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Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of tetraniliprole in the product Vayego 200 SC Insecticide

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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 Vayego 200 SC Insecticide 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 7 April 2020 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

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

All personal information, and confidential information judged by the APVMA to be confidential commercial information (CCI)[1] contained in submissions will be treated confidentially. Unless requested by the submitter, the APVMA may release a submission, with any CCI redacted, to the applicant for comment.

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

Case Management and Administration Unit

Australian Pesticides and Veterinary Medicines Authority

GPO Box 3262

Sydney NSW 2001

Phone: +61 2 6770 2300

Email: enquiries@apvma.gov.au.

Further information

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

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

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

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

1 INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Vayego 200 SC Insecticide, and approval of the new active constituent, tetraniliprole. Vayego 200 SC Insecticide, is proposed for use in almonds, macadamias, pome and stone fruit against certain Lepidopteran, Dipteran and Coleopteran pests. Tetraniliprole is classified as an Insecticide Resistance Action Committee (IRAC) group 28 insecticide for resistance management purposes.

1.1 Applicant

Bayer CropScience Pty Ltd.

1.2 Purpose of application

Bayer CropScience Pty Ltd has applied to the APVMA for registration of the new product Vayego 200 SC Insecticide, containing 200 g/L tetraniliprole, as a suspension concentrate formulation of the new active constituent tetraniliprole.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Vayego 200 SC Insecticide, and approval of the new active constituent tetraniliprole.

1.3 Proposed claims and use pattern

For the control of various pests of almonds, macadamias, pome fruit and stone fruit.

1.4 Mode of action

Tetraniliprole is an insecticide from the of the anthranilamide class of compounds. As a diamide chemical it is active by ingestion. It interferes with the ryanodine-sensitive calcium release channels which lead to loss of muscle control and subsequent insect immobility. IRAC has designated tetraniliprole as a group 28 insecticide.

1.5 Overseas registrations

Tetraniliprole is a new active ingredient that is concurrently being registered in Canada and the United States.

The applicant also indicated that Vayego Insecticide is registered in Zimbabwe, Korea and Cambodia.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

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

The purified active ingredient is a beige, solid powder with an acetous odour, while the technical material is light yellow powder with no specific odour. Tetraniliprole is neither flammable, explosive, nor oxidising. The water solubility is low. The n-octanol/water partition coefficient (log Pow) is 2.6 at pH 4 and pH7 respectively while 1.9 at pH 9. The dissociation constant (pKa) was reported to be 9.1. Tetraniliprole purified active ingredient has a melting point of 226.9–229.6°C, while the technical active constituent melts at 228.4–230.1°C.

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

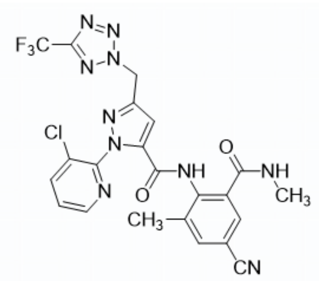
Common name (ISO):	Tetraniliprole
IUPAC name:	1-(3-chloropyridin-2-yl)-*N*-(4-cyano-2-methyl-6-(methylcarbamoyl)phenyl]-3-{[5-(trifluoromethyl)-2*H*-tetrazol-2-yl]methyl}-1*H*-pyrazole-5-carboxamide
CAS registry number:	1229654–66–3
Molecular formula:	$C_{22}H_{16}ClF_3N_{10}O_2$
Molecular weight:	544.88 g/mol
Structural formula:	

Table 2: Key physicochemical properties of the active constituent tetraniliprole

Physical form:	Technical grade—powder, purified active—solid powder
Colour:	Light yellow (technical grade), beige (purified active)
Odour:	Technical grade—odourless, purified active—acetous odour
Melting point:	Technical grade (228.4–230.1°C), purified active (226.9–229.6°C)
Boiling point:	The test item showed no boiling point under normal atmospheric pressure because it decomposed at temperatures above 230°C
Density at 20°C	Technical grade = D_4^{20} = 1.47 Purified active = D_4^{20} = 1.52
Stability:	Stable under accelerated storage (2 weeks storage at 54°C), in the presence of metals and metal ions (iron and aluminium), and under warehouse storage conditions for at least 2 years. In the accelerated study, tetraniliprole did not cause corrosion to the container materials (polypropylene and polyethylene)
Safety properties:	Not considered highly flammable. Not oxidising. Not explosive.
Solubility in water(Sample purity 98.3 % w/w):	Distilled water: 1.2 mg/L (resulting pH value: 6.31) pH 4: 1.0 mg/L pH 7: 1.0 mg/L pH 9: 1.3 mg/ L
Organic solvent solubility (at 20ºC):	Dimethyl sulfoxide >280 g/L Methanol 2.9 g/L Toluene 0.17 g/L n-heptane <0.001 g/L Ethyl acetate 6.4 g/L Dichloromethane 5.3 g/L Acetone 21.8 g/L
Dissociation constant (PKa):	pKa = 9.1
PH (1% in distilled water):	Technical grade = 5.2 at 23 oC Purified active = 5.2 at 24 oC
Octanol/water partition coefficient (Log K_{ow}/K_{ow}) at 20°C:	pH 4: log P_{ow} = 2.6 pH 7: log P_{ow} = 2.6 pH 9: log P_{ow} = 1.9

Vapour pressure	Temp(°C) vapour pressure (PA) 20 3.2×10^{-6} 25 4.6×10^{-6} 50 2.3×10^{-6}
Henry's law constant:	Distilled water (final pH = 6.3): K = 1.5×10^{-3} Pa m^3/mol^{-1} pH 4 (final pH = 4.0): K = 1.7×10^{-3} Pa m^3/mol^{-1} pH 7 (final pH = 7.0): K = 1.7×10^{-3} Pa m3/mol^{-1} pH 9 (final pH = 9.0): K = 1.3×10^{-3} Pa m^3/mol^{-1}
UV/VIS absorption spectra:	(see table below)
Complex formation ability in water:	Tetraniliprole had no complex forming ability for the measured ions compared to EDTA. No measurable complex forming ability was detected for cadmium, cobalt, copper, chromium, lead and zinc ions
Photochemical properties	The absorption properties indicated a potential for direct photolytic interactions of tetraniliprole with sunlight in aqueous solutions
Hydrolysis in aqueous solution under acid, neutral and basic conditions:	At 50°C pH 4: 10.9 days pH 7: 3.74 days pH 9: 0.04 days At 25°C pH 4: 287 days pH 7: 38.8 days pH 9: 0.75 days At 20°C pH 4: 265 days pH 7: 58.0 days pH 9: 1.27 days

UV/VIS absorption spectra:

Conditions	nm	Absorption (AU)	Molecular absorption (L/mol.cm)
neutral	204	1.11940	45774
neutral	267	0.42152	17237
acidic (pH 2)	204	1.15810	47357
acidic (pH 2)	267	0.41991	17171
basic (pH 10)	204	0.94384	38595
basic (pH 10)	267	0.39052	15969
basic (pH 10)	316	0.23587	9645

Particle size	The median particle size L_{50} of the test item deduced from the particle size distributions is 10.6 µm. The particle size L_{10} of the test item deduced from the particle size distributions is 0.9 µm. The particle size L_{90} of the test item deduced from the particle size distributions is 228.1 µm.

The APVMA has evaluated the chemistry aspects of tetraniliprole (manufacturing process, quality control procedures, batch analysis results, analytical methods, physicochemical properties, stability, and spectroscopic data) and found them to be acceptable. Technical tetraniliprole is expected to be stable for at least two years when stored under normal conditions, and shows good safety properties (not flammable, oxidising, or explosive).

Based on the data provided and the chemistry and toxicological assessments, the following APVMA Active Constituent standard is proposed for tetraniliprole:

Table 3: Proposed APVMA Active Constituent standard for tetraniliprole

Constituent	Specification	Level
Tetraniliprole	Tetraniliprole	900 g/kg minimum

2.2 Formulated product

The product Vayego 200 SC insecticide will be manufactured overseas and in Australia. Tables 4 and 5 outline some key aspects of the formulation and physicochemical properties of the product.

Table 4: Key aspects of the formulation of the product Vayego 200 SC insecticide

Distinguishing name:	Vayego 200 SC insecticide
Formulation type:	Suspension Concentrate (SC)
Active constituent concentration/s:	200 g/L tetraniliprole

Table 5: Physicochemical properties of the product Vayego 200 SC insecticide

Physical form:	White to beige liquid with a weak characteristic musty odour
PH:	4.3 (undiluted) 4.8 (1% dilution in deionized water)
Relative density:	$D4^{20}$ 1.115 g/cm^3 $D4^{40}$ 1.095 g/cm^3
Kinematic viscosity at 20 ºC:	250 x10^{-6} m^2/s at a shear rate of 20 1/s 85 x10^{-6} m^2/s at a shear rate of 100 1/s
Dynamic viscosity at 20 °C:	278 x·10^{-3} mPa·s at a shear rate of 20 1/s 95·x 10^{-3} mPa·s at a shear rate of 100 1/s
Surface tension at 25 °C Undiluted:	34 m/Nm
Surface tension at 20 °C 1 g/L in deionised water:	50 mN/m
Particle size distribution:	d (0.1) 0.45 µm d (0.5) 0.96 µm d (0.9) 2.76 µm
Safety properties:	Not explosive, no oxidizing properties and no flash point up to 100ºC. Auto-ignition temperature is 440°C.
Storage stability:	There was sufficient data to conclude that the product is expected to remain within specifications for at least 2 years when stored under normal conditions.

The APVMA has evaluated the chemistry aspects of the formulated product Vayego 200 SC insecticide, including the manufacturing process, quality control procedures, stability, physico-chemical properties, 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 two years when stored under normal conditions.

2.3 Recommendations

Based on a review of the chemistry and manufacturing details, the registration of Vayego 200 SC insecticide, and approval of the active constituent tetraniliprole, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

Chemical class

Tetraniliprole is a new insecticide of the anthranilamide class of compounds. It is a member of the group of chemicals including cyantraniliprole, flubendamide, chlorantraniliprole and cyclaniliprole that are agonists for the ryanodine receptor in insects.

Pharmacokinetics

Oral absorption of tetraniliprole in rats is rapid, with extensive excretion within the first 48 hours after dosing. Oral absorption was 41 per cent for male rats and 29 per cent for female rats. Absorption was not dose proportional at high doses, and there was minimal evidence for accumulation. Tetraniliprole was widely distributed in the tissues for oral dosing, with highest levels seen in the liver, kidneys, adrenal gland, myocardium and brown fat. Levels in tissues decreased rapidly. Metabolism was extensive, with a large number of metabolites formed, through a number of key pathways.

Dermal absorption of the active constituent was not determined, however the formulated product had a dermal absorption of 2.3 per cent in rats and estimated human dermal absorptions of 0.23 per cent.

Acute toxicity (active constituent)

Tetraniliprole had low acute oral (LD_{50} >2000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalation toxicity (LC_{50} >5010 mg/m^3/4h). Tetraniliprole was not a skin irritant in rabbits, but was a slight eye irritant and was positive for skin sensitisation in two mouse local lymph node assays.

