Australian Government

Australian Pesticides and Veterinary Medicines Authority

Public release summary

On the evaluation of the new active etofenprox in the product Trebon Insecticide

APVMA product number 84711

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This publication is available from the APVMA website.

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PREFACE

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

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

About this document

This public release summary indicates that the APVMA is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

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

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

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for approval of the active constituent etofenprox and registration of the product Trebon 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 22 October 2019 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

PO Box 6182

Kingston ACT 2604

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 Trebon Insecticide, and approval of the new active constituent, etofenprox.

1.1 Applicant

SIPCAM Pacific Australia Pty Ltd

1.2 Purpose of application

SIPCAM Pacific Australia Pty Ltd has applied to the APVMA for registration of the new product Trebon Insecticide, containing 287.5 g/L, as an emulsifiable concentrate formulation of the new active constituent etofenprox.

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

1.3 Proposed claims and use pattern

Trebon Insecticide is intended for use to control Queensland fruit fly and Mediterranean fruit fly in stone fruit (except cherries). It is applied at a rate of 50–100 mL/100L, with up to three applications per season.

1.4 Mode of action

Etofenprox, 1-{[2-(4-ethoxyphenyl)-2-methylpropoxy]methyl}-3-phenoxybenzene belongs to the class of pyrethroid ether insecticides. It acts on the nervous system of insects disturbing the function of neurons by interaction with the sodium channel. Etofenprox has insecticide activity by contact and ingestion, has a broad spectrum of action on a wide variety of pests, with fast knockdown. The Insecticide Resistance Action Committee (IRAC), has designated etofenprox as a Group 3A insecticide.

1.5 Overseas registrations

Trebon Insecticide/etofenprox is currently registered in Japan, South Korea, Philippines, Thailand, Italy, Spain, Germany, UK, France, and Greece. In the EU it is registered under the trade name of ‘Trebon 30EC’. Etofenprox is used in agriculture in these countries on oilseed rape, head cabbage, grape, peach and apple against sucking and biting insects including aphids, thrips, moths, fruit flies, leaf rollers and leafhoppers at the adult and/or larval stage.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

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

Etofenprox is a white solid with a slight aromatic odour (pure) or an amber liquid with an aromatic odour (manufactured). It has a melting point of 37.4°C and a very low vapour pressure (8.13×10^{-7} Pa at 25°C), volatility (Henry's law constant: 0.0136 Pa m^3/mol^{-1}) and solubility in water (0.0225 mg/l at 20°C). Etofenprox has no sites which can either be protonated or dissociated at pH three to 10. It is stable to hydrolysis under acidic, neutral and basic conditions (pH 4–9). Etofenprox is neither flammable nor explosive and is incapable of reacting exothermically. It has no oxidising properties.

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

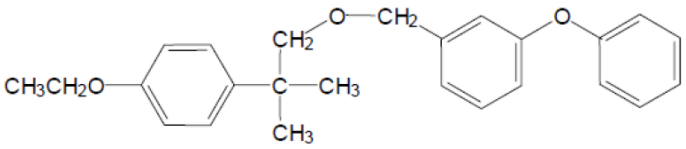
Common name (ISO):	Etofenprox
IUPAC name:	1-{[2-(4-ethoxyphenyl)-2-methylpropoxy]methyl}-3-phenoxybenzene
CAS registry number:	80844-07-1
Molecular formula:	$C_{25}H_{28}O_3$
Molecular weight:	376.5 g/mol
Structural formula:	

Table 2: Key physicochemical properties of the active constituent etofenprox

Physical form:	Crystalline powder
Colour:	White
Odour:	Slight aromatic odour
Melting point:	37.4°C
Boiling point:	The test substance thermally decomposes at about 200 °C before reaching the intrinsic boiling point under both atmospheric and reduced pressure.
Stability:	Stable under normal storage conditions.
Safety properties:	Not considered highly flammable. Not oxidising. Not explosive. No flash point observed up to 205°C.
Solubility in water (20 °C):	Water: 0.0225 mg/l pH 4 buffer: 0.0052 mg/l pH 7 buffer: 0.0225 mg/l pH 9 buffer: 0.012 mg/l
Organic solvent solubility (g/l ± S.D.) at 20 °C:	Methanol: 49 (± 5.1) g/l Ethanol: 98 (± 7.8) g/l Acetone: 877 (± 4.7) g/l Ethyl acetate: 837 (± 18.3) g/l Hexane: 667 (± 4.7) g/l Heptane: 621 (± 13.6) g/l Xylene: 856 (± 5.0) g/l Toluene: 862 (± 6.7) g/l Dichloromethane: 924 (± 7.0) g/l
Dissociation constant (PK_a):	Does not dissociate.
Octanol/water partition coefficient (Log K_{ow}/K_{OW}):	log Kow = 6.9 (20 °C)
Vapour pressure:	8.13×10^{-7} Pa at 25 °C
Henry's law constant:	0.0136 Pa m^3/mol^{-1}
UV/VIS absorption spectra:	maximum 273.5 nm in acidic and basic solution (acid methanol, pH 1 and basic methanol, pH 12) maximum 273.6 in neutral solution (methanol, pH 7)

2.2 Formulated product

The product Trebon Insecticide will be manufactured overseas. Tables 3 and 4 outline some key aspects of the formulation and its physicochemical properties.

Trebon Insecticide is an emulsifiable concentrate (EC) containing 287.5 g/L etofenprox. It is not explosive or oxidising, and has a high flash point and auto ignition temperature. Its stability allows storage under practical and normal commercial conditions. Trebon Insecticide will be available in 1–1000 L co-extruded, multilayered high density polyethylene (HDPE) containers.

