ARfD is considered unnecessary due to its low oral toxicity and the absence of any neurological effects or developmental toxicity after a single dose.

Recommendations

There are no objections on human health grounds to the approval of cyflumetofen.

There are no objections on human health grounds to the registration of the product Danisaraba Miticide, containing 200 g/L of cyflumetofen when used in accordance with the directions for use (DFU) and adhering to the recommended safety directions.

Residues assessment

Metabolism, analytical methodology, residual trial data, fate in storage, and trade aspects have been considered for cyflumetofen.

Metabolism

The metabolism of cyflumetofen was investigated in plants (apple, eggplant, and Satsuma mandarin), and in livestock (lactating goat). A confined rotational crop study also investigated the metabolism of cyflumetofen in rotational crops (lettuce, white radish, and spring wheat).

Animal metabolism

2 lactating goat metabolism studies are available; however, a metabolism study conducted on laying hens was not submitted. Given that none of the primary crops (or their processed commodities) on the proposed label are fed to poultry, a laying hen metabolism study is not required at this time.

Lactating goat

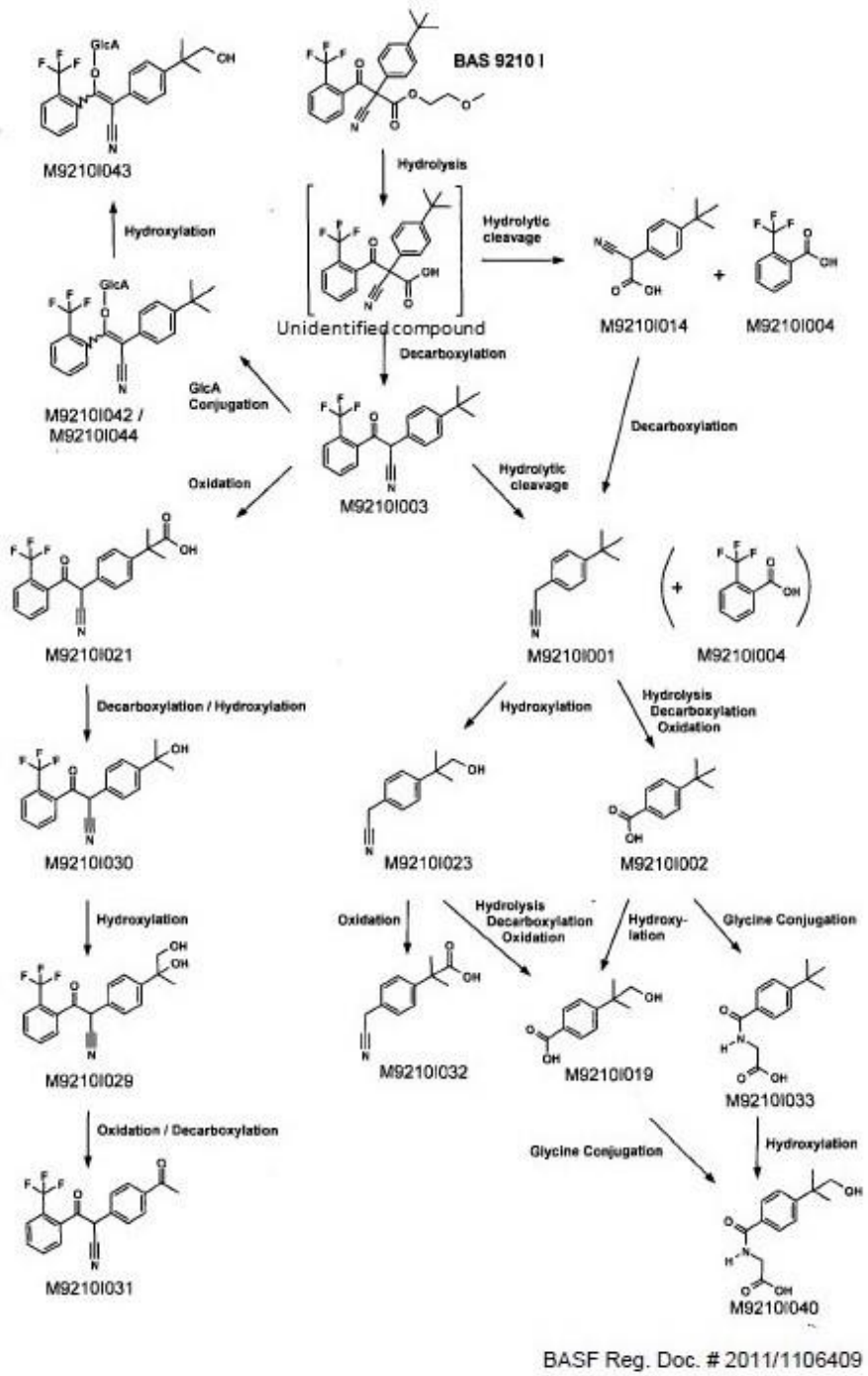
2 lactating goats were orally administered [benzoyl-ring-U-14C]-cyflumetofen (benzoyl-label) for 12 consecutive days at 0.27 or 0.30 mg/kg bw (15 or 12 ppm in feed). Another 2 goats were orally administered [t-butylphenyl-ring-U-14C]-cyflumetofen (butylphenyl-label) for 10 consecutive days at 0.43 or 0.48 mg/kg bw (13 or 12 ppm in feed). The goats were sacrificed 18 to 24 hours after the last dose. Daily samples of milk, urine, and faeces obtained for 12 and 10 consecutive days were measured for total radioactive residues for each animal.

The majority of radio-labelled cyflumetofen was excreted from lactating goats in faeces and urine (total >78% excreted during the testing periods) and only a small portion accounting for <0.3% of the administered radioactivity (AR) remained in body tissues/organs. Radioactive residues were the highest in liver (0.29 to 0.40 mg eq./kg) followed by kidney (0.17 to 0.19 mg eq./kg) but low in fat (0.028 to 0.033 mg eq./kg) and muscle tissue (0.009 to 0.020 mg eq./kg). Milk of each day contained <0.02% AR, and milk collected throughout the study period contained in total 0.008 to 0.19 mg eq./kg (0.03 to 0.14% AR).

The parent compound, cyflumetofen, was found only in fat, but at low concentration of 0.003 mg/kg accounting for 20% to 21% of the total radioactive residues (TRR). The predominant metabolite in all tissues/organs and milk was 2-trifluoromethylbenzoic acid (known as metabolite B-1) at around 0.1 mg eq./kg in liver (32% TRR) and kidney (54% TRR), and lower than 0.01 mg eq./kg in muscle tissue (46% to 51% TRR), fat (21% to 40% TRR) and milk (4.5% TRR).

The metabolism of cyflumetofen in goat involves extensive hydrolysis of formic acid esters and trifluoromethylbenzoyl moiety, decarboxylation, conjugation, hydroxylation, and oxidation.

Figure 1: Proposed metabolic pathway of cyflumetofen in lactating goats



Plant metabolism

Apples

Apples were sprayed with benzoyl- or butylphenyl-label cyflumetofen at a rate approximating 600 g ai/ha. Apple fruit samples were collected one, 7, and 30 days after treatment. The majority of the radioactivity was recovered from the acetonitrile surface rinse of fruits: 95% to 96% TRR on 1 DAT; 82% to 89% TRR on 7 DAT; and 67% to 71% TRR on 30 DAT.

The predominant radioactive residue on/in apple fruits was cyflumetofen at 0.061 to 0.066 mg/kg (58% to 61% TRR) in rinse while pulp extract contained too little radioactivity for further analysis on 1 DAT; 0.061 to 0.14 mg/kg (78% to 84% TRR) on 7 DAT; and decreased to 0.037 to 0.042 mg/kg (53% to 65% TRR) on 30 DAT.

Egg plants

Field-grown eggplants were sprayed with benzoyl- or butylphenyl-label cyflumetofen at a rate approximating 600 g ai/ha. Eggplant samples were collected one, 7, and 14 days after treatment. The majority of the radioactivity was also recovered from the acetonitrile surface rinse of fruits: 87% to 92% TRR on 1 DAT; 79% to 86% TRR on 7 DAT; and 56% to 81% TRR on 14 DAT.

The predominant radioactive residue on/in eggplant fruits was cyflumetofen accounting for 0.31 to 0.44 mg/kg (91% to 95% TRR) on 1 DAT; decreased to 0.25 to 0.39 mg/kg (67% to 71% TRR) on 7 DAT; and then to 0.18to 0.20 mg/kg (42% to 62% TRR) on 14 DAT.

Metabolites B-1, AB-6 and AB-7 were identified from the fruit rinse and/or extracts. B-1 was found at 0.059 mg eq /kg (11% TRR) on 7 DAT and at 0 061 mg eq./kg (15% TRR) on 14 DAT on/in fruits. AB-6 and AB-7 did not exceed 10% TRR.

The tentatively identified U1/U2 (likely to be acid labile conjugates of B-1) and U4 were also found in 7 DAT and 14 DAT fruits but not in 1 DAT fruits. U1 was present at 0.067 mg eq./kg (16% TRR) on 14 DAT but <10% TRR on 1 DAT and 7 DAT. U1 and U2 were found only in the fruit extracts but not in rinse, indicating that they were formed in the fruits.

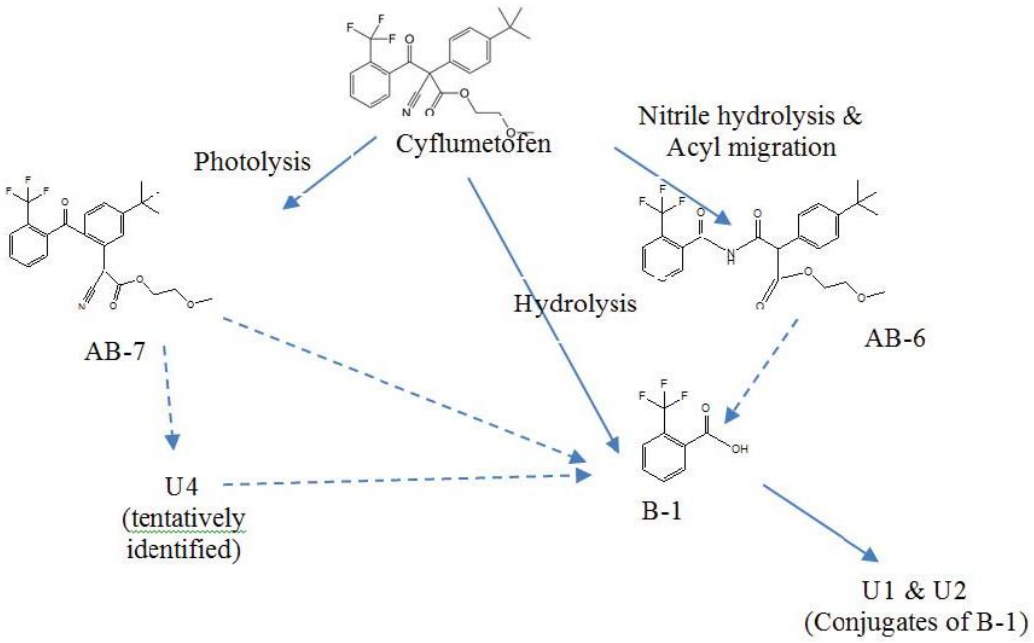
Satsuma mandarin

Field Satsuma mandarin trees were sprayed with benzoyl- or butylphenyl-label cyflumetofen at a rate approximating 600 g ai/ha. Satsuma mandarin fruit samples were collected one, 7, and 30 days after treatment. The majority of the radioactivity was recovered from the acetonitrile surface rinse of fruits: 95% to 96% TRR on 1DAT; 91% to 93% TRR on 7DAT; and 88% to 89% on 30 DAT.