Acute toxicity (product)

Vayego 200 SC is of low acute oral (LD_{50} >2000 mg/kg bw) and dermal (LD_{50} >2000 mg/kg bw) and inhalation toxicity (LC_{50} >4490 mg/m^3/4h). It was not a skin or eye irritant in rabbits, and was not a skin sensitiser in the mouse local lymph node assay.

Repeat-dose toxicity

In short term dietary studies in mice, no deaths or severe signs of systemic toxicity were seen following dietary dosing for up to 90 days, with a no observed adverse effect level of 973 mg/kg bw/day. In rats, the no observed adverse effect level for a 90 day dietary study was 608 mg/kg bw/day, based on the absence of significant toxicological findings.

In dogs given tetraniliprole in the diet for 90 days, the no observed adverse effect level was 126 mg/kg bw/day, based on increased salivation at the next highest dose. In a 52 week dietary toxicity study in dogs, the no observed adverse effect level was 88 mg/kg bw/day, based on clinical chemistry changes and decreased body weight, as well as slight microscopic changes in the adrenal gland, at 440 mg/kg bw/day.

In a short term dermal toxicity study in rats, 1000 mg/kg bw/day (six hour application) was well tolerated, with no clinical signs of toxicity or dermal irritation. No changes in the functional observation battery or reactions to stimuli were seen. The no observed adverse effect level was 1000 mg/kg bw/day.

Chronic toxicity and carcinogenicity

Tetraniliprole administered to mice in long term dietary studies (18 months) was well-tolerated, with no treatment-related effects on clinical signs, body weight, food consumption or clinical chemistry. There was no increase in tumour incidence. A slight, non-significant increase in mortality was noted at the high dose. A slight increase in liver and adrenal weights in one sex at the high dose were not associated with clinical histological changes, and were not considered to be treatment related. The no observed adverse effect level for tetraniliprole was 825 mg/kg bw/day, based on no effects at the highest dose tested.

In long term dietary studies in rats (24 months), decreased body weights, and effects on the uterus, vagina and ovaries (depletion of corpora lutea and increased epithelial hyperplasia) were observed at the highest dose. There was also a slight increase in the incidences of uterine epithelial tumours at the highest dose. Although these were only slightly above historical control values, they were considered to be treatment related. The overall no observed effect level for the study was 159 mg/kg bw/day, based on the decreased body weights seen at the highest dose in males and the decreased body weights and changes in the female reproductive organs in females at the highest dose.

Reproductive and developmental toxicity

Reproductive toxicity was investigated in a two-generation study in rats. Tetraniliprole was well tolerated, without treatment-related mortalities or serious adverse clinical signs of toxicity. There were no treatment-related effects on reproduction. Slightly delayed development was seen at the highest dose, which was attributed to decreased pup bodyweights. The no observed adverse effect level for systemic toxicity was 196 mg/kg bw/day, while the no observed adverse effect level for reproductive effects was 896 mg/kg bw/day.

In developmental toxicity studies in rats and rabbits, doses up to 1000 mg/kg bw/day were well-tolerated without treatment-related mortalities. In rats, slight decreases in foetal bodyweights and slightly delayed development were seen at the highest dose. In rabbits, there were no treatment related effects in foetuses seen. The no observed adverse effect level for both maternal foetal toxicity was 1000 mg/kg bw/day, the highest dose tested, in both rats and rabbits.

Genotoxicity

Genotoxicity was investigated in a standard battery of in vivo and in vitro tests. All tests were negative. It was concluded that tetraniliprole is unlikely to pose a genotoxicity-mediated carcinogenic risk to humans.

Toxicity of metabolites and/or impurities

No studies were performed with isolated impurities, metabolites or degradants.

Reports related to human toxicity

No adverse reports related to human toxicity were identified.

3.2 Health-based guidance values and poisons scheduling

Poisons standard

Following consideration by the Advisory Committee on Chemical Scheduling, a Delegate of the Secretary of the Department of Health has made an interim decision to amend the current Poisons Standard in relation to tetraniliprole. The proposal is to include tetraniliprole in Schedule 5 of the Poisons Standard, **except** in preparations containing 20 per cent or less of tetraniliprole. The public submission deadline in relation to this decision is 5 March 2020, and a final decision will be published by the Department of Health on 23 April 2020.

On this basis, Vayego 200 SC insecticide is exempt from scheduling.

Health-based guidance values

Acceptable Daily Intake

An Acceptable Daily Intake (ADI) for tetraniliprole was established at 0.90 mg/kg bw/d based on a NOAEL of 90 mg/kg bw/d in a 12 month dietary dog study, based on decreased body weights, clinical chemistry changes and slight histopathology changes in the adrenal gland at 440 mg/kg bw/d, and applying a 100 fold uncertainty factor to incorporate differences in toxicodynamics and toxicokinetics between and within species.

Acute Reference Dose

An Acute Reference Dose (ARfD) for tetraniliprole was not considered necessary, based on low acute toxicity, the absence of evidence for neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose or short-term exposure.

3.3 Recommendations

There are no objections on human health grounds to the approval of tetraniliprole. There are no objections on human health grounds to the registration of Vayego 200 SC Insecticide, containing 200 g/L of tetraniliprole.

4 RESIDUES ASSESSMENT

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

4.1 Metabolism

Plants

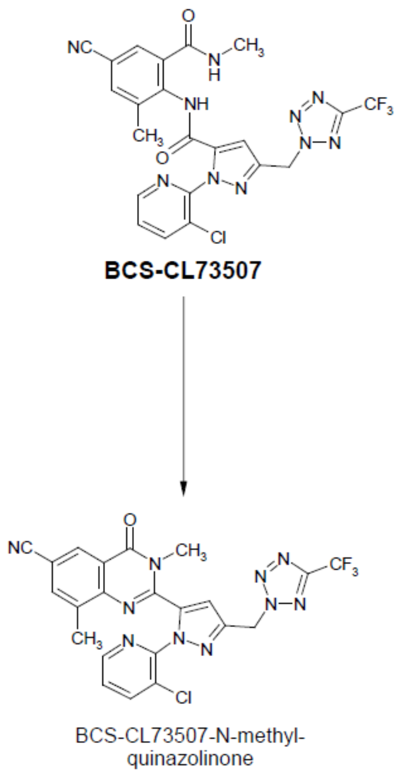
Plant metabolism studies were conducted on tomatoes (soil drench), apples (spray application), potatoes (in-furrow application and spray application), lettuce (spray application), rice (granular and spray application) and maize (seed treatment). The studies were conducted with tetraniliprole labelled with ^{14}C on either the pyrazole-carboxamide or on the phenyl-carbamoyl position.

Little metabolism of tetraniliprole was observed in these studies, with parent compound representing the main and in some cases only component of the residue in all edible matrices of primary crops.

The only other compound detected in the edible matrices was BCS-CL73507-N-methyl-quinazolinone, which accounted for ≤ 0.001 mg/kg in all edible matrices. In most of the non-edible matrices, for example in tomato leaves, N-methyl-quinazolinone was detected in higher concentrations than in edible matrices, but still far less prominent than parent compound. In general, soil drench, in-furrow application and granular treatment showed very low concentrations in the plant matrices, with a maximum of only 0.004 mg/kg for rice kernels. The concentration of parent compound and BCS-CL73507-N-methyl-quinazolinone was ≤ 0.001 mg/kg. Spray applications yielded higher concentrations of residues, especially in lettuce with a maximum concentration of 4.1 mg/kg. No metabolic degradation of parent was observed in lettuce for either label. The residues in apple fruits were mostly located in the surface wash with only small amounts in the actual fruits. 92–96 per cent of the TRR in the surface wash of apple fruits was parent.

The only observed metabolic reaction in primary crops for both labels was an intra-molecular condensation (cyclisation) leading to BCS-CL73507-N-methyl-quinazolinone as summarised below in Figure 1:

Figure 1: Proposed metabolic pathway for tetraniliprole (BCS-CL73507) in plants



Target animals

Metabolism studies were conducted on lactating goats and laying hens using tetraniliprole radio-labelled at three different positions: at the pyrazole-carboxamide, the two position of the pyridinyl ring and in the tetrazoylyl moiety.

Tetraniliprole was moderately metabolized in lactating goats. Parent compound was the main compound in all samples with the exception of fat, where the main compound was the metabolite BCS-CL73507-N-methyl-quinazolinone. Metabolite BCS-CL73507-benzylalcohol was also a predominant metabolite in goat milk.

Parent contributed 65–68 per cent TRR in goat muscle, 53–62 per cent TRR in liver, 59–71 per cent TRR in kidney and 24–30 per cent TRR in milk. In the lactating cow transfer study, parent was the predominant residue in milk and tissues with the exception of fat where BCS-CL73507-N-methyl-quinazolinone was found at higher levels.

In the goat metabolism study, metabolite BCS-CL73507-N-methyl-quinazolinone contributed 62–72 per cent TRR in goat fat, 23–28 per cent in muscle, up to 13 per cent in milk and up to 14 per cent in kidney.

Metabolite BCS-CL73507-benzyl alcohol was found at 9.0–11 per cent TRR in milk, 6.9–8.9 per cent TRR in liver and 6.0–6.2 per cent TRR in kidney. This metabolite was also included in the lactating cow transfer study with residues in each tissue and milk either being <LOQ or lower than parent and BCS-CL73507-N-methyl-quinazolinone.

Tetraniliprole was extensively metabolized in laying hens. Parent compound accounted for 4.2–13.8 per cent TRR in eggs, 3.7–10.0 per cent TRR in muscle, 25.7–54.6 per cent TRR in fat and 1.6–4.8 per cent TRR in liver. Metabolite BCS-CL73507-N-methyl-quinazolinone contributed ≤7.4 per cent TRR in eggs and tissues, while metabolite BCS-CL73507-benzyl alcohol contributed ≤8.6 per cent TRR In general, liver contained a higher number of metabolites in comparable amounts to that in muscle, fat and eggs. In the study using the pyridinyl-label, the results differed due to label specificity of metabolites originating from cleavage of the pyridinyl moiety followed by degradation and/or binding to the sample matrices.

4.2 Analytical methods and storage stability

Plant commodities

Residues of tetraniliprole and its metabolite BCS-CL73507-N-methyl-quinazolinone in/on samples of plant origin were extracted from the different matrices using water and acetonitrile. The extract was filtered and the extracted residue levels were determined by LC/MS/MS. Residues of tetraniliprole and its metabolite were quantified by comparison with stable isotope labelled standards. The LOQ was 0.01 mg/kg for each analyte in all matrices. Recoveries from control samples fortified at 0.01 mg/kg and above were within acceptable limits.