Table 3: Key aspects of the formulation of the product Trebon Insecticide

Distinguishing name:	Trebon Insecticide
Formulation type:	Emulsifiable concentrate
Active constituent concentration/s:	287.5 g/L etofenprox

Table 4: Physicochemical properties of the product Trebon Insecticide

Physical form:	Amber liquid
PH:	5.5 (1% in water at 21°C)
Specific gravity/density:	0.96 at 20°C
Kinematic viscosity:	Newtonian behaviour: slightly lower viscosity at 40 °C than at 20 °C, ie 2.0 mPa and 3.4 mPa, respectively.
Safety properties:	Flash point 62–63°C (at 101.3 kPa). Auto-ignition temperature is 410 °C. No oxidising or explosive properties (under thermal, friction or shock stresses).
Storage stability:	There was sufficient data to support that the product should remain within specifications for at least two (2) years when stored under normal conditions.

2.3 Recommendations

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

Based on a review of the chemistry and manufacturing details, the registration of Trebon Insecticide, and approval of the active constituent etofenprox, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological data submitted on the active etofenprox are considered sufficient to determine its toxicology profile and to characterise the risk to humans. The data included metabolism studies, acute toxicity studies (active constituent and product), short-term toxicity studies (oral and dermal), long-term oral toxicity studies (including carcinogenicity), reproductive and developmental toxicity studies, genotoxicity studies, neurotoxicity studies (acute), studies on metabolites and other information to address the human safety criteria.

In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels.

Chemical class

Etofenprox is a non-ester pyrethroid insecticide, which has activity via contact or ingestion against a range of insect pests. It is not structurally related to other pyrethroids which have been considered for use within Australia but does bind to voltage gated sodium channels of nerve cell axons.

Pharmacokinetics

Etofenprox was extensively absorbed after oral administration in rats. Radioactivity associated with the administration of [^{14}C]-etofenprox was widely and rapidly distributed with the highest levels detected in fat, adrenal glands, liver, ovaries and thyroid gland. Excretion proceeded rapidly, predominately via the faeces, and was almost complete within 5 days of administration. Faecal excretion amounted to 86.4–90.4 per cent of the dose, whereas urinary elimination amounted to 6.3–10.7 per cent of the administered dose, in both males and female rats.

Acute toxicity (active constituent)

Etofenprox has low acute oral (LD_{50} > 2000 mg/kg bw), dermal (LD_{50} > 2000 mg/kg bw) and inhalational (LC_{50} > 5000 mg/m^3) toxicity in rats. Etofenprox was not an eye or skin irritant in rabbits and was not a skin sensitiser in the guinea pig maximisation test.

Acute toxicity (product)

Based on submitted toxicological studies, the formulated product, containing 287.5 g etofenprox/L, has low acute toxicity in rats by the oral (LD_{50} >2000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalation (LC_{50} >5.88 mg/L) routes. The product was not a skin or eye irritant in rabbits, or a skin sensitiser in guinea pigs.

Repeat-dose toxicity

Following repeat-dosing in mice, rats and dogs, the liver was a common target organ for toxicity. The liver, kidneys and haemo-lymphoreticular system were target organs in the mouse. The liver and thyroid gland were target organs in rats. In a 90-day dietary toxicity study in mice, the NOAEL was 375 mg/kg bw/d, based on increased mortality and reduced body weight gain, minor haematological effects, histopathological alterations indicative of kidney damage, and minor changes in the liver at 1975 mg/kg bw/d. In a 90-day dietary toxicity study in rats, the NOAEL was 20 mg/kg bw/d, based on liver toxicity (hepatocyte enlargement and clinical evidence of liver dysfunction affecting fat metabolism and synthesis of clotting factors) and thyroid toxicity (increased number of microfollicles and reduced circulating T4) at 120 mg/kg bw/d. In a one-year dietary toxicity study in dogs, the NOAEL was 32.2 mg/kg bw/d, based on hepatotoxicity, including increased liver weights and histopathological alterations at 339 mg/kg bw/d. The effects were reversible.

Chronic toxicity and carcinogenicity

In an adequate range of in vitro and in vivo assays, there was no evidence that etofenprox is mutagenic, genotoxic or carcinogenic in mice and rats. JMPR and EFSA concluded that etofenprox is unlikely to pose a carcinogenic risk to humans at dietary exposure levels.

Reproductive and developmental toxicity

Etofenprox was not a reproductive toxin in rats. No reproductive toxicity was observed in two multi-generation reproduction dietary studies in rats at doses up to 246 mg/kg bw/d or by gavage at 5000 mg/kg bw/d. The NOAEL for parental toxicity was 37 mg/kg bw/d based on reduced body weight gain and histopathological findings in the liver, kidneys and thyroid at 246 mg/kg bw/d.

In two oral gavage developmental toxicity studies in rabbits, the overall NOAEL for developmental and maternal toxicity was 100 mg/kg bw/d based on reduced maternal body weight gain and feed consumption on the first day of dosing (gestation day six), mortality and increased post-implantation loss at the high dose of 250 mg/kg bw/d.

Genotoxicity

Etofenprox was not genotoxic in a range of tests including *in vivo* and *in vitro* assays.

Neurotoxicity

There was no evidence that etofenprox was neurotoxic in rats in an acute neurotoxicity study, or a 13-week neurotoxicity study, or in a neurodevelopmental toxicity study.

Mode of action (toxicology)

Induction of liver enzymes through exposure to chemicals in rodents is well-known, and is considered responsible for the liver and thyroid effects observed following dosing with etofenprox.