The predominant radioactive residue on/in mandarin fruits was cyflumetofen at 0.52 to 0.55 mg/kg (88% to 90% TRR) on 1DAT, decreasing to 0.33 to 0.37 mg/kg (79% to 83% TRR) on 7 DAT and further to 0.25 to 0.31 mg/kg (44% to 54% TRR) on 30 DAT.

Other than the parent, metabolites AB-6, AB-7, A-12 and B-1 were formed. B-1 increased over time from 0.028 mg eq./kg (4.7% TRR) on 1 DAT to 0.064 mg eq./kg (11% TRR) on 30 DAT. None of AB-6, AB-7, and A-12 exceeded 10% TRR.

Figure 2: Proposed metabolic pathway of cyflumetofen in plants



Analytical methods and storage stability

A number of acceptable analytical methods using LC-MS/MS or HPLC-MS/MS for residue analysis of cyflumetofen and B1 in plant and animal matrices were used.

Plant commodities

A range of validated LC/MS/MS or HPLC-MS/MS methods were presented for the determination of cyflumetofen and its B-1 metabolite in various plant commodities.

In general, the method for data generation and enforcement for plant matrices employ extraction by shaking with acetonitrile, and then a mixture of acetonitrile and water, or only with acetonitrile then water, or acetonitrile and acetic acid. Clean-up is performed by partitioning with a mixture of ethyl acetate and cyclohexane or magnesium sulphate and sodium acetate. The determination of the analytes was conducted using LC-MS/MS.

The LOQ was determined at 0.01 mg/kg for each analyte; LOQ for cyflumetofen equivalent B1= 0.02 mg/kg (0.024 mg/kg).

The LOD was determined at 0.002 to 0.005 mg/kg for each analyte; LOD for cyflumetofen equivalent B1= 0.005 to 0.01 mg/kg.

Animal commodities

The validated analytical method developed for cyflumetofen and B-1 in animal matrices was similar to plant matrices but employed a different clean-up procedure.

The limit of quantitation (LOQ) for residues of cyflumetofen and its metabolite B-1 in bovine tissues (meat and liver) was 0.01 mg/kg, and for bovine milk was 0.001 mg/kg for each analyte. The LOQ for cyflumetofen equivalent B1 was 0.02 and 0.002 mg/kg for bovine tissues and milk respectively.

The limit of detection (LOD) was 0.002 mg/kg for each analyte in bovine tissues and 0.0002 mg/kg in bovine milk. The LOD for cyflumetofen equivalent B1 was 0.005 and 0.0005 mg/kg for bovine tissues and milk respectively.

Stability of residues in stored analytical samples

The stability of cyflumetofen and B-1 in homogenates of almond, apple (fruit, juice) kidney bean, lettuce, orange (fruit, juice, oil), radish, and wheat grain at –20 to –10°C was tested at a spike level (each analyte separately spiked) of 0.1 mg/kg for 743 to 910 days (24 to 30 months).

Cyflumetofen was stable (>70% recovery) when stored frozen for 24 to 25 months at –20°C to –10°C in almond, apple fruit, apple juice, orange fruit, orange juice, orange oil, and wheat grain. However, it was only stable for up to 9 months in kidney bean and lettuce, and 3 months in radish root.

The metabolite, B-1 was stable when stored frozen for 30 months in almond, kidney bean, lettuce, orange fruit, orange juice, and wheat grain. It was stable up to 22 months in apple fruit, apple juice, and radish root, and 6 months in orange oil.

In the residue trials submitted, all samples were maintained under freezer conditions, (i.e.–18 °C) prior to analysis and tested within 21 months of collection. This is acceptable for the purposes of the current application.

Residue definition

Animal commodities

The 2014 JMPR recommended the following residue definition for animal commodities (for compliance with the MRL and estimation of dietary intake): Sum of cyflumetofen and 2-trifluoromethylbenzoic acid, expressed as cyflumetofen.

Based on the available information which demonstrate that B-1 is the predominate component in all edible tissues (21% to 54% TRR) and milk (4.5% TRR), while the parent is a significant residue in fat (20%TRR); it is recommended to establish a residue definition for cyflumetofen in animal commodities according to the residue definition recommended by the 2014 JMPR.

Plant commodities

The 2014 JMPR recommended the following residue definition for plant commodities:

Definition of the residue for plant commodities (for compliance with the MRL): Cyflumetofen.

Definition of the residue for plant commodities (for estimation of dietary intake): Sum of cyflumetofen and 2-trifluoromethylbenzoic acid, expressed as cyflumetofen.

Cyflumetofen was the predominant residue in Satsuma mandarin, apple and eggplant and accounted for >42% TRR in the fruits of these crops at any time point. Metabolite B-1 was found in the fruit extract of apple (30 DAT) and eggplant (14 DAT) at 1.8% and 14.8% of TRR corresponding to 0.001 and 0.061 mg eq/kg respectively. No other individual components accounted for >10% TRR. In the supervised residue trials, the concentrations of B-1 were mostly 1/10 to 1/2 of those of cyflumetofen. Based on the available information, it is recommended to establish residue definition for cyflumetofen according to the residue definition recommended by the 2014 JMPR.

Residues in food and animal feeds

Almonds

The proposed use of cyflumetofen in almonds involves a maximum of 2 foliar sprays at 20 g ai/100 L with a re-treatment interval of 14 days in conjunction with a harvest withholding period (WHP) of 7 days.

Almond kernels

In the 2 Australian trials, parent cyflumetofen residues in almond kernels following 2 applications at 1× the proposed concentration and 7 days PHI, were below the LOQ of 0.01 mg/kg [0.0027 and 0.009 mg/kg].

In the US trials, no quantifiable parent cyflumetofen residues were observed in almond or pecan kernels following 2 applications at ~0.5 to ~2× the proposed concentration at a pre-harvest interval (PHI) of 7 days (n=10; LOQ = 0.01 mg/kg).

Based on the available information, for the estimation an MRL for enforcement, a cyflumetofen MRL of 0.01 mg/kg for [TN 0660] Almonds is recommended to cover cyflumetofen residues arising in almond kernels as a result of the proposed use in conjunction with a harvest withholding period of 7 days.

For dietary risk assessment, total cyflumetofen (parent + B1) residues observed in almond and pecan kernels were: <0.03 (n=12); the STMR is 0.03 mg/kg (LOQ of 0.01 mg/kg for each analyte; LOQ for B1 equivalent to the parent = 0.02 mg/kg).

Almond hulls

The combined dataset of 2 Australian and 5 US trials suitable for MRL estimation is, in rank order: 0.40, 0.50, 0.61, 0.67, 0.99, 2.28 and 4.41 mg/kg (n=7). The OECD MRL calculator estimates a MRL of 8 mg/kg noting high uncertainty due to small dataset (STMR = 0.67 mg/kg).

Based on the available information, a MRL of 8 mg/kg for Almond hulls is recommended to cover cyflumetofen residues arising in almond hulls as a result of proposed use in conjunction with a harvest withholding period of 7 days.

Total cyflumetofen residues in almond hulls, in rank order, were: 0.44, 0.71, 0.8, 1.11, 2.0, 2.6 and 5.7 mg/kg (n=7). The median total cyflumetofen residue in almond hulls for estimation of livestock dietary exposure is 1.11 mg/kg.

Citrus

The proposed use of cyflumetofen in citrus involves a maximum of 2 foliar sprays at 20 g ai/100 L with a re-treatment interval of 14 days in conjunction with a harvest-withholding period of 7 days.

In the Australian citrus trials, following 2 applications at 1× the proposed concentration at a RTI of 14 days and a PHI of 6 to 7 days, parent cyflumetofen residues in whole citrus fruit (n=3), were mandarin: 0.06 mg/kg, lemon: 0.11 mg/kg and orange: 0.14 mg/kg.

In the US citrus trials, following 2 applications of cyflumetofen at 7.12 g ai/100 L to 69.2 g ai/100 L (0.36x to 3.46x) the proposed concentration at a RTI of 12 to 14 days and PHI of 7 days (or later if higher residues were observed) parent cyflumetofen residues in whole citrus fruit, in rank order, were:

Orange: 0.01, 0.02, 0.04, 0.07, 0.08 (2), 0.09, 0.10 (2), 0.11 (2), 0.16 mg/kg (n=12).

Grapefruit: <0.01, 0.03, 0.04 (2), 0.06 and 0.08 mg/kg (n=6).

Lemon: <0.01, 0.02 (2), 0.09 and 0.14 mg/kg (n=5).

The combined dataset suitable for MRL estimation, in rank order, is: <0.01 (2), 0.01, 0.02 (3), 0.03, 0.04 (3), 0.06 (2), 0.07, 0.08 (3), 0.09 (2), 0.10 (2), 0.11 (3), 0.14 (2) and 0.16 mg/kg (n=26). The OECD MRL calculator estimates a MRL of 0.3 mg/kg. STMR = 0.08 mg/kg.

Based on the available information, For the MRL enforcement, a cyflumetofen MRL of 0.3 mg/kg is recommended for [FC 0001] Citrus fruits to cover cyflumetofen residues arising in citrus fruit as a result of the proposed use in conjunction with a harvest withholding period of 7 days and a spray volume restraint of ‘DO NOT apply a water volume greater than 4000 L/ha’.

For the dietary risk assessment, the combined dataset for total cyflumetofen residues, in whole citrus fruit, in rank order, is: <0.03 (2), 0.03, 0.04 (3), 0.05, 0.06 (4), 0.08, 0.09 (2), 0.10 (3), 0.11, 0.12 (3), 0.13 (2), 0.15, 0.16 and 0.18 mg/kg (n=26). STMR = 0.09 mg/kg.

Citrus processed commodities

In the US citrus processing study, residues of parent cyflumetofen did not concentrate in wet pomace, juice, meal, molasses, or marmalade.

The estimated parent cyflumetofen residues in citrus pulp, dry = 0.17 mg/kg (HR 0.16 mg/kg× Pf 1.05).

Based on the available information, a cyflumetofen MRL of 0.3 mg/kg for [AB 0001] Citrus pulp, dry is recommended for the proposed use in citrus, in conjunction with a harvest withholding period of 7 days.

The median processing factor for total cyflumetofen residue in citrus pulp dry is 0.94x on a dry weight basis. Applying to the total cyflumetofen residue STMR of 0.09 mg/kg, gives an STMR-P for estimation of livestock dietary exposure of 0.08 mg/kg.

Grapes

The proposed use of cyflumetofen in grapes (wine and table) involves a maximum of 2 foliar sprays at 20 g ai/100 L, with a re-treatment interval of 14 days, in conjunction with a harvest withholding period of 14 days.

In the Australian trials, parent cyflumetofen residues in grapes following 2 treatments at 0.9× the proposed concentration, at 13 to 15 days PHI were: 0.03 (2), 0.05, 0.32 and 0.37 mg/kg (n=5).