Animal commodities

In the animal transfer study provided in support of the application, residues of tetraniliprole and its metabolites BCS-CL73507-N-methyl-quinazolinone and BCS-CL73507-benzylalcohol in milk and tissue samples were quantitated by (LC/MS/MS) using stable isotopically labelled internal standards. For milk, cream, skim milk, muscle, kidney, and liver matrices, extraction involved maceration with acetonitrile/water. Fat samples were extracted with an acetonitrile/water/hexane mixture. All extracts were filtered and extracted again with acetonitrile/water. The internal standards were added and the samples passed through a C18 cartridge prior to analysis by LC/MS/MS. The LOQ was 0.01 mg/kg for each analyte (in parent equivalents). Recoveries from fortified control samples were within acceptable limits.

Storage stability

Tetraniliprole and its metabolite BCS-CL73507-N-methyl-quinazolinone were stable for 24 months in frozen storage at ≤ –18°C, in tomato (fruit), dry bean (seed), wheat (grain), rape (seed) and grapes.

In the residue trials submitted, all samples were maintained under freezer conditions, (ie –18°C) prior to analysis and tested within 22 months of collection. This is acceptable for the purposes of the current application.

4.3 Residue definition

Plant commodities

Little metabolism of tetraniliprole was observed in the available plant metabolism studies, with parent compound representing the main and in some cases only component of the residue in all edible matrices of primary crops.

A residue definition of parent compound is recommended for commodities of plant origin. This definition is suitable for both enforcement and dietary risk assessment.

Animal commodities

In the goat metabolism study, parent compound was the main compound in all samples with the exception of fat, where the main compound was the metabolite tetraniliprole-N-methyl-quinazolinone (BCS-CQ63359). Metabolite tetraniliprole-benzylalcohol (BCS-CZ91631) was also a predominant metabolite in goat milk.

Parent is a suitable marker for enforcement as it was the main component in most matrices, except fat, in the goat metabolism studies. A residue definition of parent compound only will be recommended for commodities of animal origin for enforcement. For risk assessment the definition will also include BCS-CL73507-N-methyl-quinazolinone (BCS-CQ63359) and BCSCL73507-benzylalcohol (BCS-CZ91631).

4.4 Residues in food and animal feeds

Almonds

The proposed use on almonds is for up to two applications at 2.5 g ai/100L with a 14–21 day re-treatment interval and a 10 day withholding period. The label restricts the maximum rate for each application to 60 g ai/ha.

In Australian almond trials, sampling at the proposed withholding period of 10 days did not occur and therefore the seven day sample will be considered. Residues of parent tetraniliprole in almond kernels at seven or more days after two applications at 2 g ai/100 L (0.8× proposed) with a 14–16 day interval between applications were <0.01 and 0.01 mg/kg.

In North American almond trials, residues of parent tetraniliprole in almond nutmeat at 10 days after the last of four applications at 45 g ai/ha (0.75× proposed) were <0.01 (2), 0.01 (2) and 0.02 mg/kg.

Based on the combined Australian and overseas data set, the OECD MRL calculator recommends an MRL of 0.03 mg/kg. The STMR is 0.01 mg/kg (n = 7). An MRL of 0.05 mg/kg is recommended for tetraniliprole on TN 0660 Almonds in conjunction with a 10 day withholding period.

For almond hulls, the combined Australian and overseas data set was 0.25, 0.91, 0.97, 1.20, 1.87, 2.05 and 2.23 mg/kg. The OECD MRL calculator recommends an MRL of 5 mg/kg. The STMR is 1.20 (n = 7). An MRL of 5 mg/kg is recommended for tetraniliprole on almond hulls in conjunction with a 10 day withholding period.

Macadamias

The proposed use on macadamias is for up to three applications at 2.5 g ai/100L with a 14–28 day re-treatment interval and a 10 day withholding period. The label restricts the maximum rate for each application to 60 g ai/ha.

In Australian trials, residues of parent tetraniliprole in macadamias at seven days after the last of three applications at 3.10 g ai/100 L (1.2× proposed) were <0.01 (n = 2) mg/kg. Residues were also <0.01 (n = 2) at 14 days after the last of two applications at 4.14 g ai/100 L (1.7× proposed).

In supporting North American pecan trials, residues of parent tetraniliprole in pecan nuts at 10 days after the last of four applications at 45 g ai/ha (0.75× proposed) were <0.01 (n = 8) mg/kg. Data for pecans is considered relevant to macadamias as both are expected to have a lower residue potential than almonds.

An MRL of *0.01 mg/kg is recommended for tetraniliprole on TN 0669 Macadamia nuts in conjunction with a 10 day withholding period.

Pome fruits

The critical GAP for pome fruit is for up to three applications at 2 g ai/100 L applied 14 days apart with a seven day withholding period. The draft label restricts the total application rate to pome fruit to 60 g ai/ha for each application.

In Australian trials involving three applications at approximately 4 g ai/100 L (2× proposed), highest residues of parent tetraniliprole in apples and pears at seven or more days after the last application were 0.06, 0.11, 0.14, 0.35 and 0.38 mg/kg. Scaled for the proposed rate, residues were 0.03, 0.06, 0.07, 0.18 and 0.19 mg/kg.

In Australian trials involving three applications at 2.59 g ai/100 L (1.3× proposed), highest residues of parent tetraniliprole in apples and pears at seven or more days after the last application were 0.05, 0.06 and 0.15 (3) mg/kg. Scaled for the proposed rate residues were 0.04, 0.05 and 0.12 (3) mg/kg.

In overseas trials involving three applications at approximately 60 g ai/ha (label rate), highest residues of parent tetraniliprole in apples and pears at seven or more days after the last application were 0.04, 0.05, 0.06, 0.07, 0.08, 0.08, 0.09, 0.10, 0.10, 0.11, 0.11, 0.13, 0.13, 0.13, 0.14, 0.15, 0.15, 0.16, 0.16, 0.17, 0.17, 0.20, 0.20, 0.22 and 0.24 mg/kg.

The combined data set suitable for MRL recommendation is 0.03, 0.04, 0.04, 0.05, 0.05, 0.06, 0.06, 0.07, 0.07, 0.08, 0.08, 0.09, 0.10, 0.10, 0.11, 0.11, 0.12, 0.12, 0.12, 0.13, 0.13, 0.13, 0.14, 0.15, 0.15, 0.16, 0.16, 0.17, 0.17, 0.18, 0.19, 0.20, 0.20, 0.22 and 0.24 mg/kg. The OECD MRL calculator recommends an MRL of 0.4 mg/kg. The STMR is 0.12 mg/kg. An MRL of 0.5 mg/kg is recommended for tetraniliprole on FP 009 Pome fruits, in conjunction with a seven day withholding period.

The highest processing factor for parent tetraniliprole concentration in dried apple pomace was 7.3×. Applying this processing factor to the highest residue in fruit of 0.24 mg/kg gives a HR-P of 1.75 mg/kg. An MRL of 3 mg/kg is recommended for tetraniliprole on AB 0226 Apple pomace, dry. The STMR-P for the livestock dietary burden using the average processing factor is 0.85 mg/kg (0.12 × 7.1).

Stone fruits

The critical GAP for stone fruit is for up to three applications at 2.5 g ai/100 L at 10 day intervals in conjunction with a three day withholding period. The draft label restricts the total application rate to stone fruit to 60 g ai/ha for each application.

In Australian trials, highest residues of parent tetraniliprole in nectarines and peaches at three or more days after the last of three applications at 4 g ai/100 L (1.6× proposed) were 0.04, 0.08, 0.13, 0.17 and 0.27 mg/kg. Scaled for application rate estimated residues are 0.03, 0.05, 0.08, 0.11 and 0.17 mg/kg.

In Australian trials, highest residues of parent tetraniliprole in nectarines and peaches at three or more days after the last of three applications at approximately 2.5 g ai/100 L (label rate) were 0.05, 0.06, 0.13, 0.14 and 0.24 mg/kg.

In Australian trials, highest residues of parent tetraniliprole in cherries at three or more days after the last of three applications at approximately 2.5 g ai/100 L (label rate) were 0.04 and 0.13 mg/kg.

In overseas trials, residues of parent tetraniliprole in peaches at three days after the last of three applications at 60 g ai/ha were 0.08 and 0.15 mg/kg. If the available data at five days after the last application is considered, residues were 0.04, 0.05, 0.06, 0.06, 0.07, 0.07, 0.09, 0.10, 0.10, 0.11, 0.17, 0.17, 0.18, 0.22, 0.38 and 0.46 mg/kg.

In overseas trials, residues of parent tetraniliprole in cherries at three days after the last of three applications at 60 g ai/ha were 0.26 and 0.28 mg/kg. If the available data at five days after the last application is considered, residues were 0.09, 0.13, 0.24, 0.26, 0.28, 0.28, 0.33, 0.39, 0.45, 0.51, 0.65 and 0.67 mg/kg.

The overseas trials suggest there is a tendency towards higher residues in cherries than in other stone fruit.

If data for a three to five day PHI is considered together (noting residues often increased at later PHIs), the combined dataset for peaches and nectarines 0.03, 0.04, 0.05, 0.05. 0.05, 0.06, 0.06, 0.06, 0.07, 0.07, 0.08, 0.09, 0.10, 0.10, 0.11, 0.11, 0.13, 0.14, 0.17, 0.17, 0.17, 0.18, 0.22, 0.24, 0.38 and 0.46 mg/kg. The OECD MRL calculator recommends an MRL of 0.6 mg/kg. The STMR is 0.103 mg/kg (n = 26). An MRL of 0.7 mg/kg is recommended for tetraniliprole on FS 0012 Stone fruits (except cherries), in conjunction with a three day harvest withholding period.

If data for a three to five day PHI is considered together (noting residues often increased at later PHIs), the combined dataset for cherries is 0.04, 0.09, 0.13, 0.13, 0.24, 0.26, 0.28, 0.28, 0.33, 0.39, 0.45, 0.51, 0.65 and 0.67 mg/kg. The OECD MRL calculator recommends an MRL of 1.5 mg/kg (Unrounded MRL of 1.099 mg/kg), the STMR is 0.280 mg/kg (n = 14). An MRL of 1 mg/kg is recommended for tetraniliprole on FS 0013 cherries, in conjunction with a three day harvest withholding period.

The highest processing factor for concentration of parent tetraniliprole on processing of plums to prunes was 4.6×. Applying this processing factor to high residue of 0.46 for stone fruit (other than cherries) gives a HR-P of 2.12 mg/kg. An MRL of 3 mg/kg is recommended for tetraniliprole on DF 0014 Prunes. The STMR-P is 0.42 mg/kg (0.103 × 4.1). Given apricots are also commonly dried in Australia, a similar MRL of 3 mg/kg is also recommended for tetraniliprole on DF 240 apricots, dried.

4.5 Crop rotation

Almonds, macadamias, pome fruit and stone fruit are not considered to be rotational crops. It is not necessary to consider residues of tetraniliprole in following crops for this application.

4.6 Residues in animal commodities

Mammalian livestock

Almond hulls and apple pomace are considered to be livestock feeds in Australia. The estimated dietary burden is 0.3 ppm for beef cattle and 0.2 ppm for dairy cattle, from feeding of almond hulls at 10 per cent of the diet and apple pomace at 20 per cent for beef cattle and 10 per cent for dairy.