Toxicity of metabolites and/or impurities

No metabolites and/or impurities of toxicological significance have been identified.

Reports related to human toxicity

Extensive use overseas has not identified issues relating to human toxicity.

3.2 Health-based guidance values and poisons scheduling

Poisons standard

On 10 April 218, the Delegate of the Secretary of the Department of Health published a final Scheduling decision not to schedule etofenprox and to list it in Appendix B. The Delegate's decision took into consideration the low acute toxicity of etofenprox and that it is not a skin or eye irritant nor a skin sensitiser in animal studies. Etofenprox was listed Appendix B of the Poisons Standard on 1 June 2018. Based on the presence of liquid hydrocarbons, which are included in Schedule 5, in the product, a CAUTION signal header is required.

Health-based guidance values

Acceptable Daily Intake (ADI)

The Acceptable Daily Intake (ADI) is that quantity of a chemical compound that can safely be consumed on a daily basis for a lifetime. The ADI for humans is derived from the NOAEL in the most susceptible species in long-term toxicity studies, and an appropriate safety factor. Etofenprox is not neurotoxic, mutagenic, teratogenic or carcinogenic. Therefore, there are no specific concerns.

The ADI for etofenprox established by JMPR in 1993, and confirmed in 2011, is 0.03 mg/kg bw/d. This is based on a NOAEL of 3.1 mg/kg bw/d for renal toxicity (increased incidence of dilated and basophilic renal tubules) in a two-year dietary study in rats. It was supported by a NOAEL of 3.7 mg/kg bw/d for hepatotoxicity and reduced bodyweight gain in a two-year dietary study in mice. In 2005, EFSA also used the NOAEL of 3.1 mg/kg bw/d for renal toxicity in a two-year rat dietary study to establish an ADI for the EU Acute Reference Dose (ARfD). Following consideration of these values, the APVMA is satisfied that they are suitably protective, and the JMPR ADI is adopted for use in Australia. The Australian ADI will therefore be 0.03 mg/kg bw/d.

Acute Reference Dose (ARfD)

The Acute Reference Dose (ARfD) is the maximum quantity of a chemical that can safely be consumed over a short period of time, usually in one meal or during one day.

The ARfD for etofenprox established by JMPR is 1 mg/kg bw, based on an overall NOAEL of 100 mg/kg bw/d for reduced maternal body weight gain and feed consumption during dosing and increased post-implantation loss at 250 mg/kg bw/d in two oral gavage developmental toxicity studies in rabbits. An ARfD was established on the grounds that the observed post-implantation loss could occur after a single exposure. EFSA established an ARfD with the same numerical value on the same basis. Following consideration of these values, the APVMA is satisfied that they are suitably protective, and the JMPR ARfD is adopted for use in Australia. As the effects relate to developmental toxicity, the ARfD is only required for women of child-bearing age.

3.3 Recommendations

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

There are no objections on human health grounds to the registration of the product ‘Trebon Insecticide’ containing 287.5 g/L etofenprox.

4 RESIDUES ASSESSMENT

Metabolism, analytical methodology, residue trial data and trade aspects have been considered for etofenprox.

4.1 Metabolism

Plants

Metabolism studies in which a 1:1 mixture of benzyl and propyl radiolabelled forms of etofenprox was applied as a foliar spray were received for grape, lettuce and rape seed (canola). In each study the predominant component was the parent compound, which was observed at 85–87 per cent Total Radioactive Residues (TRR) in grape bunches treated 14 days before harvest and 69–84 per cent TRR in grape bunches treated 28 days before harvest, 88–90 per cent TRR in lettuce, 57–62 per cent TRR in rape seed and 8–35 per cent TRR in rape foliage.

Animals

The metabolism and distribution of etofenprox was investigated in hens and goats. Both were dosed orally, by capsule, with a 1:1 mixture of benzyl and propyl radiolabelled forms of etofenprox. The major component identified in goat and hen matrices was parent etofenprox. Parent was identified at 97 per cent TRR in goat fat, 93 per cent TRR in goat muscle, 33 per cent TRR in goat kidney, 38 per cent TRR in goat liver and 93 per cent TRR in milk. In hen matrices it was detected in skin at 90 per cent TRR, 93 per cent TRR in fat, 88 per cent TRR in muscle, 80–81 per cent TRR in egg yolk on days eight and 14 and 15 per cent TRR in liver.

4.2 Analytical methods and storage stability

In the submitted Australian stone fruit residue trials, residues of etofenprox and its metabolite alpha-CO were extracted from each blended homogeneous sample of stone fruit with dichloromethane. The extract was then filtered and partitioned with saturated NaCl solution. An aliquot was evaporated to dryness and reconstituted in acetonitrile/water. Etofenprox and its metabolite alpha-CO residues were determined by Ultra-Fast Liquid Chromatography coupled with a tandem mass spectrometric detection (UFLC-MS/MS). Quantitation was via external matrix standards. The limit of quantitation (LOQ) of the methods was determined as 0.01 mg/kg, for each of etofenprox and alpha-CO as individual analytes.

Studies detailing a number of other validated analytical methods suitable for determining residues of etofenprox and the metabolite alpha-CO in plant and animal matrices have been submitted. The methods involve extraction steps using organic solvents (commonly acetone), liquid/liquid partition (commonly hexane) and column chromatographic clean-up (alumina, silica gel or Florisil). Samples are quantified by GC/MS, HPLC-UV or LC-MS/MS with LOQs of 0.01 mg/kg for parent and the metabolite alpha-CO.

Methods based on the QuEChERS multi-residue method approach have been validated for both plant and animal matrices.