In the US trials, parent cyflumetofen residues in grapes following 2 treatments at 0.38× to 2.2× the proposed concentration (targeted at 0.2 kg ai/ha), at 14 days PHI were: 0.03, 0.10, 0.12, 0.13 (2), 0.15, 0.18, 0.20, 0.23, 0.27, 0.29 and 0.44 mg/kg (n=12).

The combined dataset suitable for MRL estimation, in rank order, is: 0.03 (3), 0.05, 0.10, 0.12, 0.13 (2), 0.15, 0.18, 0.20, 0.23, 0.27, 0.29, 0.32, 0.37 and 0.44 mg/kg (n=17). The OECD MRL calculator estimates a MRL of 0.7 mg/kg. STMR was 0.15 mg/kg.

Based on available information, a cyflumetofen MRL of 0.7 mg/kg for [FB 0269] Grape is recommended to cover cyflumetofen residues arising in grapes as a result of the proposed use, in conjunction with a harvest withholding period of 14 days.

For dietary risk assessment (parent + B1), the combined dataset for total cyflumetofen in grapes, in rank order, is: 0.05 (2), 0.06 (2), 0.13, 0.15, 0.17, 0.20, 0.21, 0.23, 0.24, 0.25, 0.30, 0.33, 0.35, 0.38 and 0.48 mg/kg (n=17). STMR = 0.21 mg/kg.

Grapes processed commodities

In the Australian and US grape processing studies, parent cyflumetofen residues did not concentrate in wine or juice samples (n=6). The median processing factor was 0.04x for wine and 0.23x for juice. Residues in wine and juice will be covered by the recommended MRL for grapes at 0.7 mg/kg.

The highest estimated parent cyflumetofen residues in dried grapes are calculated at 2.04 mg/kg (parent cyflumetofen HR of 0.44 mg/kg× highest Pf 4.64x).

Based on the available information, a cyflumetofen MRL of 3 mg/kg for [DF 0269] Dried grapes (= currants, raisins and sultanas) is recommended to cover cyflumetofen residues arising in dried grapes as a result of the proposed use.

The highest parent cyflumetofen residues in grape pomace, dry are estimated at 13.78 mg/kg [HR of parent cyflumetofen residues in grapes 0.49 mg/kg x HR Pf 28.13x].

Based on the available information, for the MRL enforcement, a cyflumetofen MRL of 15 mg/kg for [AB 0269] Grape, pomace, dry is recommended to cover cyflumetofen residues arising in grape pomace as a result of the proposed use in grapes, in conjunction with a harvest withholding period of 14 days.

The median processing factor for total residue in dry grape pomace is 14.1x. Applying to the total residue STMR of 0.21 mg/kg in grapes gives an STMR-P for estimation of livestock dietary exposure of 2.96 mg/kg on a dry weight basis.

Fruiting vegetables

The proposed use of cyflumetofen in fruiting vegetables (including protected tomatoes) involves a maximum of 2 foliar sprays at 200 g ai/ha, at a re-treatment interval of 14 days, in conjunction with a harvest withholding period of one day.

In the EU tomato field trials, parent cyflumetofen residues following 2 applications at 1× the proposed rate at 9 to 11 days re-treatment interval, and one day PHI (or later if higher residues were observed), were 0.05 (2) and 0.06 (2) mg/kg (n=4). Parent cyflumetofen residues in tomatoes grown in greenhouses were 0.05, 0.13 and 0.16 (2) mg/kg (n=4).

The US tomato field trials, parent cyflumetofen residues following 2 applications at 1× the proposed rate at 14 days RTI and one day PHI (or later if higher residues were observed) were 0.03 and 0.11 mg/kg (n=2).

In the Australian tomato field trials, parent cyflumetofen residues following 2 applications at 1× the proposed rate or at 20 g ai/100 L at 14 days re-treatment interval and one day PHI were 0.01 and 0.10 mg/kg (n=2). At 4 days PHI, at the trial site in Western Australia, parent cyflumetofen were 0.50 mg/kg.

In the Australian capsicum and chili field trials, parent cyflumetofen residues following 2 applications at 1× the proposed rate at 14 days re-treatment interval and one day PHI (or later if higher residues were observed), in rank order, were 0.01 (2), 0.05, 0.06, 0.41 and 0.43 mg/kg (n=6).

In the Japanese capsicum field trials, parent cyflumetofen residues following 2 applications at 2× the proposed rate at 7 days re-treatment interval and one day PHI, in rank order, were: 0.48 and 2.71 mg/kg. After scaling back to the proposed rate, parent cyflumetofen residues were: 0.24 and 1.36 mg/kg (n=2).

In the Japanese eggplant field trials, parent cyflumetofen residues following 2 applications at 2x the proposed rate at 7 days re-treatment interval and one day PHI, in rank order, were: 0.35 and 0.46 mg/kg. After scaling back to the proposed rate, parent cyflumetofen residues were: 0.18 and 0.23 mg/kg (n=2).

The combined dataset for MRL estimation, in rank order, is: 0.01 (3), 0.03, 0.05 (4), 0.06 (3), 0.10, 0.11, 0.13, 0.16 (2), 0.18, 0.23, 0.24, 0.41, 0.43, 0.50 and 1.36 mg/kg (n=23). The OECD MRL calculator estimates a MRL of 1.5 mg/kg. STMR= 0.10 mg/kg.

Based on the available information, a cyflumetofen MRL of 2 mg/kg for [VO 0050] Fruiting vegetables, other than cucurbits is recommended to cover cyflumetofen arising in fruiting vegetables as a result of the proposed use, in conjunction with a harvest withholding period of one day.

No significant difference in cyflumetofen residues was observed in the tomatoes in protected and field grown situations. The proposed use in protected grown tomatoes is supported from a residues perspective, and the recommended MRL will cover the proposed use in tomatoes grown in protected situations.

For dietary risk assessment, the combined dataset of total cyflumetofen residues, in rank order, is: 0.01, 0.02, 0.03, 0.07 (4), 0.08 (3), 0.10, 0.11, 0.15 (2), 0.18 (2), 0.25, 0.30, 0.44, 0.50, 0.52, 0.74 and 1.52 mg/kg (n=23). STMR = 0.11 mg/kg.

Tomato processed commodities

In the US tomato processing study, residues of parent cyflumetofen did not concentrate in canned or peeled tomatoes, juice, paste or puree.

The estimated highest parent cyflumetofen residues in tomato pomace (dry wt) are calculated at 13.75 mg/kg (HR parent cyflumetofen residues in tomatoes 0.50× 27.5× which was the highest Pf).

Based on the available information, a cyflumetofen MRL of 15 mg/kg for Tomato pomace, dry is recommended to cover cyflumetofen residues arising in tomato pomace as a result of proposed use, in conjunction with a harvest-withholding period of one day.

Applying the median PF for total residue in tomato pomace of 16× to the tomato total residue STMR of 0.10 mg/kg gives an STMR-P of 1.6 mg/kg dry weight for estimation of livestock dietary exposure.

Pome fruit

The proposed use of cyflumetofen in pome fruit involves a maximum of 2 foliar sprays at 20 g ai/100 L with a re-treatment interval of 14 days, in conjunction with a harvest withholding period of 7 days.

In the Australian apple trials, following 2 applications at 1× the proposed concentration, 13 to 14 days RTI and 7 days PHI, parent cyflumetofen residues in apples, in rank order, were: 0.08, 0.11 and 0.25 mg/kg (n=3).

In the 17 US pome fruit trials, there was no difference in residues observed in dilute or concentrated treatments. Following 2 applications of cyflumetofen at 10.34 g ai/100 L to 35.54 g ai/100 L (~0.52× to ~1.8×, targeted at 0.2 kg ai/ha) the proposed concentration at a RTI of 13 to 15 days and 6 to 8 days PHI, parent cyflumetofen residues were, in rank order:

Apples: 0.02, 0.05, 0.06, 0.07, 0.08, 0.10, 0.13, 0.17, 0.21 (2), 0.24, 0.25 mg/kg (n=12).

Pears: 0.07, 0.09, 0.13 (2) and 0.27 mg/kg (n=5).

The combined dataset suitable for MRL estimation, in rank order, is: 0.02, 0.05, 0.06, 0.07 (2), 0.08 (2), 0.09, 0.10, 0.11, 0.13 (3), 0.17, 0.21 (2), 0.24, 0.25 (2) and 0.27 mg/kg (n=20). The OECD MRL calculator estimates a MRL of 0.5 mg/kg. STMR= 0.13 mg/kg.

Based on the available information, a cyflumetofen MRL of 0.5 mg/kg for [FP 0009] Pome fruits is recommended to cover cyflumetofen residues arising in pome fruit as a result of the proposed use, in

conjunction with a harvest withholding period of 7 days and a spray volume restraint of 'DO NOT apply a water volume greater than 3000 L/ha per application'.

For dietary risk assessment, the combined dataset of total cyflumetofen residues, in rank order, is: 0.04, 0.07, 0.08, 0.09 (3), 0.10, 0.11 (2), 0.12, 0.15 (3), 0.19, 0.23 (2), 0.26 (2), 0.27 and 0.29 mg/kg (n=20). STMR = 0.14 mg/kg.

Apple processed commodities

In the German apple processing trials (n=2), parent cyflumetofen and B1 residues (expressed in parent equivalents) did not concentrate in apple sauce, canned apples, fruit syrup or juice. However, parent cyflumetofen residues concentrated in dried apples (Pf 3.33× and 7.21×).

In the US apple processing trials (n=2), parent cyflumetofen or B1 residues did not concentrate in apple juice, dried apples and canned apples. Parent cyflumetofen residues concentrated in applesauce (2.54× and 2.91×).

The estimated parent cyflumetofen residues in apple pomace, dry are calculated as 5.29 mg/kg (highest Pf 21.16× 0.25 mg/kg HR parent cyflumetofen in apples).

Based on the available information, a cyflumetofen MRL of 10 mg/kg for apple pomace, dry is recommended to cover cyflumetofen residues arising in apple pomace, dry as a result of proposed use in conjunction with a harvest-withholding period of 7 days.

Applying the median processing factor of 8.7× for total residue in apple pomace to the apple STMR of 0.14 mg/kg gives an STMR-P for estimation of livestock dietary exposure of 1.22 mg/kg.

Strawberries

The proposed use of cyflumetofen in strawberries (field and protected) involves a maximum of 2 foliar sprays at 200 g ai/ha at a re-treatment interval of 14 days, in conjunction with a harvest withholding period of one day.

In the AU field trials, parent cyflumetofen residues in strawberries following 2 applications at 1x the proposed rate at 14 days re-treatment interval and one day PHI, were: 0.15 and 0.34 mg/kg (n=2).

In the EU greenhouse trials, parent cyflumetofen residues in strawberries following 2 applications at 1x the proposed rate at 10 to 12 days re-treatment interval and one day PHI (or later if higher residues were observed), were: 0.07, 0.08, 0.11, 0.12 (3), 0.13 (2), 0.20 and 0.45 mg/kg (n=10).

In the Japanese greenhouse trials, parent cyflumetofen residues in strawberries following 2 applications at 2x the proposed rate at 7 days re-treatment interval and one day PHI, were: 0.92 and 1.00 mg/kg. After scaling back to the proposed rate, parent cyflumetofen residues in strawberries were: 0.46 and 0.50 mg/kg (n=2).