The estimated residues in tissues and milk and required MRLs from feeding at 0.3 ppm for beef cattle and 0.2 ppm for dairy cattle are calculated below by scaling from residues observed in the feeding study after dosing at 0.9 ppm.

Cattle

Table 6: Estimated residues in Animals

Feeding level (ppm)	Milk	Muscle	Liver	Kidney	Fat
	Parent Tetraniliprole residue (total residue for risk assessment) (mg/kg)				
0.9	<0.01 (<0.03)	<0.01 (<0.03)	0.0369 (0.0569)	<0.01 (<0.03)	<0.01 (0.0527)
0.3: beef, estimated burden	-	<0.01 (<0.03)	0.0123 (0.019)	<0.01 (<0.03)	<0.01 (0.018)
0.2: dairy, estimated burden	<0.01 (<0.03)	-	-	-	-
Established MRLs	-	-		-	-
Recommended MRLs	*0.01	*0.01		0.02 (offal)	

Poultry

The OECD feed calculator does not list almond hulls or apple pomace as feeds for poultry in Australia. Poultry commodity MRLs for tetraniliprole will be established at the LOQ for the analytical method. The following MRLs are recommended:

PE 0112 Eggs *0.01 mg/kg

PO 0111 Poultry, edible offal *0.01 mg/kg

PM 0110 Poultry meat *0.01 mg/kg

4.7 Spray drift

In the dairy cattle transfer study dosing at 0.9 ppm gave a highest parent residue of 0.0369 mg/kg in liver. The feeding level for residues of parent in liver to be at the LOQ is 0.244 ppm. If a Regulatory Acceptable Level of 0.244 ppm is entered into the APVMA spray drift risk assessment tool the following buffer zones instructions are required for protection of international trade:

Table 7: Buffer zone instructions for protection of international trade

Type of target canopy	Livestock areas
2 metres tall and smaller, maximum dilute water rate of 1000 L/ha	Not required
Taller than 2 metres (not fully-foliated), maximum dilute water rate of 2400 L/ha	10 metres
Taller than 2 metres (fully-foliated), maximum dilute water rate of 2400 L/ha	5 metres

4.8 Dietary risk assessment

The chronic dietary exposure to tetraniliprole 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 tetraniliprole is equivalent to <1 per cent of the ADI. It is concluded that the chronic dietary exposure to tetraniliprole is acceptable.

An Acute Reference Dose was considered to be unnecessary for tetraniliprole. A National Estimated Short Term Intake (NESTI) calculation for acute exposure is not required.

4.9 Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 8).

Table 8: Amendments to the APVMA MRL Standard—Table 1

Amendments to Table 1			
Compound		Food	MRL (mg/kg)
ADD:			
Tetraniliprole			
TN	0660	Almonds	0.05

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
DF	0240	Apricots, dried	3
FS	0013	Cherries	1
MO	0105	Edible offal (mammalian)	0.02
PE	0112	Eggs	*0.01
TN	0669	Macadamia nuts	*0.01
MM	0095	Meat (mammalian)	*0.01
ML	0106	Milks	*0.01
FP	0009	Pome fruits	0.5
PO	0111	Poultry, edible offal of	*0.01
PM	0110	Poultry meat	*0.01
DF	0014	Prunes	3
FS	0012	Stone fruits (except Cherries)	0.7

Table 9: Amendments to the APVMA MRL Standard—Table 3

Amendments to Table 3	
Compound	**Residue**
ADD:	
Tetraniliprole	Commodities of plant origin: Tetraniliprole Commodities of animal origin for enforcement: Tetraniliprole Commodities of animal origin for dietary exposure assessment: Sum of tetraniliprole, 2-[1-(3-chloropyridin-2-yl)-3-{[5(trifluoromethyl)-2H-tetrazol-2-yl]methyl}-1H-pyrazole-5-yl]-3,8-dimethyl-4-oxo-3,4-dihydroquinazoline-6-carbonitrile (BCS-CQ63359) and 2-(3-chloro-2-pyridyl)-N-[4-cyano-2-(hydroxymethyl)-6-(methylcarbamoyl)phenyl]-5-[[5-(trifluoromethyl)tetrazol-2-yl]methyl]pyrazole-3-carboxamide (BCS-CZ91631), expressed as tetraniliprole

Table 10: Amendments to the APVMA MRL Standard—Table 4

Amendments to Table 4		
Compound	**Animal feed commodity**	**MRL (mg/kg)**
ADD:		
Tetraniliprole		
	Almond hulls	5
AB 0226	Apple pomace, dry	3

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Pome fruit and stone fruit are considered to be major export commodities, as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed feeds produced from treated pome fruit pomace and almond hulls. Residues in these commodities resulting from the use of Vayego 200 SC Insecticide may have the potential to unduly prejudice trade.

Australia typically exports between 2000–5000 tonnes of apples per year (Australian Horticulture Statistics Handbook 2017–18). For the year ending 2018, Australia exported 5060 tonnes. The main markets were PNG, the UK, Italy, Sri Lanka and Hong Kong.

For the year ending 2018, Australia exported 12,467 tonnes of pears. The main markets were New Zealand, Indonesia, Canada, Singapore and India.

For the year ending June 2018, Australia exported 17,769 tonnes of fresh summerfruit (apricots, nectarines/peaches and plums). Major export markets for apricots were Saudi Arabia, UAE, Hong Kong, Singapore and Kuwait. Major export markets for nectarines/peaches were China, UAE, Singapore, Saudi Arabia and Hong Kong. Major export markets for plums were Hong Kong, Singapore, China and Indonesia.

For the year ending June 2018, Australia exported 4114 tonnes of cherries. The main export markets were Hong Kong, China, Singapore, Vietnam and Taiwan.

The significant export markets for Australian beef, sheep, pig meat and offals are listed in the APVMA Regulatory Guidelines—Data Guidelines: Agricultural, Overseas trade (Part 5B).

5.2 Overseas registrations and approved label instructions

The applicant indicated that tetraniliprole products are undergoing regulatory consideration in Canada, USA and Mexico. Canada has recently published its proposed MRLs for tetraniliprole[2]. The applicant also indicated that Vayego Insecticide is registered in Zimbabwe, Korea and Cambodia.

5.3 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

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[2] canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/consultations/proposed-maximum-residue-limit/2020/tetraniliprole/document.html

Codex CXLs when importing foods. Tetraniliprole has not been considered by Codex. The following relevant international MRLs have been established for tetraniliprole (Table 11).

Table 11: Proposed Australian and current international MRLs for Tetraniliprole

Commodity	Tolerance for residues arising from the use of tetraniliprole (mg/kg)					
	Australia	EU	Japan	Korea	New Zealand	Canada (proposed)
Residue definition	Tetraniliprole (for MRLs)	-	Tetraniliprole (for compliance)	-	Tetraniliprole (for compliance)	Tetraniliprole
Pome fruit	0.5	-	-	-	0.2	0.5
Apple		-	1	0.7	-	-
Pear		-	0.5	0.2	-	-
Stone fruit {except cherries}	0.7	-	-	-	-	1 (Stone fruit)
Apricot		-	1	-	-	-
Peach		-	1	0.5	-	-
Plum		-	1 (mume plum)	0.2	-	-
Prunes	3	-	0.1 (Japanese plum including prune)	-	-	-
Apricots, dried	3	-	-	-	-	-
Cherries	1	-	1	-	-	-
Edible offal (mammalian)	0.02	-	-	-	-	0.3
Meat (mammalian)	*0.01	-	-	-	-	0.02
Milks	*0.01	-	-	-	-	0.05

No MRLs for tetraniliprole are established in Taiwan

5.4 Potential risk to trade

A final determination on if the proposed uses on stone fruit and pome fruit pose an undue risk to international trade will be made following completion this consultation. Industry stakeholders are invited to comment on the potential risk to trade and the ability for relevant industries to manage that risk.

Export of treated produce containing finite (measurable) residues of tetraniliprole 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.

Appropriate MRLs have generally not been established in overseas markets. Noting that overseas registrations of Vayego are on-going and that the applicant plans to submit to Codex based on the NAFTA Joint Review outcomes, the following export advice statement has been proposed:

Export of treated produce

Growers should note that suitable MRLs or import tolerances may not exist in all markets for produce treated with Vayego 200 SC. If you are growing produce for export, please check with Bayer CropScience for the latest information on MRLs and import tolerances and for advice on any potential trade issues and their management.

For animal commodities, LOQ MRLs are proposed for all commodities except for mammalian offal where a MRL of 0.02 mg/kg is proposed based on an estimated level of parent tetraniliprole residue in liver of 0.0123 mg/kg. The depuration phase of the feeding study involving dosing at 90 ppm suggests that the half-live for parent tetraniliprole in liver is ~one days. By-products such as almond hulls and apple pomace would not normally be fed within 60 days of slaughter for export without declaration. Detectable residues of tetraniliprole are not expected to occur in animal commodities for export as a result of the proposed uses.

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Vayego 200 SC Insecticide was of low oral, dermal and inhalational toxicity. It was not a skin or eye irritant, and was not a skin sensitiser. A dermal study with tetraniliprole had a no observed adverse effect level of 1000 mg/kg bw/day. Additional supporting information for low toxicity by dermal exposure was the estimated dermal absorption factor for the product in humans of 0.23 per cent.

6.2 Occupational exposure

Exposure during use

The product is proposed to be used as an insecticide in pome and stone fruit, almonds and macadamias via spray application. The recommended maximum use rate is 0.3 L product/ha, equivalent to 60 g tetraniliprole/ha, with a recommended maximum of three applications per season. A quantitative assessment of exposure was not required, due to the low systemic hazard of the product.

Exposure during re-entry or rehandling

A quantitative assessment of exposure during re-entry to treated crops was not required, due to the low systemic hazard of the product.

6.3 Public exposure

The product is intended for professional use only and is not intended for application to areas accessible to the general public. An assessment of potential exposure by spray drift indicated that bystander buffer zones are not required, due to the low systemic hazard of the product.

6.4 Recommendations

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

First aid instructions

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

Safety directions

Wash hands after use.

Precautionary (warning) statements

Not required.

7 ENVIRONMENTAL ASSESSMENT

7.1 Fate and behaviour in the environment

Soil

The degradation of tetraniliprole was examined in ten aerobic soils and three anaerobic soils under laboratory conditions at 20°C. After 120 days, mineralisation reached a maximum of 19 per cent of applied radioactivity (AR) and bound residues accounted for up to 10 per cent AR. The degradation of tetraniliprole followed bi-phasic kinetics with aerobic DT50 values derived for modelling ranging 28–171 days (geomean 86 days) and anaerobic DT50 values ranging 161–178 days (geomean 171 days). The rate of dissipation was relatively variable under field conditions with DT50 values ranging 25–433 days (geomean 165 days).