4.3 Residue definition

An Australian residue definition is currently established as parent etofenprox.

Plants

Parent etofenprox was shown to be the predominant component of the radioactive residues in the submitted plant metabolism studies (grape, lettuce and rape).

In the submitted Australian field trials conducted on apricots, nectarines and peaches, residues of parent etofenprox and the metabolite alpha-CO were determined. In all 12 trials, parent etofenprox was observed to be the predominant residue in fruit in every sample and at all sampling timings. Furthermore, in over 80 per cent of the samples, the amount of alpha-CO was less than 10 per cent of the total (etofenprox + alpha-CO) residue. Etofenprox was similarly observed to be the predominant residue in peach, plum and nectarine samples in 21 trials conducted in Europe. It is noted that the alpha-CO metabolite (lowest NOAEL 54 mg/kg bw) is considered to be approximately 2.5× less toxic than the parent compound (NOAEL 20 mg/kg bw).

Animals

Parent etofenprox was shown to be the predominant component of the radioactive residues in the submitted hen and goat metabolism studies. The exposure of livestock to etofenprox is not expected from the proposed use on stone fruit (except cherries).

Summary

Based on the major metabolites identified in the available plant and animal metabolism data, the results of the available stone fruit residue trials where parent and alpha-CO were measured, the capability of the analytical methods and toxicological advice, it is concluded that a residue definition of etofenprox is appropriate for enforcement and risk assessment of etofenprox residues for commodities of plant and animal origin. There are therefore no proposed changes to the established residue definition for etofenprox, noting also that the established residue definition for Codex and in most overseas markets is also parent only.

4.4 Residues in food and animal feeds

The proposed Good Agricultural Practice (GAP) for Trebon Insecticide for use on stone fruit (except cherries) is for a maximum of three applications of etofenprox per season, at 50–100 mL product/100L (14–29 g a.i./100L). Applications should be made as maturity approaches (fruit turning colour) and if re-application is required, a minimum of seven days is required between applications. The proposed harvest withholding period (WHP) is three days, with the following grazing restraint “DO NOT graze any treated area or cut for stockfood”.

In 12 trials conducted in Australia, residues in stone fruit (apricots, nectarines and peaches) after three applications at 29 g a.i./100L (1× the maximum proposed application concentration), or in one peach trial after one application at 29 g a.i./100L, at a 3–4 day harvest WHP (or longer if a higher residue was observed), and in apricots after three applications at 28.8 g a.i./100L at a five-day WHP were, in rank order:

0.25, 0.59, 0.64 (one application), 0.77, 0.84, 0.99, 1.9, 2.0, 2.4 (apricots at a five day WHP), 2.5, 2.5 and 2.7 mg/kg (STMR = 1.4 mg/kg, n = 12).

In nine European peach, nectarine and plum trials in which sampling was carried out at three days after the last application residues in peaches after two applications at 14-24 g a.i./100L (0.47-0.82× the maximum proposed concentration) and conversion to expected residues after application at the maximum proposed concentration of 28.8 g a.i./100L were in rank order:

0.16, 0.17, 0.19, 0.30, 0.43, 0.51, 0.56, 0.80 and 0.89 mg/kg (STMR = 0.43 mg/kg, n = 9).

The combined dataset of residues from Australian and European trials conducted on stone fruit and suitable for MRL estimation is, in rank order:

0.16, 0.17, 0.19, 0.25, 0.30, 0.43, 0.51, 0.56, 0.59, 0.64, 0.77, 0.80, 0.84, 0.89, 0.99, 1.9, 2.0, 2.4, 2.5, 2.5 and 2.7 (STMR = 0.77 mg/kg, n = 21).

An MRL set at five mg/kg for FS 0012 Stone fruit [except cherries] is considered appropriate for the proposed use of etofenprox on stone fruit (except cherries) in conjunction with a harvest WHP of three days.

It is noted that a number of the Australian trials were reverse decline trials with sampling carried out at 14–18 days after the last application. The dataset of residue values from sampling at the last sampling timing (14–18 DALA) in the Australian reverse decline trials was, 0.24, 0.45, 0.46, 0.95, 1.1 and 1.2 mg/kg (STMR = 0.705 mg/kg, n = 6). Half-lives of the decline in residues from zero days to 14–18 days in the Australian reverse decline trials, ranged from 8.3–25 days (median 13 days).

4.5 Crop rotation

As stone fruits are not considered to be rotational crops, it is not necessary to consider residues in following crops/animal feeds.

4.6 Residues in animal commodities

A lactating dairy cattle feeding study was submitted by the Applicant. Three treatment groups of three dairy cows each were dosed orally for 28–30 consecutive days with etofenprox. The nominal dose levels of etofenprox based on concentration in the diet (DM feed basis) were 0.5, 1.5 ppm and 50 ppm. Depuration data was obtained for two other cows in the 50 ppm feeding group.

Although commodities from stone fruit are not fed to cattle and other mammals or poultry, etofenprox mammalian and poultry commodity MRLs will be established at the LOQ for enforcement purposes.

MO 0105 Edible offal (mammalian)	*0.01 mg/kg
PE 0112 Eggs	*0.01 mg/kg
MM 0095 Meat (mammalian) [in the fat]	*0.01 mg/kg

ML 0106 Milks	*0.01 mg/kg
PO 0111 Poultry, Edible offal of	*0.01 mg/kg
PM 0110 Poultry meat [in the fat]	*0.01 mg/kg

4.7 Dietary risk assessment

Estimated dietary intake

The chronic dietary exposure to etofenprox 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[2] and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for etofenprox is equivalent to <10 per cent of the ADI.