In the US field trials, parent cyflumetofen residues in strawberries following 2 applications at 1x the proposed rate at 7 to 15 days re-treatment interval and one day PHI (or later if higher residues were observed), were: 0.04, 0.11, 0.16 (2), 0.18, 0.23, 0.25 and 0.44 mg/kg (n=8).

The combined dataset suitable for MRL estimation, in rank order, is: 0.04, 0.07, 0.08, 0.11 (2), 0.12 (3), 0.13 (2), 0.15, 0.16 (2), 0.18, 0.20, 0.23, 0.25, 0.34, 0.44, 0.45, 0.46 and 0.50 mg/kg (n=22). The OECD MRL calculator estimates a MRL of 0.8 mg/kg (STMR = 0.16 mg/kg).

Based on the available information, a cyflumetofen MRL of 0.8 mg/kg for [FB 0275] Strawberry is recommended to cover parent cyflumetofen residues arising in strawberries grown in field or greenhouses as a result of the proposed use, in conjunction with a harvest withholding period of one day. Use on protected grown strawberries is supported from a residues perspective.

For dietary exposure assessment, the combined dataset for total cyflumetofen (parent+ B1) in strawberries, in rank order is, 0.06, 0.09, 0.10, 0.14, 0.15 (3), 0.17, 0.18 (2), 0.19 (2), 0.21 (2), 0.22, 0.26, 0.35, 0.37, 0.47, 0.48, 0.52 and 0.59 mg/kg (n=22). STMR = 0.19 mg/kg.

Crop rotation

Of the use patterns currently proposed, fruiting vegetables and strawberries are considered to be rotational crops. The proposed use on fruiting vegetables and strawberries involves 2 applications at 200 g ai/ha for a maximum seasonal rate of 400 g ai/ha.

A field rotational crop study was conducted in the US to determine the magnitude of cyflumetofen residues in/on lettuce, radishes or wheat planted 30, 60 or 90 days after a soil application of Cyflumetofen 20 SC.

The supported residue definition for compliance with the MRL is parent cyflumetofen. No parent compound (LOD of 0.002 ppm) was detected from any of the crop extracts at any plant back interval following treatment at 400 g ai/ha (1× the maximum proposed seasonal rate for rotational crops). It is concluded that residues in rotational crops above the LOQ for parent cyflumetofen should not occur as a result of the proposed use, and that MRL coverage for rotational crops and animal feeds or re-cropping intervals are not required from a residues or trade perspective.

Residues in animal commodities

According to the OECD animal feed calculator, in Australia:

- almond hulls may be fed at 10% of the diet of beef and dairy cattle
- apple pomace may comprise 20% of the diet of beef and 10% of the diet of dairy cattle
- citrus pulp may compromise 30% of the diet for beef and dairy cattle
- grape pomace maybe fed to beef and dairy cattle at 20% of their diet
- tomato pomace maybe fed to beef and dairy cattle at 10% of their diet.

According to the OECD feed calculator, the estimated dietary burden as a result of the proposed uses in almond, apples, citrus, grapes, and tomatoes is calculated at 0.71 ppm. The OECD animal feed calculator estimates a total of 40% of the cattle (beef and dairy) diet consisting of processed commodities: grape pomace, almond hulls, and citrus pulp.

A lactating cow transfer study has not been submitted; however, a lactating goat metabolism study is available. The observed total cyflumetofen (parent + B1) residues in goat milk and tissues following feeding at 13.5 ppm in the feed and the estimated residues associated with the proposed use are presented in Table 5.

Table 5: Required mammalian commodity MRLs - Cattle

Feeding level (ppm)	Milk	Muscle	Liver	Kidney	Fat
	Total cyflumetofen residue (mg/kg)				
13.5	0.001	0.005	0.125	0.102	0.009
0.71 – estimated burden	<0.003	<0.03	<0.03 (0.006)	<0.03	<0.03
Recommended MRLs	*0.003	*0.03		*0.03 (offal)	*0.03

The following MRLs are appropriate for cyflumetofen based on the animal commodity MRL definition of parent+ B1:

MO 0105 Edible offal (mammalian): *0.03 mg/kg

MM 0095 Meat (mammalian): *0.03 mg/kg

ML 0106 Milks: *0.003 mg/kg

None of the primary crops (or their processed commodities) on the label are poultry feed. A poultry feeding study was not submitted. Therefore, the dietary burden for poultry cannot be assessed.

Spray drift

The APVMA Spray Drift Risk Assessment was based on a Regulatory Acceptable Level (RAL) of 3.24 mg/kg. See the *Spray drift* and *Label recommendations* sections for details of the relevant restraints and buffer zones.

Dietary risk assessment

The chronic dietary exposure to cyflumetofen 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 cyflumetofen is <5% of the ADI. It is concluded that the chronic dietary exposure to cyflumetofen is acceptable.

An ARfD has been considered unnecessary for cyflumetofen by the APVMA. Therefore, consideration to acute dietary exposure is not required.

Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 6).

Table 6: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
Add:			
Cyflumetofen			
TN	0660	Almonds	0.01
FC	0001	Citrus	0.3
DF	0269	Dried grapes (= currants, raisins and sultanas)	3
MO	0105	Edible offal (mammalian)	*0.03
VO	0050	Fruiting vegetables, other than cucurbits	2
FB	0269	Grapes	0.7
MM	0095	Meat (mammalian)	*0.03
ML	0106	Milks	*0.003
PF	0009	Pome fruits	0.5
FB	0275	Strawberry	0.8

Amendments to Table 3	
Compound	**Residue**
Add:	
Cyflumetofen	For enforcement in plant commodities: cyflumetofen For assessment of dietary risk in plant commodities: sum of cyflumetofen and 2-trifluoromethylbenzoic acid, expressed as cyflumetofen For enforcement and assessment of dietary risk in animal commodities: sum of cyflumetofen and 2-trifluoromethylbenzoic acid, expressed as cyflumetofen

Amendments to Table 4			
Compound		**Animal feed commodity**	**MRL (mg/kg)**
Add:			
Cyflumetofen			
		Almond hulls	8
AB	0226	Apple pomace, dry	10
AB	0001	Citrus pulp, dry	0.3
AB	0269	Grape pomace, dry	15
		Tomato pomace, dry	15

Assessment of overseas trade aspects of residues in food

Commodities exported and main destinations

Citrus fruit, grapes (including dried grapes), wine, and pome fruit are considered to be major export commodities[1], as are commodities of animal origin, such as meat, offal, and dairy products, which may be derived from livestock fed feeds produced from treated citrus, grapes, apple almond, and tomato. Residues in these commodities resulting from the use of Danisaraba Miticide may have the potential to unduly prejudice trade.

Overseas registrations and approved label instructions

The applicant indicated that cyflumetofen products are registered for use on a range of fruit and vegetable crops in the USA, Brazil, and Japan.

Comparison of Australian MRLs with Codex and international MRLs

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. Cyflumetofen has been considered by Codex. The following relevant international MRLs have been established for cyflumetofen (Table 7).

[1] Australian Pesticides and Veterinary Medicines Authority, *APVMA Regulatory Guidelines – Data Guidelines: Agricultural - Overseas trade (Part 5B)*, APVMA website, 20 July 2020.

Table 7: Proposed Australian and current international MRLs for cyflumetofen

Commodity	Tolerance for residues arising from the use of cyflumetofen (mg/kg)							
	Australia (proposed)	EU[2]	Japan[3]	Codex[4]	USA[5]	Korea[6]	Taiwan[7]	China[8]
Residue definition	Plant commodities MRL enforcement: cyflumetofen Animal commodities MRL enforcement & dietary exposure: Cyflumetofen + B1	Cyflumetofen	Agricultural products: cyflumetofen For animal products: sum of cyflumetofen and B1	Plant commodities MRL enforcement: cyflumetofen Animal commodities: MRL enforcement and dietary exposure Cyflumetofen + B1	Cyflumetofen	Cyflumetofen	Cyflumetofen	Cyflumetofen
Almonds	0.01	*0.01	0.01	*0.01 (Tree nuts)	0.01 (Tree nuts)	–	0.01	0.01 (nuts)
Citrus	0.3	0.5	Citrus 10 (exc. natsudaidai, 5)	0.3	0.30	0.3 (exc. mandarin, 0.5; Korean lemon, 1.0)	1	0.3 (exc. citrus)
Citrus oil, edible	–	–	–	36	16	–	–	–
Dried grapes	3	–	–	1.5	–	–	–	(Raisin, 1.5)

[2] European Union website.
[3] Japan Food Chemistry Research Foundation, *Residual pesticide standard value search system*.
[4] Food and Agriculture Organization of the United Nations, *Pesticides Database Search – 273 – Cyflumetofen*, FAO website.
[5] Code of Federal Regulations, *Cyflumetofen; tolerances for residues*, National Archives and Records Administration website.
[6] Food Safety Korea, *Integrated Search for Residues – Cyflumetofen*, Food Safety Korea website.
[7] Taiwan Food and Drug Administration, *Standards for Pesticide Residue Limits in Foods*, Taiwan FDA website.
[8] United States Department of Agriculture, *China Notifies Draft Maximum Residue Limits for Pesticides*, 20 March 2018.

Commodity	Tolerance for residues arising from the use of cyflumetofen (mg/kg)							
	Australia (proposed)	EU[2]	Japan[3]	Codex[4]	USA[5]	Korea[6]	Taiwan[7]	China[8]
Eggplant	2	0.4	2	–	–	1	1	–
Grapes	0.7	0.6	3	0.6	0.60	2	1	0.6
Pepper	2	–	–	–	–	2 (sweet pepper)	1 (hot pepper)	
Pome fruits	0.5	0.4	2 (apples and pears)	0.4	0.30	0.5 apple 1.0 pear	1 apple 2 pear	0.4
Strawberries	0.8	0.6	2	0.6	0.6	2	2	0.6
Tomato	2	0.4	0.4	0.3	0.7	–	0.2	0.3
Mammalian fats		*0.01	0.01	*0.01 (except milk fats)	–	–	–	–
Mammalian meat	*0.03	*0.01	0.01	*0.01	–	–	–	–
Mammalian offal	*0.03	0.02	0.02	0.02	–	–	–	–
Milks	*0.003	*0.01	0.01	*0.01		–	–	–

Potential risk to trade

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

The proposed cyflumetofen MRL of 0.3 mg/kg for citrus is equivalent to the citrus MRLs of 0.3 mg/kg currently established by the Codex, China, EU, Korea, and the USA. The EU has citrus MRL established at 0.5 mg/kg. In Japan, the citrus MRL is established at 10 mg/kg (except natsudaidai at 5 mg/kg).

The proposed cyflumetofen MRL of 0.7 mg/kg for grapes is slightly higher than grape MRLs of 0.6 mg/kg established by Codex, EU, USA, and China. Grape MRLs are established in Japan at 3 mg/kg, Korea at 2 mg/kg, and Taiwan at 1 mg/kg. The proposed Australian dried grape MRL of 3 mg/kg is higher than the dried grapes MRLs of 1.5 mg/kg established by the Codex and China.

The proposed cyflumetofen MRL of 0.5 mg/kg for pome fruit is slightly higher than the pome fruit MRLs of 0.4 mg/kg currently established by Codex, EU, and China. The USA has a pome fruit MRL established at 0.3 mg/kg. In Japan, the pome fruit MRL is established at 2 mg/kg. It is noted that the highest residues in relevant trials was 0.25 mg/kg in apples and 0.27 mg/kg in pears which are lower than the lowest international MRL for pome fruit at 0.3 mg/kg.