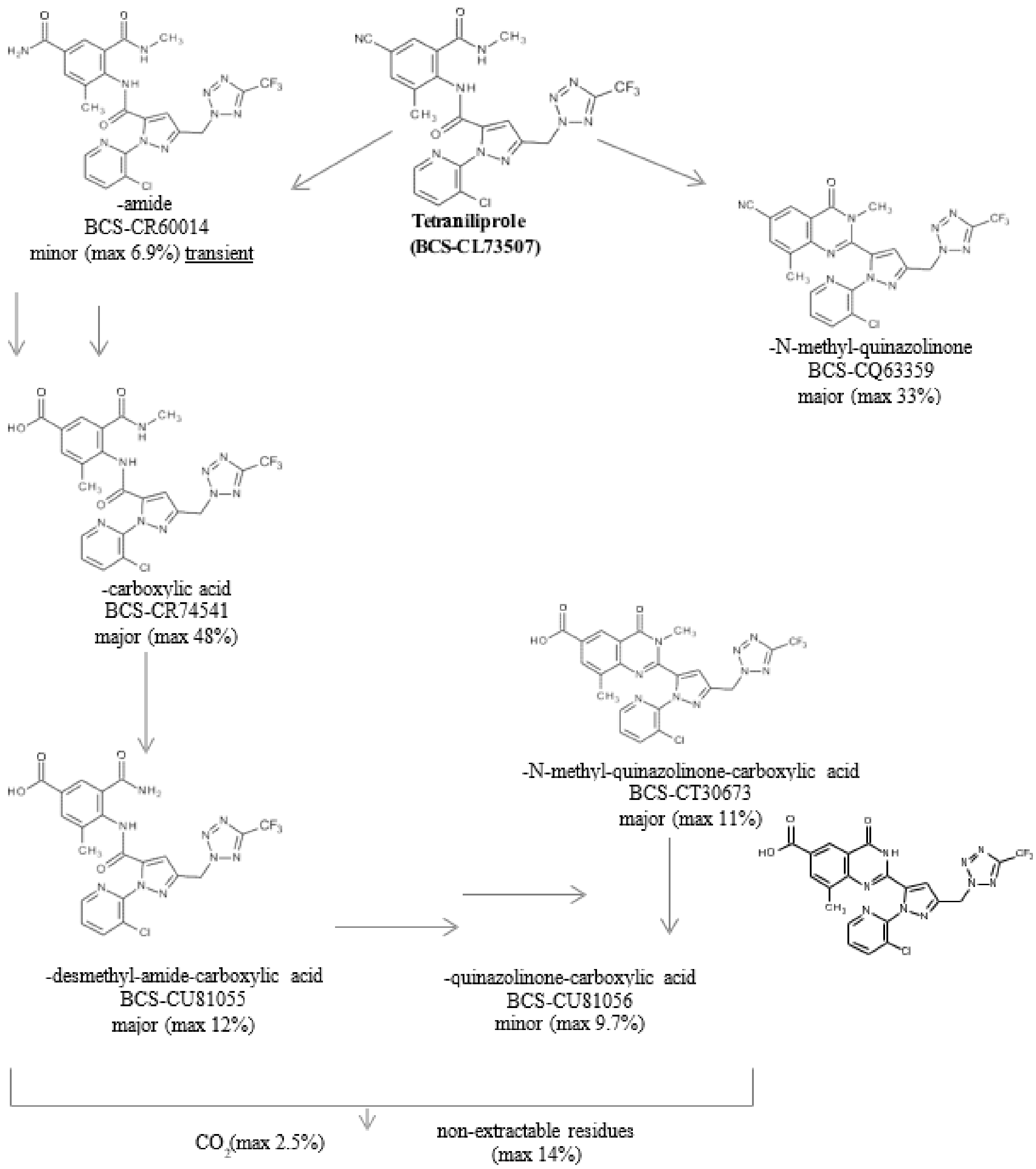
For photolytic degradation in soil, the experimental half-lives for tetraniliprole were 27 and 44 days in the irradiated and dark samples, respectively. The DT50 of tetraniliprole under environmental conditions was calculated to be 82 solar summer days at Phoenix, USA.

The major routes of dissipation of tetraniliprole in soil are transformation and biodegradation with the following processes involved (Figure 2):

- cyclization of tetraniliprole to result in the formation of BCS-CQ63359 and BCS-CT30673
- hydrolysis of the nitrile group of tetraniliprole to result in BCS-CR60014
- hydrolytic deamination of the amino group to result in BCS-CR74541
- demethylation of the carboxylic acid amide of BCS-CR74541 to result in BCS-CU81055
- cyclization of BCS-CR74541 to result in formation of BCS-CT30673
- cyclization of BCS-CU81055 to result in BCS-CU81056
- demethylation of the pyrimidine ring of BCS-CT30673 to result in BCS-CU81056.

The adsorption of tetraniliprole has been determined in six soils and one sediment. KF values ranged 1.2–10 mL/g (mean 5.9 mL/g). Based on regression analysis, the KF was predicted to be 2.9 mL/g at 1 per cent OC. Binding of tetraniliprole strengthened once adsorbed to the soil. KF, OC values ranged 133–411 mL/g in soils and 1920 mL/g in sediment, indicating high adsorption/ low mobility in soil.

Figure 2: Proposed degradation pathway for tetraniliprole in soil



Water and sediment

Tetraniliprole has low solubility in water (~1.0 mg/L). Hydrolysis of tetraniliprole is pH dependent with DT50 values of 265–287 days at pH 4, 39–58 days at pH 7, and 0.75–1.3 days at pH 9. One degradation product was identified as BCS-CQ63359 with a maximum amount of 100 per cent AR at 30 days after treatment (pH 9, 20°C). Therefore, hydrolysis is relatively slow in acidic and neutral water, but is an important route of dissipation in alkaline water.

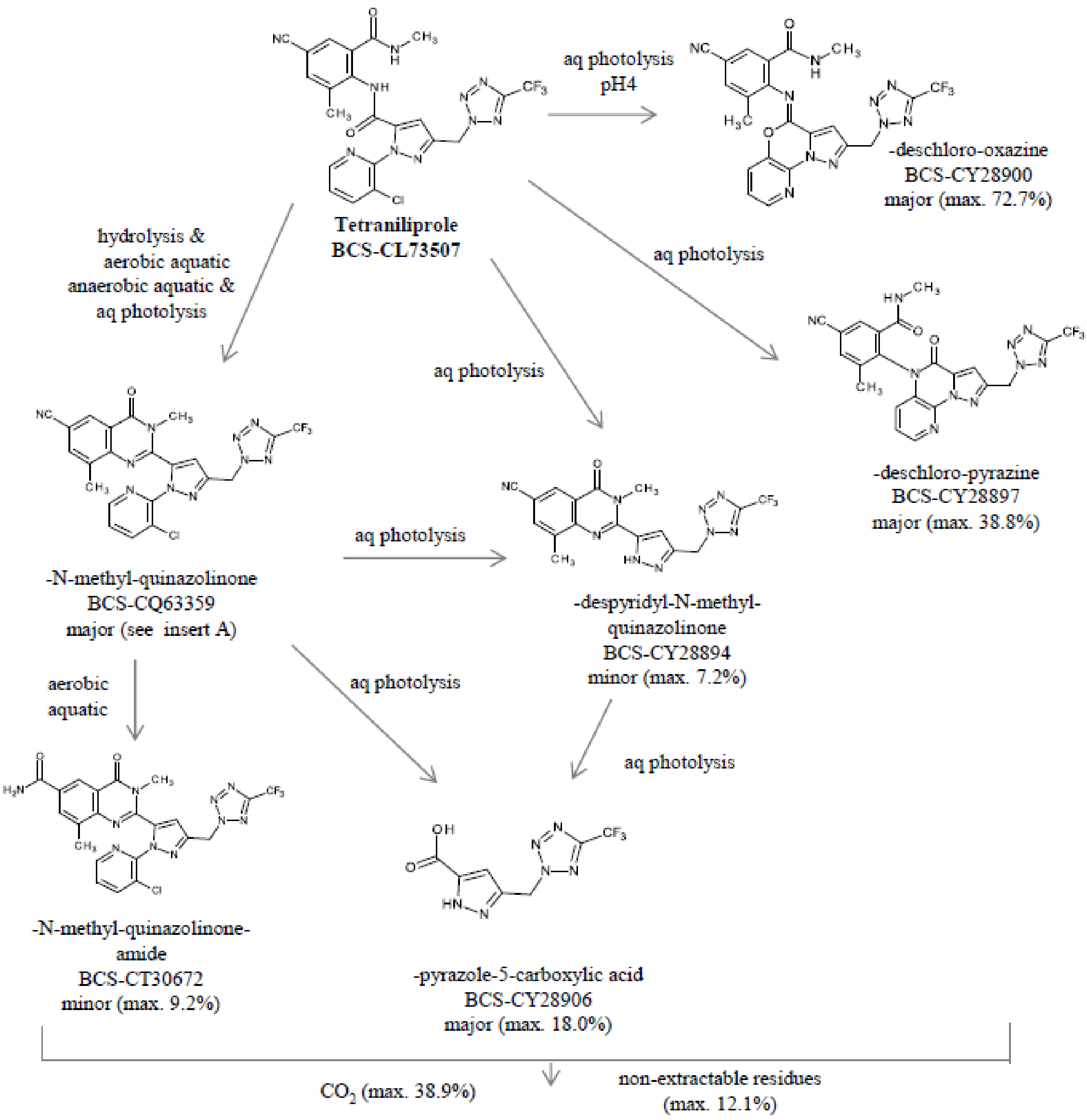
Rates of aqueous photolysis were determined in sterile pH 4 buffer (DT50 10 summer days at Phoenix, USA) and in sterile natural water at pH 8.5–9.0 (DT50 4.7–4.9 summer days at Tokyo, Japan).

Aquatic metabolism of tetraniliprole was studied in four water sediment systems. Mineralization and bound residues were low (up to 0.2 per cent and 10 per cent AR, respectively). DT50 values were variable and ranged 11–218 days in the entire system. The longest half-life in the system was applied in the risk assessment. The proposed degradation pathway for tetraniliprole in water is provided in Figure 3.

Air

Tetraniliprole has low vapour pressure and low Henry's Law constant indicating that this chemical is unlikely to volatilise from soil or water surfaces. The half-life for tetraniliprole in the atmosphere by photochemical oxidative degradation is less than 10 hours indicating that it does not have potential for long range transport in the atmosphere.

Figure 3: Proposed degradation pathway for tetraniliprole in water



[A] BCS-CQ63359 max occurence %AR: hydrolysis 99.6%, aerobic aquatic 84.8%, anaerobic aquatic 40.4%, photolysis at pH 4 0%, photolysis in natural water 39.2%

7.2 Effects and associated risks to non-target species

Terrestrial vertebrates

Tetraniliprole has low toxicity to mammals (LD_{50} >2000 mg ac/kg bw, *Rattus norvegicus*) and birds (LD_{50} >2000 mg ac/kg bw, three species tested). Following long-term dietary administration in reproduction studies, reduced body weights of F2 generation was observed in mammals at doses as low as 1361 mg ac/kg bw/d (NOEL 307 mg ac/kg bw/d, *Rattus norvegicus*) and reduced 14 day old survivor weights was observed in birds at doses as low as 128 mg ac/kg bw/d (NOEL 43 mg ac/kg bw/d, *Anas platyrhynchos*).