It is concluded that the chronic dietary exposure of etofenprox is acceptable.

The acute dietary exposure is estimated by the National Estimated Short Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR with 97.5th percentile food consumption data derived primarily from the 2011–12 National Nutritional and Physical Activity Survey. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food.

An ARfD at one mg/kg bw was established for women of child-bearing age only. The highest acute dietary intake was estimated at <5 per cent of the ARfD. It is concluded that the acute dietary exposure is acceptable.

4.8 Recommendations

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

Table 5: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
ADD:			
Etofenprox			
MO	0105	Edible offal (Mammalian)	*0.01
PE	0112	Eggs	*0.01

[2] WHO (2008), Consultations and workshops: Dietary Exposure Assessment of Chemicals in Food: Report of a joint FAO/WHO Consultation, Annapolis, Maryland, USA, 2–6 May 2005.

Amendments to Table 1			
Compound		Food	MRL (mg/kg)
MM	0095	Meat (mammalian) [in the fat]	*0.01
ML	0106	Milks	*0.01
PO	0111	Poultry, Edible offal of	*0.01
PM	0110	Poultry meat [in the fat]	*0.01
FS	0012	Stone fruits [except cherries]	5

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Stone fruit are considered to be major export commodities[3]. Residues in these commodities resulting from the use of Trebon Insecticide may have the potential to unduly prejudice trade.

The Applicant has indicated that the leading markets for Australian summer fruit commodities (apricots, nectarines, peaches and plums) relevant to this application are Hong Kong, Singapore, Malaysia, Indonesia, Saudi Arabia, Kuwait and UAE for the year ending June 2016[4].

Updated information shows that in the year ending June 2018, apricots were mainly exported to (in descending exports by tonnes) Saudi Arabia, UAE, Hong Kong, Singapore and Kuwait, nectarines and peaches were mainly exported to China, UAE, Singapore, Saudi Arabia and Hong Kong and plums were mainly exported to Hong Kong, Singapore, China, Indonesia and Malaysia[5].

Stone fruit and stone fruit by-products are not considered to be livestock (including cattle and poultry) feeds. Although commodities from stone fruit are not fed to cattle and other mammals, etofenprox mammalian and poultry commodity MRLs will be established at the LOQ for enforcement purposes. As quantifiable residues will not be present in animal commodities, the risk to trade in animal commodities is low and requires no further consideration.

5.2 Overseas registrations and approved label instructions

The Applicant indicated that etofenprox products (various formulations) are registered for use on various crops in a large number of overseas countries. Uses on stone fruit crops are registered in Cambodia, Chile, Israel, Italy, Japan, Korea and Spain.

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 GAP employed by various countries. Some countries may accept Codex CXLs when importing foods. Etofenprox has been considered by Codex.

The following relevant international MRLs have been established for etofenprox (Table 6).

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[3] APVMA Regulatory Guidelines—Data Guidelines: Agricultural—Overseas trade (Part 5B)

[4] Information from Australian Horticulture Statistics Handbook 2015–2016

[5] Australian Horticulture Statistics Handbook Fruit 2017–2018; horticulture.com.au/growers/help-your-business-grow/research-reports-publications-fact-sheets-and-more/australian-horticulture-statistics-handbook/

Table 6: Proposed Australian and current international MRLs for etofenprox

Country	Residue definition (plant commodities)	Commodity	MRL (mg/kg)
Australia (proposed)	Parent	Stone fruit (except cherries)	5
Codex	Parent	Nectarine, Peach	0.6
China		Nectarine, Peach	0.6
EU	Parent + alpha-CO	Peach	0.6
		Apricot, Cherries, Plum, Other stone fruit	1.0
Japan	Parent	Peach	0.1
		Nectarine	0.6
Korea	Parent	Apricot, Cherries	1.0
		Other stone fruit	2.0
		Chinese bush cherry	3.0
		Korean plum	5.0
Taiwan		Nectarine	0.6
		Peach	0.6
USA	Parent	All food commodities apart from those listed	5.0

5.4 Potential risk to trade

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

The established residue definition for etofenprox (parent) which will not be amended, is the same as established by Codex and in most major overseas markets, except the EU, which includes the metabolite alpha-CO for plant commodities. This metabolite is usually present at significantly smaller amounts compared to the parent, so the difference in residue definition is of limited significance when considering the use proposed here for Trebon Insecticide.

The proposed MRL for stone fruit (except cherries) is 5 mg/kg. The MRLs for stone fruit established by CODEX, the EU, Japan and Taiwan are generally either 0.6 or 1 mg/kg. Korea has various stone fruit MRLs from 1–5 mg/kg, while the USA has an MRL for 5 mg/kg for all food commodities apart from those listed separately (and is therefore applicable to stone fruit).

The Applicant has proposed the following statement to mitigate the risk to trade in stone fruit:

Trade advice information: Treated crop commodities destined for export may require extra time being allowed between application and harvest, as some export markets have either no Maximum Residue Limit (MRL) or different MRL to those of Australia. Details of overseas standards and export interval can be obtained by contacting Sipcam Pacific Australia Pty Ltd before using this product.

5.5 Recommendations

Comment is sought from the stone fruit industry on the potential risk to international trade associated with the proposed use of Trebon Insecticide, containing 287.5 g/L etofenprox, and the ability of industry practices to manage potential risks to trade.

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Repeat dose studies in animals are considered relevant for the assessment of worker exposure.

6.2 Occupational exposure

Exposure during use

Workers may be exposed to the product when opening containers, mixing/loading/application, cleaning up spills, maintaining equipment and entering treated crops. The main route of exposure to the product spray will be dermal and inhalation, with potential for ocular exposure.