The proposed animal commodity MRLs are recommended at the LOQ of *0.03 mg/kg for total cyflumetofen residues, according to the supported residues definition of parent cyflumetofen plus is B1 metabolite. As finite residues are not expected in animal commodities, the risk to trade associated with animal commodities derived from animals fed treated animal feeds is considered low.

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

Export of treated commodities:

Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for labelled crops treated with DANISARABA MITICIDE. Additionally, some export markets have established MRLs different to those in Australia. If you are growing crops for export, please check with BASF Australia Ltd for the latest information on MRLs and import tolerances BEFORE using this product.

Recommendations

Comment is sought on the potential for the proposed uses to prejudice Australian trade.

Work health and safety assessment

Health hazards

Danisaraba Miticide was of low, acute oral, dermal, and inhalation toxicity, and was not a skin or eye irritant. Due to the testing methodology used, potential for skin sensitisation could not be eliminated. A 28-day dermal study showed no adverse effects at the highest dose tested of 1,000 mg/kg bw/day. A dermal absorption of 11% was determined using a rat in vivo study supported by a human in vitro study.

Occupational exposure

Exposure during use

Exposure during use is likely to result from mixing and loading and applying the product. The Occupational Pesticide Handler Exposure Calculator was used to model expected risks resulting from use of the product at the proposed label rate using default work rate assumptions. Risks were acceptable for all mixing and loading activities with high margins of exposure (MoE). Combined mixing/loading/applicator margins of exposure were acceptable using airblast application with single layer clothing and no gloves. Combined mixing/loading/applicator risks for use by hand-held equipment (protected and outdoors) were also acceptable, however the use of gloves is recommended for these uses.

Exposure during re-entry or rehandling

Risks associated with re-entry to treated areas were calculated using the US EPA Occupation Pesticide Re-entry Calculator, along with consideration of a dislodgeable foliar residue study provided by the applicant. Risks associated with systemic exposure following treatment were acceptable on day 0; however, based on the acute hazard of the product formulation, a re-entry statement is recommended.

Public exposure

The product is intended for professional use and is not expected to be used or applied by members of the public. The RAL for bystanders spray drift risk assessment is 724 g /ha. No buffer zones are required for the protection of bystanders from spray drift associated with the application of the product. See the *Spray drift* and *Label recommendations* sections for the general spray drift restraints.

Recommendations

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

First aid instructions

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

Safety directions

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

Precautionary (warning) statements

WARNING – contains cyflumetofen, which may cause skin sensitisation. Sensitive individuals should avoid contact with this substance.

Restraints

For PROFESSIONAL use only

DO NOT apply by aircraft

Re-entry or re-handling statement

DO NOT enter treated areas until spray has dried. If prior entry is necessary, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

Environmental assessment

Fate and behaviour in the environment

Soil

Photolysis on soil is not expected to be a significant removal process for cyflumetofen in the environment as there was no difference in degradation rates between irradiated and dark soils (DT_{50} 1.2 days). Furthermore, irradiation of cyflumetofen-treated soil did not result in the formation of specific photodegradation products compared to non-irradiated soil.

Metabolism of cyflumetofen was assessed in 8 different soils (3 studies) in the laboratory. Degradation was considered through 2 different radiolabel positions which followed both single order, and biphasic degradation patterns. Modelling DT_{50} values ranged from 2.4 to 13 days (geomean DT_{50} 3.8 days).

Under aerobic conditions in soil, cyflumetofen degraded to CO_2 (1.7 to 39%) and metabolites B-1 (max 63%), B-3 (max 23%) and AB-1 (max 22%). Non-extractable residues were 19 to 40%. The primary mechanisms of degradation were by cleavage (hydrolysis) of the ester linkage followed by decarboxylation with formation of AB-1, hydrolysis of the keto-functional group with the formation of B-1, and cleavage of the keto-function through reaction with amine functionality to yield B-3 (possibly also intra-molecular reaction with CN group). All 3 reactions may occur simultaneously in soil.

Laboratory soil degradation tests were performed for the 3 major soil metabolites in 3 soils. Degradation of B-1 and B-3 followed single, first order kinetics, while AB-1 was best described by double first-order in parallel kinetics. Modelling DT_{50} results for B-1, B-3 and AB-1 (geomean of 3 values) were 16, 13 and 107 days, respectively. AB-1 was rapidly degraded over the first short period, but then degradation slowed considerably. The slow phase half-life relates to <20% of the initially applied substance.

Field testing was available for 4 sites in the USA, with 2 applications at each site. Degradation was similar to that observed in the laboratory and followed either first order or biphasic kinetics. A total of 7 half-lives could be calculated from these studies, with $DegT_{50}$ values of 0.35 to 8.0 days (geomean 1.7 days). These results were not considered reliable due to the potential instability of cyflumetofen observed under storage conditions of the samples prior to analysis.

Adsorption of cyflumetofen was determined by an HPLC method. Due to the instability of cyflumetofen in $CaCl_2$ solutions, it was not possible to determine a K_{OC} for cyflumetofen using the batch adsorption method. The K_{OC} for cyflumetofen was 131826 L/kg, indicating that cyflumetofen will be strongly adsorbed onto soil. 1/n is set at the default of 1.

Adsorption of metabolite B-1 was studied by the batch adsorption experiment, but because of the low adsorption of B-1, even at soil:solution ratios of 1:1, it was not possible to determine an accurate K_d from these experiments. Therefore, a column leaching experiment was performed with B-1, and the average K_{OC} was determined to be 3.7 L/kg. Based on 1% organic carbon in soil, a representative K_F is 0.027 L/kg.

Adsorption of metabolite B-3 was studied in a total of 9 soils by the batch adsorption method. Adsorption of B-3 on soil could be described by Freundlich adsorption isotherms. K_F values ranged from 0.11-0.58 L/kg with an average of 0.23 L/kg. 1/n is set at the default of 1.

Adsorption of metabolite AB-1 was studied in a batch adsorption experiment but because of the very high adsorption of AB-1 even at soil:solution ratios of 1:100 to 1:200, it was analytically not possible to determine Freundlich isotherms. Therefore, K_{OC} values were based upon a measurement at a single concentration. K_{OC} values (duplicate experiment), determined at a 1:200 soil:solution ratio and an initial concentration of 0.05 mg/L were 6,200 to 450,000 L/kg. Based on 1% organic carbon in soil, a representative K_d is 620 L/kg from the lowest K_{OC}.

Water and sediment

Cyflumetofen was susceptible to hydrolysis in acidic, neutral, and basic buffer solutions. The hydrolysis rate increased with increasing pH, i.e., DT_{50}s 7.7 days (pH 4), 6.0 days (pH 5), 9.8 hours (pH 7) and 10 minutes (pH 9) at 25°C as described by first order kinetics. At environmentally relevant pH values, hydrolysis products that exceeded 10% of applied radioactivity were A-1 (max 10% AR at pH 5 to 7), A-2 (max 15% AR at pH 4; max A-1+A-2 44% AR at pH 7), A-18 (max 36% AR at pH 5-7), AB-1 (max 45% AR at pH 5-7) and B-1 (max 53% AR at pH 5 to 7).

Cyflumetofen was susceptible to aquatic photolysis in aqueous buffer solution (pH 5) with DT_{50} values of 1.3 hours under irradiated conditions (20 W/m^2, 290 to 400 nm), and 134 hours under dark conditions. In irradiated natural water, the DT_{50} was 1.1 hours. Aquatic photolysis products (in buffer pH 5) that exceeded 10% of applied radioactivity were B-1 (max 12% AR), AB-7 (max 11% AR) and AB-15 (max 55% AR). B-1 was also a significant degradation product under dark conditions (max 13% AR). In natural water (dark and irradiated), AB-1 was also observed in significant amounts. The only specific photolytic degradation products of cyflumetofen were AB-15 and AB-7.

The aerobic degradation of cyflumetofen was studied in 4 different water/sediment systems in 2 studies. Upon addition of cyflumetofen to the water layer, cyflumetofen was partitioned between the water and sediment layers. Degradation was generally biphasic in water and total system but did occasionally follow first order kinetics. Based on derived modelling endpoints, the geometric mean DT_{50} in water and total system were calculated to be 0.42 days and 5.1 days, respectively. Mineralisation to CO_2 was a minor process in all systems accounting for <7% AR at the end of the studies. Bound residues accounted for up to 32% AR. Major metabolites found in the water phase were B-1 (max 64% AR at 0.7 days), B-3 (max 15% AR at 0.7 days) and A-12 (max 15% AR at 15 days), while major metabolites found in sediment (B-ring label) were B-1 (max 22% AR at 29 days) and B-3 (max 28% AR at 15 days).

Air

Cyflumetofen is predicted to have an atmospheric half-life of 0.53 days based on 12 hours of sunlight per day. Additionally, cyflumetofen has a low vapour pressure (<5.9×10-6 Pa at 25 ^oC) and low Henry's law constant (<9.4×10^{-2} $Pa.m^3/mol$) and is not expected to partition significantly to the air compartment. It is therefore unlikely to be transported short or long distances in air.

Effects and associated risks to non-target species

Terrestrial vertebrates

Cyflumetofen had low toxicity to mammals (LD_{50} >2000 mg ac/kg bw, *Rattus norvegicus*) and birds (LD_{50} >2250 mg ac/kg bw, *Anas platyrhynchos*). Cyflumetofen was similarly not toxic to birds following short-term dietary exposure (LC_{50} >5,000 mg ac/kg diet, 2 species tested). Following long-term dietary administration in reproduction studies, an increased incidence of cracked eggs was observed at a test rate of 389 mg ac/kg diet resulting in the NOEC of 154 mg ac/kg diet (lowest NOEL 13.6 mg ac/kg bw/d, *Colinus virginianus*), while reproduction success in mammals was not affected up to the highest dose, resulting in a study NOEL of 34.6 mg ac/kg bw/d (1,500 mg ac/kg diet; *Rattus norvegicus*).

Risks of cyflumetofen to terrestrial vertebrates were determined to be acceptable assuming direct dietary exposure within the treatment area at the maximum rate. Although the log K_{ow} of 4.3 indicates potential for bioaccumulation of cyflumetofen, a food chain assessment indicated that any accumulated residues in earthworms or fish were not expected to reach levels harmful to predators under the proposed conditions of use. In addition, based on toxicokinetic studies, biomagnification is not expected in the food chain. No protection statements are therefore required for terrestrial vertebrates.

Aquatic species

Cyflumetofen has low toxicity to fish (LC_{50} >29 µg ac/L, *Pimephales promelas*), aquatic invertebrates (>LC_{50} 6.3 µg ac/L, *Crassostrea virginica*), algae (E_rC_{50} >34 µg ac/L, *Skeletonema costatum*), and aquatic plants (EC_{50} >38 µg ac/L, *Lemna gibba*) at the limit of solubility, and is not toxic to sediment dwellers (LC_{50} >787 mg TRR/kg dw, *Leptocheirus plumulosus*). Following long-term exposure, reduced growth in fish at 179 µg ac/L (NOEC 72 µg ac/L, *Cyprinus carpio*); no adverse effect at highest tested dose in aquatic invertebrates (NOEC >16.2 µg ac/L, *Daphnia magna*); and reduced emergence in sediment dwellers at 102 mg ac/kg dw (NOEC 44.7 mg ac/kg dry sediment, *Chironomus riparius*) were recorded.