The major potential routes of exposure to terrestrial vertebrates are considered to be feeding on food items (eg vegetation and invertebrates) directly contaminated from spray application of the product. The screening level assessment assumed that terrestrial vertebrates feed exclusively on over sprayed food items within the treatment area. Risks were determined to be acceptable at the screening level. Therefore, risks to terrestrial vertebrates were considered to be acceptable and no specific protection statements are required.

Aquatic species

Tetraniliprole has relatively low toxicity to aquatic vertebrates such as fish (LC_{50} >10 mg ac/L, four species tested), high toxicity to aquatic invertebrates (lowest EC_{50} 0.071 mg ac/L, *Daphnia magna*), high toxicity to sediment-dwellers (lowest EC_{50} 0.23 mg ac/L or LC_{50} 0.034 mg ac/kg dry sediment, *Chironomus* spp.), moderate toxicity to algae (lowest ErC50 1.4 mg ac/L, *Skeletonema costatum*), and relatively low toxic to aquatic plants (E_rC_{50} >6.6 mg ac/L, *Lemna gibba*). Following long-term exposure, tetraniliprole reduced total length of fish fry at concentrations as low as 5.0 mg ac/L (NOEC 2.5 mg ac/L, *Pimephales promelas*), reduced reproduction and increased immobilisation of aquatic invertebrates at concentrations as low as 0.024 mg ac/l (NOEC 0.013 mg ac/L, *Daphnia magna*), and reduced emergence of sediment-dwellers in a dose-dependent manner (EC_{10} 0.00071 mg ac/L or EC_{10} 0.0060 mg ac/kg dry sediment, *Chironomus riparius*). Tetraniliprole does not bioconcentrate in fish (BCF <1).

The major potential routes of exposure of aquatic species are considered to be spray drift or runoff from the treatment area. Although the product is not applied to water, a screening level risk assessment assumed the worst-case scenario of a direct overspray of shallow aquatic habitat in order to determine which aquatic species are not at risk. Acceptable risks could be concluded at the screening level for aquatic vertebrates, algae and aquatic plants.

The Regulatory Acceptable Level (RAL) for protection of sensitive aquatic species (invertebrates and sediment dwellers) was based on the NOEC of 0.00071 mg ac/L for chronic toxicity to sediment dwellers. A spray drift assessment for vertical sprayers at 60 g ac/ha determined that buffer zones of five to 25 metres are required for the protection of natural aquatic areas, depending on the height of target canopy and the degree of foliation. Runoff risks were determined to be acceptable provided the slope of the treatment area is relatively gentle (ie, no greater than a four per cent slope). In addition to general spray drift restraints, protection statements and restraints are required for aquatic species.

Bees

Tetraniliprole has high toxicity to bees. Following acute contact exposure to tetraniliprole, *Apis mellifera* was considerably more sensitive than *Bombus terrestris* (LD_{50} 0.41–0.44 µg ac/bee versus 22–94 µg ac/bee). In an aged foliar residues test at rates up to 100 g ac/ha, the RT_{25} value was determined to be less than three hours indicating that foliar residues are unlikely to cause adverse effects if the product is applied in the time period between two hours prior to sunset and eight hours prior to sunrise. Following acute oral exposure to tetraniliprole, the LD_{50} values ranged 0.010–0.050 µg ac/bee for both species of bees. Long-term (10 day) dietary exposure to 0.014 µg ac/bee resulted in 50 per cent mortality and 23 per cent with behavioural abnormalities (NOAEL 0.0072 µg ac/bee). Acute and chronic effects bee brood occurred at similar exposure levels as adult bees. The acute LD_{50} is 0.013 µg ac/bee and chronic NOEL 0.01 µg ac/bee (100 per cent mortality of larvae was observed at 0.030 µg ac/bee).

A screening level risk assessment assumed the worst-case scenario of a direct overspray of blooming plants that are frequented by bees. Acceptable risks of contact toxicity to bees were concluded at the screening level. Therefore, mandatory buffer zones are not required for the protection of bees.

Residue studies demonstrated that tetraniliprole can move into bee relevant matrices in crop species. Even when applied post-bloom, residue data indicate that bees will be exposed to residues in pollen and nectar in the following season. Seven field studies examining post-bloom applications of a representative SC formulation at rates ranging from 45 to 78 g ac/ha in almonds, cherries, apples and citrus were undertaken to determine the specific uptake into bee-relevant matrices. Maximum residues of tetraniliprole at the next blooming period (3–87 DAA in citrus; 200–300 DAA in almonds, cherries and apples) were 454 µg ac/kg in pollen and 24 µg ac/kg in nectar. A risk assessment using these empirical maximum values indicate risks to larvae are acceptable; however, acceptable RQ values were marginally exceeded for acute and chronic dietary exposure of adults.

In addition to the standard laboratory tests for bees, a range of semi-field studies using honeybees and bumble bees were undertaken using a representative SC formulation of tetraniliprole. One study looked at effects on colony performance and loss under free foraging field conditions when exposed to tetraniliprole in sucrose solutions for 42 days. The observations were continued for 12 months. The NOAEL was 624 µg ac/kg diet, which is higher than the maximum measured concentration in pollen (454 µg ac/kg).

In conclusion, available data suggest that observable effects on bees in the field are unlikely at the proposed application rates. Based on the outcome of the assessment, protection statements and restraints are required for bees.

Other non-target arthropods

For other non-target arthropods, data were provided on contact toxicity of fresh dried residues of a representative SC formulation of tetraniliprole to the indicator species of predatory mite (*Typhlodromus pyri*) and parasitic wasp (*Aphidius rhopalosiphi*). The respective Tier 1 (glass plate) studies resulted in LR_{50} values of >44 g ac/ha and 0.63 g ac/ha. To further address the toxicity to *Aphidius rhopalosiphi*, an extended laboratory test on natural substrate (barley plants) was performed, which resulted in an LR_{50} 0.70 g ac/ha and an ER_{50} 0.40 g ac/ha. No adverse effects were observed in two additional species of predatory arthropods in extended laboratory tests on natural substrates (LR_{50} and ER_{50} >44 g ac/ha, *Coccinella septempunctata* and *Chrysoperla carnea*).

Beneficial (predatory and parasitic) arthropods could be directly exposed to the active constituent within the crop during treatment or as a result of spray drift. A Tier 2 assessment was conducted which considers higher-tier tests conducted under progressively more natural, realistic conditions. Risks to predatory arthropods were considered to be acceptable.

A higher tier assessment was necessary for parasitic arthropods. Semi-field studies were undertaken for three species of parasitic arthropods in three different vegetable crops (cabbage, tomato, and aubergine) at relevant rates from 20 to 60 g ac/ha, which indicated <50 per cent impact on parasitisation and hatching rates. Similarly, an orchard field study (apples) demonstrated low impact on parasitisation rates at environmentally relevant rates. As such, the proposed use of Vayego 200 SC Insecticide was considered to be compatible with IPM programs using beneficial arthropods.

Two full fauna off-crop field tests were also undertaken at rates up to 4.0 g ac/ha to examine the impact of spray drift on off-field communities. The community level NOER was determined to be 4.0 g ac/ha (highest rate tested) after eight weeks of observation. Although the highest rate tested is slightly lower than potential accumulated residues, it is expected that off-field communities are unlikely to be impacted under the proposed conditions of use. The off-field communities are considered to be a refuge for recolonization of communities that may be impacted within the treatment area.

In conclusion, risks to beneficial arthropods were considered to be acceptable and no specific protection statements are required.

Soil organisms

Tetraniliprole has low toxicity to soil macro-organisms such as earthworms (LC_{50corr} >448 mg ac/kg dry soil, *Eisenia fetida*). Following long-term exposure, reduced reproduction was observed at concentrations as low as 112 mg ac/kg dry soil (NOEC 63 mg ac/kg dw soil, *Folsomia candida*). Tetraniliprole did not affect soil processes such as nitrogen transformation at exaggerated soil concentrations (NOEC 3.0 mg ac/kg dry soil).

A screening level risk assessment assumed the worst-case scenario of a direct overspray of soil without interception. Risks to soil organisms were determined to be acceptable at the screening level, and therefore no specific protection statements are required.

Non-target terrestrial plants

Both Tier 1 and Tier 2 tests were undertaken for a representative SC formulation of tetraniliprole. Tier 1 tests used 10 different crop species at the limit rates of 15 or 200 g ac/ha to assess effects following pre-emergent or post-emergent exposure. Less than 25 per cent effect was observed in the tests (ie, ER_{25} and ER_{50} values >200 g ac/ha). Tier 2 tests were conducted on the most sensitive species from the Tier 1 tests, which confirmed ER_{25} and ER_{50} values are >200 g ac/ha. Based on the submitted data, it was concluded that risks of tetraniliprole to non-target terrestrial plants were acceptable and no specific protection measures are required.

7.3 Recommendations

The following restraints and protection measures are advised from the viewpoint of environmental safety:

RESTRAINTS:

DO NOT apply by a boom sprayer

DO NOT apply by aircraft.

DO NOT apply if heavy rains or storms are forecast within three days.

DO NOT irrigate to the point of runoff for at least three days after application.

DO NOT apply where the slope exceeds 4 per cent.

Table 12: Buffer zones for vertical sprayers

Type of target canopy and dilute water rate	Mandatory downwind buffer zones Natural aquatic areas
2 metres tall and shorter, maximum dilute water rate of 1000 L/ha	5 metres
Taller than 2 metres (not fully-foliated), maximum application rate of 300 mL/ha	25 metres
Taller than 2 metres (fully-foliated), maximum application rate of 300 mL/ha	15 metres

Protection statements

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

Highly toxic to bees. Tetraniliprole has a systemic action. DO NOT apply to crops pre-bloom or from the onset of flowering until flowering is complete. DO NOT allow spray drift to flowering weeds or flowering crops in the vicinity of the treatment area. Before spraying, notify beekeepers to move hives to a safe location with an untreated source of nectar and pollen, if there is potential for managed hives to be affected by the spray or spray drift. Risk to bees is reduced by spraying in early morning or late evening while bees are not foraging.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Tetraniliprole is an insecticide from the diamide chemical class and is active by ingestion. The product is intended to be used in Australia in almonds, macadamias, pome and stone fruit against certain Lepidopteran, Dipteran and Coleopteran pests. Tetraniliprole is classified as an IRAC group 28 insecticide for resistance management purposes. Tetraniliprole interferes with the ryanodine-sensitive calcium release channels which lead to loss of muscle control and subsequent insect immobility.

Tetraniliprole differs from most other group 28 insecticides as the spectrum of control expands beyond Lepidoptera control to include Coleoptera and Diptera plus other specific sucking pests. When applied to the plant, it has translaminar and xylem movement in and across plant material, allowing it to be ingested by the feeding insect. Once ingested the insect will rapidly stop feeding and subsequently die.