In the absence of specific exposure data for the proposed mode of application, the US EPA Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure.

The toxic endpoints of concern and the identified NOAEL for risk assessment were derived from a repeat dose study in animals; and therefore in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account both potential inter-species extrapolation and intra-species variability. Based on the risk assessment, the proposed use of the product does not require any personal protective equipment. However, while basic PPE for mixing/loading/application has not been deemed necessary, the applicant has proposed to include safety directions as outlined below which the APVMA does not oppose.

Exposure during re-entry or rehandling

Workers may be exposed through re-entry into treated areas. Based on the low risks identified during spray application, and the absence of relevant acute toxicity endpoints, there were no identifiable risks from re-entry once the spray had dried. However, while basic PPE for entry prior to the spray drying has not been deemed necessary, the applicant has proposed to include a re-entry statement as outlined below which the APVMA does not oppose.

6.3 Public exposure

The product is not intended for use by the public. Bystander risk is possible, but expected to be limited based on the proposed use pattern. Potential routes of exposure for bystanders are dermal, inhalational and ocular. Adherence to good agricultural practices will minimise potential exposures.

6.4 Recommendations

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

First aid instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26; New Zealand 0800 764 766. If swallowed, do NOT induce vomiting

Safety directions

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

Precautionary (warning) statements

RE-ENTRY PERIOD

DO NOT enter treated areas before the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and PVC gloves. Clothing must be laundered after each day's use.

7 ENVIRONMENTAL ASSESSMENT

7.1 Fate and behaviour in the environment

Soil

Etofenprox was rapidly degraded in eight laboratory soils under aerobic conditions at 20°C with DT50 values ranging 7.0 to 58 days (geomean DT_{50} 16 days) and DT90 values ranging 17–192 days. In one soil incubated at 10°C, the DT_{50} was 13 days and the DT_{90} was 41 days. Under fully anaerobic conditions in one soil, the degradation rate was less rapid with an overall DT_{50} of 174 days. Under field conditions at three sites in the United States, etofenprox dissipated rapidly in soil with DT_{50} values ranging 4.8–14 days (DT_{90} 15–45 days).

Studies using radiolabelled material show that etofenprox is initially degraded in soil by one of four different routes:

- oxidation resulting in α-CO
- hydroxylation of the benzene ring leading to 4'-OH
- de-ethylation resulting in DE
- cleavage of the ether linkage between the two benzene rings to give DP.

Once formed, these four metabolites do not accumulate and are themselves quickly degraded to CO_2 (up to 46 per cent mineralisation) and a degree of bound residue is incorporated into the organic matter of the soil (up to 53 per cent bound residues). Under aerobic conditions, no metabolite exceeded 10 per cent of the applied radioactivity. Under anaerobic conditions, the metabolite 4'-OH reached a maximum level of 12 per cent of the applied dose after 90 days of incubation.

Irradiation does not markedly accelerate the degradation of etofenprox on soil as indicated by a DT50 of 19 days compared to 22 days for the dark control. No degradate exceeded 10 per cent of the applied radioactivity and the metabolic profiles were similar under irradiated and dark conditions.

Etofenprox is classified as slightly mobile to immobile in eight soils based on K_d values ranging 23–872 mL/g (mean K_d 254 mL/g). This was confirmed in column leaching tests where etofenprox was not leached out from all the soils tested.

Water

Etofenprox was not hydrolysed in sterile buffer solutions at pH 4, 7 and 9 incubated for five days at 50°C in the dark. The metabolite α-CO was found to be stable at pH 4 and pH 7, but was hydrolysed at pH 9 to form PENA and m-PBAcid.

Etofenprox was rapidly photodegraded under simulated sunlight with DT50 values of 4.7 days in sterile buffer conditions and 7.9 days in natural water. The two major degradates were α-CO (38–65 per cent) and PENA (12–14 per cent). These results clearly demonstrate that direct phototransformation may represent a

major factor contributing to disappearance of etofenprox in the aquatic environment. α-CO did not show any further photolytic degradation.

The results of a water/sediment study confirmed an average DT_{50} value of 18 days for etofenprox in the entire system. In the water phase, etofenprox decreased to < 1 per cent between days 14 and 59. The only major metabolite was 4'-OH, which reached a maximum level of 21 per cent of the applied radioactivity on day seven in the sediment, and, thereafter, decreased to ≤10 per cent of the applied radioactivity after 30 days. The average DT_{50} value for the metabolite 4'-OH was 26 days in the entire system. Incorporation to bound residues and mineralization to CO_2 are the significant routes of disappearance of etofenprox in water/sediment systems.

Data on the degradation of etofenprox in aquatic systems are also available from a mesocosm study. Enclosures in outdoor mesocosms were treated with etofenprox at six nominal concentrations. From the enclosure treated with the highest nominal concentration (22 µg/L), water and sediment samples were analysed for concentrations of etofenprox and α-CO. In the water phase, etofenprox concentration decreased rapidly and disappeared almost completely from day seven onwards (DT_{50} 1.4 days). The maximum concentration of α-CO measured did not exceed 10 per cent of the maximum concentration of the parent item. The concentration of the metabolite α-CO also decreased rapidly and disappeared almost completely from day 14 onwards (DT_{50} 3.8 days). In the sediment phase, etofenprox reached its maximum concentration after 14 days and, thereafter, decreased constantly until the end of the study (day 112). Concentrations of α-CO in the sediment remained very low during the course of the study.