A representative SC formulation increased the toxicity levels to fish (LC_{50} >837 µg ac/L, *Oncorhynchus mykiss*), aquatic invertebrates (EC_{50} >700 µg ac/L, *Daphnia magna*), and algae (E_rC_{50} >952 µg ac/L, *Pseudokirchneriella subcapitata*) at exposure levels approaching 1 mg ac/L, and the results from the formulation testing were used to determine the acute regulatory acceptable levels.

The major metabolites tested (B-1, B-2, A-2, AB-1) did not demonstrate greater toxicity than the parent compound. Due to the low solubility of cyflumetofen in water, the exact toxicity of cyflumetofen or the tested metabolites could not be established from the studies on aquatic organisms. Metabolites were chosen for testing based on their occurrence in different environmental media (water or sediment), with B-1 being the most dominant degradate that is water soluble and found in virtually all environmental fate studies.

Spray drift risks to aquatic species are driven by the high chronic toxicity of cyflumetofen to aquatic invertebrates (RAL 0.016 mg ac/L). Mandatory buffer zones of up to 5 metres for boom sprayers, and up to 15 metres for vertical sprayers are required to mitigate these risks.

Runoff risks of cyflumetofen were determined to be acceptable when accounting for real-world slopes in growing regions and different soil profiles, provided the product is not applied when a runoff event is expected soon after application. General runoff restraints are required to mitigate this risk.

Bees

Cyflumetofen has low toxicity to bees (*Apis mellifera*) by contact exposure (LD_{50} >102 µg ac/bee) and oral exposure (LD_{50} >116 µg ac/bee). The representative SC formulation does not enhance toxicity effects on bees. No behavioural effect, and acceptable mortality were observed in the oral test at the highest dose tested (NOEL 116 µg ac/bee, *Apis mellifera*). In a semi-field test with an application rate of 200 g ac/ha to flowering *Phacelia tanacetifolia*, there were no effects on honey bee mortality, foraging behaviour, or honey bee colonies.

Risks of cyflumetofen to bees were determined to be acceptable, assuming direct dietary and/or contact exposure following application to blooming plants within the treatment area at the maximum rate. No protection statements are therefore required for bees.

Other non-target arthropods

A representative SC formulation of cyflumetofen was not toxic to the indicator species for predatory arthropods (LR_{50} >1,400 g ac/ha, *Typhlodromus pyri*) and parasitic arthropods (LR_{50} >1,400 g ac/ha, *Aphidius rhopalosiphi*) in Tier 1 (glass plate) laboratory toxicity tests. An extended laboratory study on predatory mites at much lower rates had no effects on mortality or reproduction (LR_{50} >600 g ac/ha *Typhlodromus pyri*), while Tier 1 (glass plate) laboratory tests on other predatory arthropods showed similar results (LR_{50} >40 g ac/ha; *Amblyseius cucumeris*, *Chrysoperla carnea* and *Orius strigicollis*).

Risks of cyflumetofen to beneficial arthropods were determined to be acceptable, assuming direct contact exposure to fresh-dried residues on foliage or soil within the treatment area at the maximum rate. No protection statements are therefore required for beneficial arthropods.

Soil organisms

Cyflumetofen was not toxic to earthworms through acute exposure (LC_{50corr} >500 mg ac/kg dry soil, *Eisenia fetida*). In a reproduction test, the $NOEC_{corr}$ was 500 mg ac/kg. Cyflumetofen does not adversely affect soil microbial processes, such as nitrogen or carbon transformation at the highest tested soil concentration (NOEC 1.4 mg ac/kg dry soil).

Risks of cyflumetofen to soil organisms were determined to be acceptable, assuming direct exposure to maximum predicted residues in the top 5 cm of soil without interception by the crop. No protection statements are therefore required for soil organisms.

Non-target terrestrial plants

A representative SC formulation of cyflumetofen 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 following pre-emergent exposure was tomato (ER_{25} 44 g ac/ha, ER_{50} 178 g ac/ha,

Lycopersicon esculentum) and all 10 species were not sensitive following post-emergent exposure (ER_{25} >400 g ac/ha, ER_{50} >400 g ac/ha, 10 species).

Spray drift risks to non-target terrestrial plants are driven by the high toxicity of the cyflumetofen following pre-emergent exposure (RAL 18 g ac/ha). Mandatory buffer zones of up to 10 metres for boom sprayers and up to 20 metres for vertical sprayers are required to mitigate these risks.

Recommendations

In considering the environmental safety of the proposed use of Danisaraba Miticide, the APVMA had regard to the toxicity of the active constituent and its residues, including metabolites and degradation products, in relation to relevant organisms and ecosystems. Based on the outcome of the risk assessment, the APVMA is satisfied that the proposed use of the product meets the environmental safety criteria when used according to label directions, which includes the following restraints and protections statements to address environmental risks:

Restraints

DO NOT apply by aircraft

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.

[See *Spray drift* and *Label recommendations* sections for specific spray drift restraints and buffer zones.]

Protection of wildlife, fish, crustaceans and environment

DO NOT contaminate wetlands or watercourses with this product or used containers.

Efficacy and safety assessment

Proposed product use pattern

Danisaraba Miticide, containing 200 g/L of cyflumetofen in a suspension concentrate (SC) formulation, is proposed for use as a miticide in pome fruit, citrus fruit, strawberries, grapes, fruiting vegetables, tree nuts (almonds) and ornamentals. Proposed target pest species include: two-spotted mite (*Tetranychus urticae*), European red mite (*Panonychus ulmi*), citrus red mite (*Panonychus citri*), oriental spider mite (*Eutetranychus orientalis*) and Bryobia mite (*Bryobia spp.*).

The product is to be applied at a rate of 100 mL/100 L (20 g ai/100 L) or 1L/ha (200 g ai/ha), mechanically by airblast or ground-boom application methods and manually by handheld spray equipment in greenhouse settings. No aerial spray treatment will be applied to crops. In all crops, a maximum of 2 sprays per season are proposed, after a 14-day interval, where necessary.

Cyflumetofen, either as Danisaraba, Sultan or Nealta Miticide, has been registered for a number of years in over 30 countries, including USA, Canada, Japan, South Korea, and several state members of the EU. The use patterns sought in the Australian registration are similar to its uses in other countries.

Efficacy and target crop safety

Data from 128 trials were submitted, together with scientific argument, to support the label claims of product efficacy and crop safety for Danisaraba Miticide. 22 trials were conducted in Australia with the remainder conducted in USA, Japan, and various European countries. Trials used Danisaraba Miticide (coded BAS 9210 01) and/or the equivalent products registered overseas under the trade names Nealta Miticide (coded BAS 9210 2l and BAS 9210 4l) or Sultan Miticide (coded BAS 9210 2l). All formulations were closely similar, containing the same loading of active constituent (200 g/L cyflumetofen) and formulated as a suspension concentrate. Side-by-side comparisons, undertaken in 37 trials, confirmed bioequivalence of these formulations.

Pome fruit

Proposed uses in pome fruit (apples and pears) are for the control of two-spotted mite, European red mite and Bryobia mite, at a rate of 100 mL product/100 L. Data from 38 efficacy trials were submitted (37 in apples and one in pears), conducted in Australia and overseas, to demonstrate efficacy against two-spotted mite (17 trials) and European red mite (21 trials), as well as a claim of product safety to predatory mites and crop safety in apples and pears. The overall trend of the data supported a label claim for the control of these mite pests in apples and pears at the proposed label rate. The applicant provided argument to justify a label claim for the control of Bryobia mite in pome fruits, without further data, based on efficacy against two-spotted mite and European red mite. Cyflumetofen is expected to be equally effective against Bryobia mites given their taxonomic closeness (all species belong to the family *Tetranychidae*) and similarity of feeding behaviour. Furthermore, trial results demonstrated that cyflumetofen was equally as efficacious as industry standard miticides that are currently registered for the control of Bryobia mite in pome fruit, at the same label rates as used for two-spotted mite and European red mite. Bryobia mites are also listed as a target species for cyflumetofen in Japan. These arguments for extrapolation were considered acceptable.

Almonds

Proposed uses in almonds are for the control of two-spotted mite, European red mite, and Bryobia mite, at 100 mL product/100 L. The results from 2 trials, conducted in the US, demonstrated product efficacy for control of two-spotted mites in almonds at the proposed label rate. The applicant provided argument to justify the extrapolation of uses for the control of European red mite in almonds based on the substantial body of data presented in this submission to determine the efficacy of cyflumetofen on this species in other crops, at the same application rate of 100 mL/100 L. Trials in almonds confirmed the activity of cyflumetofen on two-spotted mite at the proposed label rate and crop safety when applied at twice the label rate. Given the similarity of plant architecture, application timing, and spray techniques, extrapolation of efficacy data from pome fruits to almonds is considered appropriate. Arguments presented for the extrapolation of uses to include the control of Bryobia mites in pome fruit were also considered to be valid for a similar label claim in almonds.

Citrus

Proposed uses in citrus are for the control of Oriental Spider mite, Citrus Red Mite, and two-spotted mite, at 100 mL product/100 L. Efficacy and crop safety data from 20 field trials conducted in Australia and overseas from 2001–18 were provided to support these uses. Two Australian trials, undertaken in limes, assessed the efficacy and crop safety of Danisaraba Miticide and BAS 9210 2I (Nealta Miticide) against Oriental spider mite. Five trials conducted in the EU on mandarin, orange, and clementine, tested BAS 9210 2I and BAS 9210 0I (DANISARABA) against two-spotted mite. Nine single/multi plot trials were conducted in Japan to test the efficacy of Danisaraba Miticide to control citrus red mite in mandarins. The data set collectively confirmed the efficacy and crop safety of cyflumetofen formulations for the control the 3 mite species in citrus at the proposed label rate when mite populations reach economic thresholds and supported a follow-up spray 14 days later if required. Extrapolation of efficacy and crop safety to all of the citrus crop group is considered appropriate based on the trial results for limes, mandarin, orange, and clementine.

Grapes (wine and table)

Proposed use in grapes is for the control of two-spotted mite, at a rate of 100 ml/100 L. Data from 18 trials, conducted in Australia and overseas (US and Japan), were submitted to demonstrate efficacy (one trial) and crop safety (all trials). In the efficacy trial, Danisaraba Miticide achieved a high level of control against two-spotted mite at the proposed label rate and was equivalent or better than industry standards. The results were consistent with trials which tested efficacy of cyflumetofen to control two-spotted mite in other crops and considered to be sufficient to support registration. No phytotoxicity was observed in any trials conducted on several varieties of wine and table grapes and the data is supportive of a label claim of crop safety in grapevines.

Strawberries

Proposed uses in strawberries (field and protected) are for the control of two-spotted mite and European red mite, at a rate of 1 L/ha. Data from 8 trials was provided to demonstrate product efficacy to control two-spotted mites in strawberries. One replicated trial, conducted in Victoria, assessed efficacy and crop safety following a single application of Nealta Miticide. Other efficacy trials were conducted in the EU in strawberries grown under protected cropping (Spain (×4), Germany (×1), Italy (×2) and included both the

Nealta formulation (BAS 9210 2I) and BAS 9210 0I (DANISARABA). The combined data set showed that cyflumetofen was efficacious against all two-spotted mite life-stages and performed as well as, or better than, the commercial standards used in the trials, often with a faster knock down response on motile stages. As a rate response was evident in some trials, the proposed label rate of 1 L/ha was supported. In the Australian trial, the addition of an adjuvant increased the efficacy of cyflumetofen against two-spotted mites.