8.2 Efficacy and target crop/animal safety

Bayer CropScience Pty Ltd submitted data from 45 scientific trials conducted in Australia to satisfy the efficacy and crop safety criteria for Vayego 200 SC Insecticide, to control of the following insect pests when applied as a foliar broadcast spray:

- codling moth (*Cydia pomonella*), light brown apple moth (*Epiphyas postvittana* syn *Tortrix postvittana*, LBAM), garden weevil (*Phlyctinus callosus*), apple weevil (*Otiorhynchus cribricollis*) and Fuller's rose weevil (*Asynonychus cervinus*) in pome fruit
- oriental fruit moth (*Laspeyresia molesta*, syn *Cydia molesta*), carpophilus beetles (*Carpophilus* spp.), Mediterranean fruit fly (*Ceratitis capitata*), garden weevil (*Phlyctinus callosus*), apple weevil (*Otiorhynchus cribricollis*) and Fuller's rose weevil (*Asynonychus cervinus*) in stone fruit
- carpophilus beetles (*Carpophilus* spp.) in almonds
- sigastus weevil (also known as macadamia seed weevil) (*Kuschelorhynchus macadamiae*) in macadamias.

Efficacy

45 scientific trials in support of registration of new product Vayego 200 SC Insecticide, were conducted between 2015 and 2018.

Reference Products

A range of reference products were used across the major crops in the presented trials. The reference products were applied according to the respective label in most trials and provided appropriate treated controls for comparison with Vayego's efficacy.

Crops Tested

Data was derived from 44 small plot field trials and one laboratory trial, conducted in all Australian states except the Northern Territory, in pome and stone fruit, macadamia nuts and almonds. All major crops listed on the draft label were tested through a number of species and varieties for each group.

The pome group included apple varieties Gala, Pink Lady, Red Delicious, Granny Smith, Fuji and Rosy Glo, which was a reasonable range of varieties tested for codling moth and weevils in Queensland, New South Wales, Victoria, South Australia and Tasmania. Pears were only tested in one trial in Queensland, representing the proportion of pears grown to apples across the pome group in Australia.

The stonefruit group was tested in 19 trials, including peaches, nectarines and plums, proportionate to the volumes of stonefruit types in Australia. Apricots were not tested in the field, but do not have any specific pests that were not already targeted in the stonefruit trials undertaken. Cherries were not included in any trial data, and the 'stonefruit' criteria in the Directions for Use table does not exclude Vayego from being applied to cherries. Targeted pests for the stonefruit crop group on the Vayego label do not include any major cherry pests, pests listed in the DFU for stonefruit are common to cherries (weevils, light brown apple moth and efficacy is expected to be acceptable for these pests). The peach and nectarine varieties tested were appropriate, noting that stonefruit varieties change frequently with market preferences.

Macadamia varieties included 246, 741 and 816, and were only trialled in New South Wales. Almond varieties tested in Victoria and South Australia included Price, California Paper Shell, Carmel, Nonpareil and Johnston.

Target Pest

All target species listed on the draft label were tested in two or more trials.

Extensive testing was done in pome fruit for control of codling moth (*Cydia pomonella*), Fuller's rose weevil (*Asynonychus cervinus*), apple weevil (*Otiorhynchus cribricollis*) and garden weevil (*Phlyctinus callosus*) Light brown apple moth (*Epiphyas postvittana*) in apples and pears. All trials supported efficacy of these pests in pome fruit. Weevils can also be a considerable pest in stonefruit in specific regions, efficacy against weevils in stonefruit was provided in support of the label claim.

Extensive data was provided in support of efficacy against carpophilus beetles in stonefruit, specifically *Carpophilus davidsonii, C.hemipterus,* and *C. humeralis* as major pests for fruit damage and for spread of fungal diseases that reduce marketable fruit pre- and post-harvest. *(Carpophilus near dimidiates* was tested in almonds). Oriental fruit moth (*Cydia molesta*) and Mediterranean fruit fly (*Ceratitis capitata*) were also tested and the trial data was supportive.

Data from the macadamia trials reported supportive pest assessments on sigastus weevil, also known as macadamia seed weevil (*Kuschelorhynchus macadamiae*), as well as fruit spotting bug (*Amblypelta nitida*).

Target Pressure

Pest abundance for most pests tested in the majority of trial data presented was adequate to challenge Vayego efficacy (moderate to high pressure). Artificial introduction of carpophilus beetles to peach, nectarine and plum trees was appropriate to ensure adequate pressure with this highly mobile pest.

Efficacy at Rates tested

The presented data supported Vayego label claims. Vayego consistently showed efficacy as reduced levels of fruit damage in comparison to the untreated control across all major crop groups.

CODLING, LIGHT BROWN APPLE, AND ORIENTAL FRUIT MOTHS

Vayego was consistently equivalent to industry standards for codling moth control when applied in season-long programs.

Light brown apple moth damage in pome fruit was significantly reduced by Vayego applied at label rate in comparison to the UTC and industry standards.

Vayego efficacy on oriental fruit moth was less significant in peaches. At final assessment following four and five applications beginning at first sign of leaf-rolling, Vayego applied at label rate reported significantly lower branch tip damage than the UTC at final assessment.

CARPOPHILUS BEETLES

Data from stonefruit field trials reported moderate to high carpophilus pressure through the artificial inundation of plots with seven to 20 adult beetles each, following a single application of treatments, according to label. Efficacy of Vayego in these trials was compared to industry standard, maintaining significantly less fruit damage than the untreated control at harvest.

Laboratory assays of Vayego and Talstar on *Carpophilus hemipterus* confirmed Vayego had greater effect ingested than as a contact spray. Efficacy in the ingestion assay reported Vayego as being comparable to the industry standard.

SIGASTUS BEETLES

Trials were undertaken to assess sigastus weevil in macadamia nuts. Vayego applied prior to shell hardening was effective in reducing nut damage when assessed in fallen nuts and at on-tree assessments, and was equally as effective as the industry standard at 36 days after fourth application.

WEEVILS

Efficacy of Vayego was tested against garden weevil, apple weevil and fullers rose weevil. Trunk applications of Vayego were not as effective as foliar applications for reducing weevil numbers, or leaf and fruit damage. At 40 days following a single application in apples, garden weevil prevalence measured as leaf damage showed Vayego applied at 2.0 gai/100 L was effective in comparison to the industry standard.

MEDITERRANEAN FRUIT FLY

Under reasonable pressure in peaches and nectarines, Vayego applied at 2.5 gai/100 L was effective. Greater reduction in fruit damage was realised with four applications in comparison to two. In one peach trial Vayego applied at label rate was equivalent to the industry standards in marketable fruit percentages at harvest.

Crop safety

Crop safety was challenged most trials at 2× or 2.5× label rates, no phytotoxic symptoms were recorded at two assessments times between three and 30 days following one or several spray applications, which was appropriate to show acute phytotoxicity. In all other trials phytotoxicity was recorded and supportive up to the tested rates of 1.25×.

Resistance management

Tetraniliprole is an insecticide from the diamide chemical class and is active by ingestion. It interferes with the ryanodine-sensitive calcium release channels which lead to loss of muscle control and subsequent insect immobility. For resistance management, tetraniliprole is classed as group 28 insecticide under the IRAC guidelines.

Specific resistance management guidelines for insecticides in Australia are set out by CropLife and can be found on their website. As resistance management guidelines are subject to change as strategies evolve, it is proposed that the directions pertaining to these guidelines will be updated through CropLife. A statement directing the applicator to the CropLife website for the most up to date recommendation will be included on the label. Any specific limitations in product use required by relevant resistance management strategies will be added to the label as required. Currently, there has not been a need to develop a specific RMS for tetraniliprole. No current resistance management strategies exist for the pests included on the proposed product label.

8.3 Recommendations

Based on a review of the efficacy and crop safety, the registration of Vayego 200 SC insecticide is supported from an efficacy and crop safety perspective.

9 LABELLING REQUIREMENTS

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Vayego® 200 SC INSECTICIDE

ACTIVE CONSTITUENT: 200 g/L TETRANILIPROLE

For the control of various pests of almonds, macadamias, pome fruit and stone fruit as specified in the DIRECTIONS FOR USE table

GROUP 28 INSECTICIDE
IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

1-110 L

STORAGE AND DISPOSAL
Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.

All pack sizes except 60 L and 110 L
Triple rinse container 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 for appropriate disposal 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. Do not re-use empty container for any other purpose.

60 L packs only
If tamper evident seals are broken prior to initial use then the integrity of the contents cannot be assured. Empty container by pumping through dry-break connection system. Do not attempt to breach the valve system or the filling point, or contaminate the container with water or other products. Ensure that the coupler, pump, meter and hoses are disconnected, triple rinsed and drained after each use.
When empty, or contents no longer required, return the container to the point of purchase. This container remains the property of Bayer CropScience Pty Ltd. Do not re-use empty container for any other purpose.

110 L packs only
If tamper evident seals are broken prior to initial use then the integrity of the contents cannot be assured. Empty container by pumping through dry-break connection system. Do not attempt to breach the valve system or the filling point, or contaminate the container with water or other products. Ensure that the coupler, pump, meter and hoses are disconnected, triple rinsed and drained after each use. When empty, or contents no longer required, return the container to the point of purchase. This container remains the property of Bayer CropScience Pty Ltd.

Do not re-use empty container for any other purpose.

SAFETY DIRECTIONS
Keep out of reach of children. When opening the container, mixing and loading and using the prepared spray, wear cotton overalls (or equivalent clothing) buttoned to the neck and wrists and elbow-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

FIRST AID
First aid is not generally required. If in doubt, contact a Poisons Information Centre (phone Australia 13 11 26) or a doctor.

SAFETY DATA SHEET
Additional information is listed in the Safety Data Sheet, which can be obtained from www.crop.bayer.com.au.

EXCLUSION OF LIABILITY
This product must be used strictly as directed, and in accordance with all instructions appearing on the label and in other reference material. So far as it is lawfully able to do so, Bayer CropScience Pty Ltd accepts no liability or responsibility for loss or damage arising from failure to follow such directions and instructions.
Vayego® is a Registered Trademark of the Bayer Group.

APVMA Approval No.: 86756/116512

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Draft 21.02.2020 Vayego 200 SC Insecticide Page **3** of **9**
www.crop.bayer.com.au
Technical Enquiries: 1800 804 479

FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY PHONE 1800 033 111
Batch Number: DOM: Barcode

VAYEGO® 200 SC INSECTICIDE

ACTIVE CONSTITUENT: 200 g/L TETRANILIPROLE

For the control of various pests of almonds, macadamias, pome fruit and stone fruit as specified in the DIRECTIONS FOR USE table

DIRECTIONS FOR USE

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.
DO NOT apply where the slope exceeds 4%.

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 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 hazardous surface temperature inversion conditions present at the application site during the time of application. Surface temperature inversion 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.