Similarly, under field conditions at two sites in the United States, etofenprox dissipated rapidly with DT_{50} values ranging 1.6–1.7 days in the water phase (DT_{90} 21–27 days) and 7.3–15 days in the sediment phase (DT_{90} 24–52 days).

In conclusion, etofenprox does not hydrolyse in acidic, neutral or basic buffer solutions in the dark. Irradiation contributes significantly to the degradation of etofenprox in aquatic systems. Therefore, significant degradation of etofenprox in natural systems that are exposed to natural sunlight is expected. Main metabolites are α-CO in the water phase and 4'-OH in the sediment phase.

Air

Etofenprox has low vapour pressure and low Henry's law constant indicating that this chemical is unlikely to evaporate from soil or water surfaces. The half-life for this chemical in the atmosphere is around 2.1 hours indicating that this chemical is susceptible to photochemical degradation if it enters the atmosphere during spray application and does not have potential for long range transport in the atmosphere.

7.2 Effects and associated risks to non-target species

Terrestrial vertebrates

Etofenprox was not toxic to mammals (LD_{50} >2000 mg ac/kg bw, *Rattus norvegicus*) or birds (LD50 >2000 mg ac/kg/bw, two species tested) following oral administration. Etofenprox was similarly not toxic to birds following short-term dietary exposure (LC_{50} >5000 mg ac/kg diet, two species tested). Following long-term

dietary exposure in a mammalian multi-generation reproduction study, increased pup mortality and reduced pre-weaning weight gain was observed at 246 mg ac/kg bw/d (NOEL 37 mg ac/kg bw/d, *Rattus norvegicus*). No adverse effects were observed following long-term dietary exposure in birds in a one-generation reproduction study (NOEL 90 mg ac/kg bw/d, *Colinus virginianus*).

Risks of etofenprox toxicity to terrestrial vertebrates were determined to be acceptable at the screening level, which assumed direct exposure to maximum possible cumulative concentrations in the diet. Although etofenprox has high potential to partition to fat (log Kow 6.9), a food chain assessment indicated that any accumulated residues in earthworms or fish, for example, will not reach levels harmful to predators. Risks of biomagnification were also determined to be low due to rapid elimination rates in mammals and fish.

Aquatic species

Etofenprox is considered to be highly toxic to fish (lowest LC_{50} 0.0027 mg ac/L, *Onchorhynchus mykiss*), aquatic invertebrates (lowest EC_{50} 0.00044 mg ac/L, *Daphnia magna*), and sediment dwellers (EC_{50} 0.00052 mg ac/L, *Chironomus riparius*). It is considered to be moderately toxic to algae (E_rC_{50} 31 mg ac/L, *Pseudokirchneriella subcapitata*) and no adverse impacts are expected in aquatic plants at the limit of solubility (EC_{50} >0.026 mg ac/L, *Lemna gibba*). Following long-term exposure, reduced survival of fish hatchlings was observed at concentrations as low as 0.00019 mg ac/L (NOEC 0.000062 mg ac/L, *Danio rerio*), reduced reproduction was observed in aquatic invertebrates at concentrations as low as 0.000079 mg ac/L (NOEC 0.000054 mg ac/L, *Daphnia magna*), and reduced emergence was observed in sediment dwellers at concentrations as low as 6.4 mg ac/kg dry sediment (NOEC 2.9 mg ac/kg dry sediment, *Chironomus riparius*).

Two mesocosm tests were conducted containing aquatic communities of zooplankton, macro-invertebrates, emergent insects, and macrophytes. Effects on Asellidae and total numbers of macro-invertebrates were observed at concentrations as low at 0.00075 mg ac/L with recovery within eight weeks (NOEC 0.00025 mg ac/L). Effects on Asellidae and Glossiphonidae were observed at concentrations as low as 0.0022 mg ac/L with no recovery (NOEAEC 0.00075 mg ac/L).

A regulatory acceptable concentration of 0.00075 mg ac/L was established based on mesocosm studies with the most sensitive effect being on populations of crustaceans and leaches. Runoff risks were determined to be acceptable with standard restraints to minimise runoff. Spray drift risks were determined to be acceptable with buffer zones of 20 to 55 metres depending on the canopy height, degree of foliation, and the spray volume. A precautionary statement is required identifying high toxicity to aquatic species.

Bees

Etofenprox is highly toxic to adult bees (lowest oral LD_{50} 0.014 µg ac/bee; lowest contact LD_{50} 0.024 µg ac/bee, *Apis mellifera*), and moderately toxic to bee larvae (LD_{50} 4.5 µg ac/bee, *Apis mellifera*). Following long-term exposure of adult bees in dietary toxicity tests, increased mortality was observed at doses of 0.16 µg ac/bee/d (NOAED 0.059 µg ac/bee/d).

Semi-field studies on flowering phacelia and mustard plants at rates ranging from 200 to 280 g ac/ha demonstrated a strong repellent effect. No adverse effects were observed on colonies for the first five days at 200 g ac/ha; however, a number of adverse effects were observed in the 28-day test at 280 g ac/ha.

These effects included short-term effect on pupae mortality, reduced foraging activity, increased brood termination rate, and decreased brood and compensation indices. Abnormal behaviour was also observed on the first day of bee flight after application.

Trebon Insecticide is applied at the first sign of fruit maturity. This does not coincide with flowering times and etofenprox is not systemic, so direct exposure to bees is not expected. However, indirect exposure through spray drift may occur.