The applicant considered the efficacy data presented with this application for control of European red mite in other crops at the same label rate as sufficient to extrapolate uses for this pest in strawberries. This argument was accepted.

Crop safety data was provided from 5 trials conducted on field-grown strawberries and 10 trials conducted on strawberries grown under protected cropping (glasshouse, polytunnel) using DANISARABA/BAS 9210 0I and Nealta Miticide (BAS 9210 2I, BAS 9210 4I). The data supported the crop safety of cyflumetofen in strawberries at up to 2.8× the proposed rate (2.88 L/ha) and with a follow-up spray after 14 days, if required.

Fruiting vegetables

Proposed uses in fruiting vegetables are for the control of two-spotted and European red mites, at a rate of 1 L/ha. Fruiting vegetables includes tomatoes (field grown and protected), capsicums, chili peppers, and eggplants. Efficacy and crop safety data on two-spotted mite from 3 Australian field trials conducted in tomatoes using BAS 9210 2I (Nealta Miticide) were provided in support of this use. Overall, the data demonstrated that cyflumetofen gave equivalent or better control than the commercial standards for the control of two-spotted mite in tomatoes. They also demonstrated equivalence between all cyflumetofen formulations when applied at the same rate of active ingredient per hectare. The data support a label claim in fruiting vegetables and are consistent with the efficacy trials provided against two-spotted mite in other crops when applied at the proposed label rate of 1 L/ha.

The applicant argued that efficacy data for the control of two-spotted mite in tomatoes can be extrapolated to other crops within the fruiting vegetable crop group (capsicums, chili peppers, and eggplants), as proposed application rates are the same at 1 L/ha. It was further argued that the data generated for European red mite control in apples and stone fruit can be extrapolated to fruiting vegetables. Based on the substantial body of data provided in this application demonstrating product efficacy against two-spotted and European red mite under multiple crops and conditions, extrapolation of uses was supported.

Crop safety data were obtained from 27 trials undertaken in representative fruiting vegetable crops (field grown and protected cropping) using the DANISARABA, BAS 9210 2I and BAS 9210 4I formulations. The data provided demonstrated crop safety in tomatoes, capsicum, chili, and eggplants at the proposed label rate and over 6 times (1 to 6.4×) the proposed label rate with follow up sprays after 10 to15 days apart (14 days apart as a label claim) and were supportive of a label claim for crop safety in fruiting vegetables for the proposed label rate of 1 L/ha.

Ornamentals

Proposed uses in ornamentals are for the control of two-spotted mite, European mite, and Bryobia mite in field-grown and protected crops, at a rate of 100 mL/100 L. Species of ornamentals include: Chrysanthemum, Cyclamen, Fuchsia, Gerbera daisy, Rose, and African violets (*Saintpaulia spp.*). Data from

53 overseas trials were provided to support efficacy and crop safety in ornamentals, including a summary of the US EPA submission for the registration of Sultan Miticide (the same formulation as Nealta Miticide). Trials were conducted in field-grown carnations, chrysanthemums, and roses as well as in carnations, chrysanthemums, roses, New Guinea Impatiens, and African daisies grown under protected cropping, between 2004 and 2013. Trials in the EU were conducted using BAS 9210 2I (Nealta Miticide) and BAS 9210 0I, while Japanese trials used Danisaraba Miticide. No trials were conducted in Australia in these assessments.

Overall, the trial data confirmed the efficacy cyflumetofen in controlling two-spotted mites infesting a range of ornamental species. Levels of control were equivalent to, or better than, industry standard treatments when applied at recommended label rate. The application, therefore, is supportive of a label claim for the control of two-spotted mite in ornamental plants at the proposed label rate of 100 mL/100 L. The applicant provided argument for the extrapolation of data on European red mite in apples and stone fruit to support control of this species in ornamentals. Given the body of efficacy data provided on European red mite in this application and levels of control achieved against two-spotted mites infesting ornamentals, this argument was accepted.

In crop safety trials, no phytotoxicity was observed in a range of ornamental species tested under field and protected cropping situations. Data presented showed that the cyflumetofen formulations were safe to use in roses following 2 applications, 7 days apart, at rates up to 2.5× the proposed label rate. Phytotoxicity data from the Sultan Miticide registration showed that one to 2 applications of cyflumetofen, at up to 2× the proposed label rate, was safe to use on: Euonymus, daylily, Kentia palm, pansy, butterfly bush, Phormium, marigold, zinnia, chrysanthemum, cyclamen, fuchsia, gerbera daisy, rose, African violets, Ficus, and hibiscus. The label General Instructions includes an appropriate statement advising users to conduct a small test application to assess for phytotoxicity before spraying ornamentals not listed on the label. A label claim for crop safety in ornamental is, therefore, supported.

Resistance management

Cyflumetofen is a novel benzoylacetonitrile acaricide with a mode of action classified by the Insecticide Resistance Action Committee (IRAC 2021) as Group 25A beta-ketonitrile derivative (mitochondrial complex II electron transport inhibitors). Currently, there are no other products containing a Group 25A active constituent registered for use in Australia. Therefore, Danisaraba Miticide is expected to provide growers with a useful control agent, with a different mode of action, for rotation in resistance management programs.

Recommendations

Trial data demonstrated that Danisaraba Miticide will be effective in controlling mite infestations when applied at the proposed label rates of 100 mL/100 L or 1 L/ha, as a single application or as 2 applications with a 14-day interval between treatments, where necessary. The product was safe to use at the proposed label rate in all the crops tested at more than twice the label rate.

There are no objections on efficacy or target-crop safety grounds to the registration of the product Danisaraba Miticide, containing 200 g/L of cyflumetofen, when used as directed.

Spray drift assessment

Regulatory Acceptable Levels (RALs) were established for each risk area in order to calculate the appropriate spray drift buffer zones for Danisaraba Miticide, using in the APVMA Spray Drift Assessment Tool (SDRAT).

Residues

From a lactating goat metabolism study, dosing with cyflumetofen at 13.5 ppm which gave a maximum residue according to the residue definition (parent cyflumetofen plus the B1 metabolite) of 0.125 mg/kg in liver, it was established that a RAL of 3.24 ppm was appropriate to use to calculate buffer zones for livestock areas. No buffer zones are required for livestock areas when Danisaraba Miticide is applied by ground boom sprayers. Buffer zones of between 0 and 10 metres are required when the product is applied by vertical sprayers, depending on the dilute water rate and type of target canopy (see label).

Human Health

Risks to bystanders from spraying activities were based on potential risks to children (as the most sensitive sub-population) using a NOAEL of 16.5 mg/kg bw/day, a maximum application rate of product of 1 L/ha with and minimum droplet size of COARSE. Using these parameters, a RAL of 724 g/ha was established for calculating bystanders buffer zones in the SDRAT. Based on these calculations, no buffer zone is required for bystanders when Danisaraba Miticide is applied by ground boom or vertical sprayers.

Environment

Cyflumetofen has low toxicity to bees by contact exposure (LD_{50} >102 µg ac/bee, Apis mellifera) and oral exposure (LD50 >116 µg ac/bee, *Apis mellifera*). Spray drift risks to bees are therefore considered to be acceptable and no buffer zones for pollinators are required.

Spray drift risks to aquatic species are driven by chronic toxicity of cyflumetofen to aquatic invertebrates (RAL 16 µg ac/L). Mandatory buffer zones for natural aquatic areas were determined to be up to 5 metres for boom sprayers, depending on the boom height, and up to 15 metres for vertical sprayers, depending on the dilute water rate and type of target canopy.

Cyflumetofen was not phytotoxic to terrestrial plants following post-emergent exposure (in vegetative vigour test); however, one species (tomato) did show sensitivity at drift-relevant rates in the seedling emergence test (RAL 18 g ac/ha). Mandatory buffer zones for natural vegetation areas were determined to be up to 10 metres for boom sprayers, depending on the boom height, and up to 20 metres for vertical sprayers, depending on the dilute water rate and type of target canopy.

Table 8: Summary of RALs for Danisaraba Miticide (200 g/L cyflumetofen)

Sensitive area	Regulatory Acceptable Level	
	Level of active	Units
Natural aquatic	16	µg/L
Vegetation	18	µg/L
Pollinator	999999	g/ha
Bystander	724	g/ha
Livestock	3.24	ppm

Buffer zones calculated by the SDRAT, using the above RALs, were incorporated into the Danisaraba Miticide label spray drift instructions (see below).

Labelling requirements

BASF
We create chemistry

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

DANISARABA® MITICIDE

ACTIVE CONSTITUENT: 200g/L CYFLUMETOFEN

GROUP	25A	INSECTICIDE

For the control of Two spotted mite, European red mite and Bryobia mite in pome fruit, almonds and ornamentals; for Two spotted mite, Citrus red mite and Oriental spider mite in citrus; for Two spotted mite in grapes; for Two spotted mite and European red mite in fruiting vegetables and strawberry, as per the Directions for Use table.

IMPORTANT: READ THE LEAFLET BEFORE USING THIS PRODUCT

CONTENTS: 1L-1000L

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Website: www.crop-solutions.basf.com.au

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APVMA Approval No.: XXXXX/XXXXX

DIRECTIONS FOR USE

RESTRAINTS

For PROFESSIONAL use only.

DO NOT apply by aerial spraying.

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

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 table/s 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 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 not smaller than a **COARSE** spray droplet size category
- minimum distances between the application site and downwind sensitive areas (see 'Mandatory buffer zones' section of the following table titled 'Buffer zones for boom sprayers') are observed.

Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Mandatory downwind buffer zones				
		Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas	Livestock areas
Up to maximum label rate	0.5 m or lower	0 metres	0 metres	0 metres	0 metres	0 metres
	1.0 m or lower	0 metres	5 metres	0 metres	10 metres	0 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 'Mandatory buffer zones' section of the following table titled 'Buffer zones for vertical sprayers') are observed.