Vertical sprayers
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

Type of target canopy and dilute water rate	Mandatory downwind buffer zones				
	Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas	Livestock areas
2 metres tall and shorter, maximum dilute water rate of 1000 L/ha (maximum application rate of 300 mL/ha)	Not required	5 m	Not required	Not required	Not required
taller than 2 metres (not fully-foliated), maximum dilute water rate of 2400 L/ha (maximum application rate of 300 mL/ha)	Not required	25 m	Not required	Not required	10 m
taller than 2 metres (fully- foliated), maximum dilute water rate of 2400 L/ha (maximum application rate of 300 mL/ha)	Not required	15 m	Not required	Not required	5 m

Directions for use table

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
Almonds	Carpophilus beetles (incl. *Carpophilus near dimidiatus)*	12.5 mL/ 100 L	H 10 days	Monitor orchards during hull split for the presence of carpophilus beetles. If numbers have the potential to cause economic loss, apply at mid hull split before the shells of soft- shelled varieties dry, exposing the kernel. Apply a follow up application 14–21 days later if there is a continual influx of carpophilus beetles from surrounding areas. Apply a maximum of two applications Kernel damage can still occur if carpophilus beetles enter the orchard just prior to harvest, when the shell is open, and feed directly on the kernel. Ensure thorough coverage of the target crop as thorough coverage of all hulls is essential – refer 'Application' section in GENERAL INSTRUCTIONS. Concentrate spraying for this pest is not appropriate. A non-ionic wetter eg Agral® 600 should be added at 10 mL/100 L of spray solution. Do not apply more than 300 mL of Vayego per hectare in a single application. Vayego should form part of an integrated program to manage carpophilus beetle populations with a focus on orchard hygiene.
Macadamias	Sigastus weevil (macadamia seed weevil, *Kuschelorhynchus macadamiae)*	12.5 mL/ 100 L	H 10 days	Monitor the weevil population and commence applications when weevils are active and after petal fall. Apply a maximum of three applications, with a 14–28 day interval between applications as required until shell hardening. Apply as a dilute application ensuring thorough and uniform spray coverage of foliage and branches–refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application. The addition of a non-ionic wetter eg Agral 600 added at 10 mL/100 L of spray solution, may improve control. Vayego 200 SC should be used as part of an integrated pest management approach which should include the use of other measures for control of sigastus weevil.

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
Pome fruit	Codling moth (*Carpocapsa pomonella* syn (*Cydia pomonella*), light brown apple moth (*Epiphyas postvittana* syn *Tortrix postvittana*)	10 mL/ 100 L	H 7 days	Apply a maximum of three applications, with 14–21 day intervals between each application. Commence no earlier than post petal fall (or 110 degree days for codling moth or 140 degree days for light brown apple moth as detected in pheromone traps but after petal fall) until late December. Ensure thorough coverage of the target crop—refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application. Further treatments should be made with alternate mode-of-action insecticides.
Pome fruit, stone fruit	Weevils eg apple weevil *(Otiorhynchus cribricollis)*, Fuller's rose weevil (*Asynonychus cervinus*), garden weevil *(Phlyctinus callosus)*	10 mL/ 100 L	Pome fruit H 7 days Stone fruit H 3 days	Monitor the orchards in early spring and commence applications no earlier than post petal fall when weevils begin to emerge. Apply a second application 14 days later if required. Apply a maximum of two applications Ensure thorough coverage of the target crop–refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application.
Stone fruit	Oriental fruit moth *(Laspeyresia molesta* syn *Grapholita molesta)*	10 mL/ 100 L	H 3 days	Commence applications post petal fall, when predictive models from local monitoring agencies indicate egg hatch of a generational peak. Apply a maximum of three applications, with 14–21 day intervals between applications. Ensure thorough coverage of the target crop – refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application.

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
	Dried fruit beetles (*Carpophilus* spp.) – suppression			Monitor stone fruit orchards for beetles as fruit approaches maturity and become susceptible to attack. Commence application before beetle populations reach damaging levels and re-apply treatments if necessary at an interval of 10–14 days. Apply a maximum of three applications. Ensure thorough coverage of the target crop – refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application.
	Mediterranean fruit fly (*Ceratitis capitata*)	12.5 mL/ 100 L		Commence applications when monitoring indicates fruit fly activity and fruit are vulnerable to damage (eg fruit ripening). Apply a maximum of three sprays, with 10 day intervals between applications. Ensure thorough coverage of the target crop – refer 'Application' section in GENERAL INSTRUCTIONS. Do not apply more than 300 mL of Vayego per hectare in a single application. Vayego applications should form part of an integrated fruit fly management program including baiting, trapping and a focus on orchard hygiene.

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

WITHHOLDING PERIODS

Harvest (H)
Stone fruit: DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION
Pome fruit: DO NOT HARVEST FOR 7 DAYS AFTER APPLICATION
Tree nuts: DO NOT HARVEST FOR 10 DAYS AFTER APPLICATION

Grazing (G)
Pome fruit, stone fruit, tree nuts: DO NOT GRAZE TREATED ORCHARD

EXPORT OF TREATED PRODUCE
Growers should note that MRLs or import tolerances may not exist in all markets for edible produce treated with Vayego 200 SC Insecticide. If you are growing edible produce for export, please check with Bayer CropScience Pty Ltd for the latest information on MRLs and import tolerances before using Vayego 200 SC.

GENERAL INSTRUCTIONS

Mixing
Shake the container well before using. Partially fill the spray tank with clean water and add the required volume of product to the water whilst agitating. Where recommended, add non-ionic surfactant, then top up the tank with clean water to the required volume. Vayego 200 SC should be agitated constantly before and during application and applied as soon as possible after mixing.

Application
Dilute spraying—all crops

- Use a sprayer designed to apply high volumes of water up to the point of run-off and matched to the crop being sprayed.
- Set up and operate the sprayer to achieve even coverage throughout the crop canopy. Apply sufficient water to cover the crop to the point of run-off. Avoid excessive run-off.
- The required water volume may be determined by applying different test volumes, using different settings on the sprayer, from industry guidelines or expert advice.
- Add the amount of product specified in the Directions for Use table for each 100 L of water up to a maximum of 300 mL Vayego per hectare in a single application. Spray to the point of run-off.
- The required dilute spray volume will change and the sprayer set up and operation may also need to be changed, as the crop grows.

Concentrate spraying—macadamias, pome fruit, stone fruit

- Use a sprayer designed and set up for concentrate spraying (that is a sprayer which applies spray volumes less than those required to reach the point of run-off) and matched to the crop being sprayed.
- Set up and operate the sprayer to achieve even coverage throughout the crop canopy using your chosen spray 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

1. Dilute spray volume as determined above: For example 1500 L/ha
2. Your chosen concentrate spray volume: For example 750 L/ha
3. The concentration factor in this example is 2 X (ie 1500 L ÷ 750 L = 2)
4. If the dilute label rate is 10 mL/100 L, then the concentrate rate becomes 2 x 10, which is 20 mL/100 L of concentrate spray.

- The chosen spray volume, amount of product per 100 L of water, and the sprayer set up and operation may need to be changed as the crop grows.
- Do not use at a concentration factor greater than 2X (eg at a rate higher than 25 mL/ 100 L where a dilute spraying rate of 12.5 mL/ 100 L is specified).
- Note that the concentration mixing rate is applicable only to Vayego. The adjuvant remains unchanged (ie no concentration factor applies).
- For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training and follow industry best practice.

COMPATIBILITY
For the latest compatibility recommendations contact the Bayer Crop Science Technical Information Line 1800 804 479 or your local Bayer Crop Science representative.

INSECTICIDE RESISTANCE WARNING GROUP 28 INSECTICIDE
For insecticide resistance management Vayego 200 SC Insecticide is a Group 28 insecticide. Some naturally occurring insect biotypes resistant to Vayego 200 SC and other Group 28 insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if Vayego 200 SC or other Group 28 insecticides are used repeatedly. The effectiveness of Vayego 200 SC on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Bayer CropScience Pty Ltd accepts no liability for any losses that may result from the failure of Vayego 200 SC to control resistant insects.

Resistance management strategy
Vayego 200 SC may be subject to specific resistance management strategies. For further information contact your local supplier, Bayer Crop Science representative, local agricultural department agronomist or visit www.croplife.org.au.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with the chemical or used containers.

PROTECTION OF HONEY BEES AND OTHER INSECT POLLINATORS
Highly toxic to bees. Tetraniliprole has a systemic action. DO NOT apply to crops pre-bloom or from the onset of flowering until flowering is complete. DO NOT allow spray drift to flowering weeds or flowering crops in the vicinity of the treatment area. Before spraying, notify beekeepers to move hives to a safe location with an untreated source of nectar and pollen, if there is potential for managed hives to be affected by the spray or spray drift. Risk to bees is reduced by spraying in early morning or late evening while bees are not foraging.

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ABBREVIATIONS

ACCS/ACMS	Advisory Committee for Chemicals Scheduling/Advisory Committee for Medicines Scheduling
ac	active constituent
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
APVMA	Australian Pesticides and Veterinary Medicines Authority
AR	Applied radioactivity
ARfD	Acute Reference Dose
BCF	Bioconcentration factor
bw	Bodyweight
CAS	Chemical Abstracts Service
d	Day
D_4^{20}	Density at 20 ºC
DAA	Days after application
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EC_{10}	concentration at which 10% of the test population is impacted
EC_{50}	concentration at which 50% of the test population is impacted
EDTA	Ethylenediaminetetraacetic acid
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
ER_{25}	rate at which 25% of the test population is impacted
ER_{50}	rate at which 50% of the test population is impacted
g	gram
GAP	Good Agricultural Practice
GLP	Good Laboratory 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
IRAC	Insecticide Resistance Action Committee
ISO	International Organization for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_F	Freundlich partitioning coefficient
$K_{F,OC}$	Freundlich organic carbon partitioning coefficient
L	Litre
LC/MS/MS	Liquid chromatography–mass spectrometry
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 P_{OW}
LOQ	Limit of Quantitation—level at which residues can be quantified
LR_{50}	rate that kills 50% of the test population of organisms
m^3	Cubic metre
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NAFTA	North America free trade agreement
NEDI	National Estimated Daily Intake

NESTI	National Estimated Short Term Intake
ng	nanogram
NOEC/NOEL	No Observable Effect Concentration Level
NOAEL	No Observed Adverse Effect Level
OC	Organic Carbon
OM	Organic Matter
PA	Vapour pressure
pH	How acidic or basic a water-based solution is
PHI	Pre harvest interval
PK	Dissociation constant
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RAL	Regulatory acceptable level
RBC	Red Blood Cell Count
REI	Re-Entry Interval
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
STMR	Supervised Trials Median Residue
TGAC	Technical grade active constituent
vmd	volume median diameter
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	Repels water
in vitro	Test/research that's performed outside of a living organism
in vivo	Test/research that's performed with or within an entire, living organism
Leaching	Removal of a compound by use of a solvent
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

REFERENCES

APVMA 2019, *Spray drift risk assessment manual*, Australian Pesticides and Veterinary Medicines Authority, Canberra 2019, available at apvma.gov.au/node/51826.

APVMA 2015, *Data Guidelines,* Australian Pesticides and Veterinary Medicines Authority, Canberra, available at apvma.gov.au/registrations-and-permits/data-guidelines.

WHO 1997, *Guidelines for predicting dietary intake of pesticide residues*, World Health Organization, Geneva, available at: who.int/foodsafety/publications/pesticides/en/.