Buffer zones for vertical sprayers

Application rate	Type of target canopy and dilute water rate	Mandatory downwind buffer zones				
		Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas	Livestock areas
100 mL/100 L	2 metres tall and shorter, maximum dilute water rate of 1000 L/ha	0 metres	0 metres	0 metres	0 metres	0 metres
	Taller than 2 metres (not fully-foliated), maximum dilute water rate of 4000 L/ha	0 metres	20 metres	0 metres	20 metres	10 metres
	Taller than 2 metres (fully-foliated), maximum dilute water rate of 4000 L/ha	0 metres	10 metres	0 metres	15 metres	5 metres

DFU Table

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
Pome fruit (apple and pears) Almond	Two-spotted mite (*Tetranychus urticae*) European red mite (*Panonychus ulmi*) Bryobia mite (*Bryobia* spp.)	100 mL/100 L	7 days	Monitor crops and commence applications before local threshold levels are reached. Continue to monitor crops and make subsequent applications after 14 days where necessary. Apply a maximum of 2 sprays per season. Alternate the applications of DANISARABA MITICIDE with a miticide from a different Mode of Action. Refer to the Crop Life

Citrus fruit	Two-spotted mite (*Tetranychus urticae*) Citrus red mite (*Panonychus citri*) Oriental spider mite (*Euteranychus orientalis*)			Australia Guidelines for resistance management. DANISARABA MITICIDE is not systemic and does not have translaminar activity. Apply in sufficient water to ensure thorough coverage to the point of runoff of the target crop. It is recommended that on larger tree and vine crops, water volumes of 1000 L/ha and above are used. If concentrate spraying, ensure through coverage of the target crop, ensuring a minimum of 1 L/ha of product is applied. For CONCENTRATE spraying, refer to APPLICATION section below. The addition of an adjuvant appropriate for the crop being sprayed may aid in speed of knockdown and the overall control. Pome fruit: DO NOT apply a water volume greater than 3000 L/ha per application. Citrus fruit: DO NOT apply a water volume greater than 4000 L/ha per application.
Grape (Wine and Table)	Two-spotted mite (*Tetranychus urticae*)		14 days	
Strawberry Fruiting Vegetables, including tomatoes, capsicums, chili peppers and eggplants	Two-spotted mite (*Tetranychus urticae*) European red mite (*Panonychus ulmi*)	1 L/ha	1 day	Monitor crops and commence applications before local threshold levels are reached. Continue to monitor crops and make subsequent applications after 14 days where necessary. Apply a maximum of 2 sprays per season. Alternate the applications of DANISARABA MITICIDE with a miticide from a different Mode of Action. Refer to the Crop Life Australia Guidelines for resistance management. DANISARABA MITICIDE is not systemic and does not have translaminar activity. Apply in sufficient water to ensure thorough coverage to the point of runoff of the target crop. For CONCENTRATE spraying, refer to APPLICATION section below. The addition of an adjuvant appropriate to the crop being sprayed
Protected Strawberry Protected Tomatoes		100 mL/100 L	1 day	

				may aid in speed of knockdown and the overall control.
Ornamentals including Chrysanthemum, Cyclamen, Fuchsia, Gerbera daisy, Rose and African violets (*Saintpaulia* spp.) (field and protected)	Two-spotted mite (*Tetranychus urticae*), European red mite (*Panonychus ulmi*) and Bryobia mite (*Bryobia* spp.)	100 mL/100 L	-	Monitor crops and commence applications before local threshold levels are reached. Continue to monitor crops and make subsequent applications after 14 days where necessary. Apply a maximum of 2 sprays per season. Alternate the applications of DANISARABA MITICIDE with a miticide from a different Mode of Action. Refer to the Crop Life Australia Guidelines for resistance management. DANISARABA MITICIDE is not systemic and does not have translaminar activity. Apply in sufficient water to ensure thorough coverage to the point of runoff and penetration of the target plants. The addition of an appropriate adjuvant may aid in speed of knockdown and the overall control. Test the safety and compatibility of all adjuvants before use. Always read and follow the specific adjuvant label using the correct concentration of adjuvant to avoid plant injury. For ornamentals not listed on the label, a small test application to assess for phytotoxicity should be made before spraying the whole crop.

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

WITHHOLDING PERIODS

HARVEST:
POME FRUIT, ALMOND, CITRUS: DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION
GRAPES: DO NOT HARVEST FOR 14 DAYS AFTER APPLICATION
TOMATO, STRAWBERRY, FRUITING VEGETABLES: DO NOT HARVEST FOR 1 DAY AFTER APPLICATION
ORNAMENTALS: NOT REQUIRED WHEN USED AS DIRECTED

GRAZING:
POME FRUIT, ALMOND, CITRUS AND GRAPES: DO NOT ALLOW LIVESTOCK TO GRAZE IN TREATED AREAS.

ORNAMENTALS: DO NOT ALLOW LIVESTOCK TO GRAZE IN TREATED AREAS OR CUT FOR STOCK FEED.

Export of treated commodities
Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for labelled crops treated with DANISARABA MITICIDE. Additionally, some export markets have established MRLs different to those in Australia. If you are growing crops for export, please check with BASF Australia Ltd for the latest information on MRLs and import tolerances BEFORE using this product.

GENERAL INSTRUCTIONS
DANISARABA MITICIDE is a miticide which acts by inhibiting electron transport in the respiration system of insects. Monitor crops and apply DANISARABA MITICIDE as threshold levels are reached. DANISARABA MITICIDE has low toxicity to beneficial insects and is suitable for use in Integrated Pest Management programs.

APPLICATION
To be effective, thorough crop coverage is required. Adjust water volumes according to the crop growth stage to ensure thorough coverage and apply to the point of run-off. The additional of a non-ionic surfactant may aid in speed of knockdown and the overall control. DANISARABA MITICIDE is not systemic and does not have translaminar activity meaning good spray coverage is essential. Tank mixes with Summer oil or an organophosphate insecticide IS NOT recommended.

Before spraying Ornamentals not listed on the label, a small test application should be made to assess for phytotoxicity.

Mixing Instructions
Measure the required amount of DANISARABA MITICIDE, add to partly filled spray tank, and then add the remainder of the water. Where required, add a non-ionic surfactant at the end of the filling process.

DANISARABA MITICIDE is a suspension concentrate (SC) formulation. When using in a tank mix with other products, the following mix order should be observed:

- half fill the spray tank. Maintain constant agitation
- add any granule (WG) formulated products first and allow dispersion, followed by any suspension concentrates (SC/flowable) including DANISARABA MITICIDE
- add any other EC formulations
- add any water-soluble salts
- add any adjuvants as required.

Compatibility
DANISARABA MITICIDE is physically compatible with the following products (maintain constant agitation): Fungicides: Polyram, Delan, Luna Sensation, Fontelis, Toledo, Serifel, Systhane, Belanty, Switch, Bravo, Merivon, Vivando, Pristine, Cabrio, Nimrod, Kocide Blue Xtra, Tri-Base Blue and Captan.

Insecticides: Versys, Success Neo, Belt, Movento and Altacor.

DANISARABA MITICIDE is not compatible with Mancozeb 750 WG.

As formulations of other manufacturer's products are beyond the control of BASF, and the quality of water may vary with location, all mixtures should be tested prior to mixing commercial quantities.

Dilute Spraying
Use a sprayer designed to apply high volumes of water up to the point of run-off and matched to the stage of growth of crop being sprayed. Calibrate 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 specialist advice. Spray to the point of run-off. The required dilute spray volume, sprayer calibration and operation may all need to be changed as the crop grows.

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

Example only – Dilute spray volume, as determined above to achieve coverage near the point of run-off, for example is 1000 L/ha. Your chosen concentrate spray volume is 500 L/ha. The concentration factor in this example is: 2×(1000 L÷500 L= 2). If the dilute label rate is 100 mL/100 L, then the concentrate rate becomes 2× 100, which is 200 mL/100 L of water. 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.

IPM compatibility
DANISARABA MITICIDE has low toxicity to insect predators and is suitable for use where IPM is practiced.

INSECTICIDE RESISTANCE WARNING

GROUP	25A	INSECTICIDE

For insecticide resistance management DANISARABA MITICIDE is a Group 25A insecticide. Some naturally-occurring insect biotypes resistant to DANISARABA MITICIDE and other Group 25A mites may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the mite population if DANISARABA MITICIDE or other Group 25A insecticides are used repeatedly. The effectiveness of DANISARABA MITICIDE on resistant individuals could be significantly reduced. Since occurrence of resistant insects is difficult to detect prior to use, BASF Australia Ltd accepts no liability for any losses that may result from the failure of DANISARABA MITICIDE to control resistant mites. DANISARABA MITICIDE may be subject to specific resistance management strategies. For further information, contact your local supplier, BASF Australia Ltd representative or local agricultural department agronomist.

RE-ENTRY PERIOD
DO NOT enter treated areas until spray has dried. If prior entry is necessary wear cotton overalls buttoned to

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

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

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight. Triple rinse containers before disposal. Add rinsings to spray tank. **DO NOT** dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and 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
Avoid contact with skin. When opening the container, preparing the spray and using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow-length chemical resistant gloves. Wash hands after use. After each day’s use, wash gloves and contaminated clothing.

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

ADDITIONAL USER SAFETY INFORMATION

WARNING: contains cyflumetofen, which may cause skin sensitisation. Sensitive individuals should avoid contact with this substance.

SAFETY DATA SHEET
Additional information is listed in the Safety Data Sheet available from your supplier.

CONDITIONS OF SALE
All conditions and warranties rights and remedies implied by law or arising in contract or tort whether due to the negligence of BASF Australia Ltd or otherwise are hereby expressly excluded so far as the same may legally be done provided however that any rights of the Buyer pursuant to non- excludable conditions or warranties of the *Competition and Consumer Act 2010* or any relevant legislation of any State are expressly preserved but the liability of BASF Australia Ltd or any intermediate Seller pursuant thereto shall be limited if so permitted by the said legislation to the replacement of the goods sold or the supply of equivalent goods and all liability for indirect or consequential loss or damage of whatsoever nature is expressly excluded. This product must be used or applied strictly in accordance with the instructions appearing hereon. This product is solely sold for use in Australia and must not be exported without the prior written consent of BASF Australia Ltd.

APVMA Approval No: XXXXX/XXXXX

Batch No:

Date of Manufacture:

® = Registered trademark

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Acronyms and abbreviations

Shortened term	Full term
ac	active constituent
ADI	acceptable daily intake (for humans)
ai	active ingredient
ARfD	acute reference dose
bw	bodyweight
d	day(s)
DAT	days after treatment
DT_{50}	time taken for 50% of the concentration to dissipate
EC_{50}	concentration at which 50% of the test population are immobilised
ErC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
ER_{25}	effective rate, 25th percentile
ER_{50}	effective rate, median
ESI	export slaughter Interval
FTIR	fourier-transform infrared spectroscopy
g	gram
GAP	good agricultural practice
h	hour
ha	hectare
HPLC	high pressure liquid chromatography or high-performance liquid chromatography
IPM	integrated pest management
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
kPa	kilopascal

Shortened term	Full term
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
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
MS	mass spectrometry
MSDS	material safety data sheet
NEDI	national estimated daily intake
NESTI	national estimated short-term intake
ng	nanogram
NMR	nuclear magnetic resonance spectroscopy
NOEC/NOEL	no observable effect concentration level
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
Pa	pascal
ph	acidity or alkalinity of a solution
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
RAL	regulatory acceptable level
s	second
SC	suspension concentrate
STMR	supervised trial median residue

Shortened term	Full term
STMR-P	supervised trial median residue-processed
SUSMP	standard for the uniform scheduling of medicines and poisons
TGAC	technical grade active constituent
TRR	total radioactive residue
µg	microgram
WHO	World Health Organisation
WHP	withholding period

Glossary

Term	Description
Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
CAS number	Unique numerical identifier assigned by the Chemical Abstracts Service (CAS) to every chemical substance
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Cytotoxic	A substance or process which results in cell damage or cell death
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
Henry's law constant	A gas law that states that the amount of dissolved gas in a liquid is proportional to its partial pressure above the liquid
Hydrophobic	Repels water
Immunotoxicity	Adverse effect on the structure or function of the immune system, or on other systems as a result of immune system dysfunction
IUPAC name	International Union of Pure and Applied Chemistry naming scheme for organic compounds
Leaching	Removal of a compound by use of a solvent
Metabolism	The chemical processes that maintain living organisms
Pharmacokinetics	The study of the movement of substances within the body
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Racemic mixture	A mixture of equal quantities of 2 enantiomers
Toxicology	The study of the nature and effects of poisons

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