Considering no adverse effects were observed on adult foraging bees at 200 g ac/ha under semi-field conditions, a spray drift assessment according to APVMA's updated approach to spray drift management[6] considered an RAL of 200 g ac/ha, vertical sprayer application and the maximum application rate of 100 mL/100L. The assessment determined that buffer zones are not required to mitigate risks of contact toxicity to bees. However, precautionary language is still required to avoid spray drift to flowering weeds or crops that are in the vicinity of the treatment area, in order to minimise oral exposure of bees and subsequent exposure of larvae. Any nearby hives should also be moved to a safe location with an untreated source of nectar and pollen.

Non-target arthropods

Available toxicity data on a representative EC formulation of etofenprox indicate high toxicity to other beneficial (predatory and parasitic) arthropods. Tier one laboratory tests investigating toxicity of fresh-dried residues on inert (glass) substrate for the standard indicator species indicated LR_{50} values of 0.70 g ac/ha (*Typhlodromus pyri*) and 0.42 g ac/ha (*Aphidius rhopalosiphi*). Extended laboratory tests on natural (foliage) substrate indicated LR_{50} values of 4.8 g ac/ha (*Typhlodromus pyri*), 24 g ac/ha (*Aphidius rhopalosiphi*), 18 g ac/ha (*Chrysoperla carnea*), and 2.4 g ac/ha (*Orius laevigatus*).

Aged residues tests were available for rates up to 153 g ac/ha; however, these data are of limited value considering the cumulative rate was estimated to be 860 g ac/ha under the proposed conditions of use in Australia. Community studies were also undertaken to investigate spray drift risks to off-field arthropod communities. Pronounced effects with no recovery were observed for the order Caelifera at 53 g ac/ha which is an environmentally relevant rate under the proposed conditions of use.

Adverse effects on beneficial arthropods could not be excluded within the treatment area or field margin. Therefore, the use of etofenprox is not considered compatible with IPM programs utilising beneficial arthropods. Precautionary measures must also be taken to minimise spray drift to non-crop areas.

Soil organisms

Etofenprox is not considered to be acutely toxic to soil macro-organisms at exaggerated soil concentrations such as earthworms (LC_{50corr} >24 mg ac/kg dry soil, *Eisenia fetida*). Following long-term exposure, a dose-response effect on reproduction rates were observed in three species of soil macro-organisms (lowest EC_{10} 0.41 mg ac/kg dry soil, *Folsomia candida*). Etofenprox did not affect soil processes such as carbon and nitrogen mineralisation at the maximum rate tested (NOEC 0.89 mg ac/kg dry soil).

[6] apvma.gov.au/node/28071

Risks to soil organisms were determined to be acceptable when foliar interception and incorporation into a 15-cm soil depth over the long-term were considered.

Non-target terrestrial plants

Etofenprox is not considered to be phytotoxic based on pre- and post-emergent toxicity testing of a representative EC formulation on ten crop species (ER_{25} >100 g ac/ha; ER_{50} >100 g ac/ha). Therefore, risks of etofenprox to non-target terrestrial plants are considered to be acceptable.

7.3 Recommendations

In considering the environmental safety of the use of Trebon Insecticide, the APVMA had regard to the toxicity of the active constituent and its residues, including metabolites and degradation products, in relation to relevant organisms and ecosystems. Based on the outcome of the risk assessment, the APVMA was satisfied under s14 of the Agricultural and Veterinary Chemicals Code Act 1994 that the use of the product meets the safety criteria with respect to s5A(1)(c); and the label meets the labelling criteria under s5D(1), with respect to environmental considerations.

The following mitigation/labelling statements are recommended based on the outcome of the risk assessment and current label standards.

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.

SPRAY DRIFT RESTRAINTS

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

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

DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The advisory buffer zones in the relevant buffer zone table below provide guidance but many 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 three and 20 kilometres per hour at the application site during the time of application.

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

DO NOT apply by a 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.

Table 7: Buffer zones for vertical sprayers

Type of target canopy	Natural aquatic areas
2 metres tall and smaller, maximum dilute water rate of 1000 L/ha	20 metres
Taller than 2 metres (not fully-foliated), maximum dilute water rate of 1500 L/ha	55 metres
Taller than 2 metres (fully foliated), maximum dilute water rate of 1500 L/ha	45 metres

INTEGRATED PEST MANAGEMENT

Toxic to beneficial arthropods. Not compatible with integrated pest management (IPM) programs utilising beneficial arthropods. Minimise spray drift to reduce harmful effects on beneficial arthropods in non-crop areas.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

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

PROTECTION OF HONEY BEES AND OTHER INSECT POLLINATORS

Highly toxic to bees. Harmful to bee brood. DO NOT apply to crops 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.

DISPOSAL

Triple-rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not

recycling, break, crush, or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500mm 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.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Trebon Insecticide is a pyrethroid-like insecticide containing the active ingredient etofenprox (1-{[2-(4-ethoxyphenyl)-2-methylpropoxy]methyl}-3-phenoxybenzene). The product is intended to be used in Australia for the control of Queensland fruit fly (*Bactrocera tryoni*) and Mediterranean fruit fly (*Ceratitis capitata*) in stone fruit (except cherries).

The product is to be applied at a single rate of application 50–100 mL/100 L sprayed to the point of runoff when adult fruit fly numbers warrant spraying. If re-application is needed, a minimum of seven days is required between treatments. No more than three applications of Trebon Insecticide may be applied per growing season.

Trebon Insecticide cover sprays should be used along with other control measures such as orchard hygiene, pest monitoring, mating disruption or lure and kill products to ensure effective season-long control. Trebon Insecticide will not control eggs or larvae present in fruit at spraying.

8.2 Efficacy and target crop safety

Efficacy

The applicant presented results from efficacy trials conducted in Australia (against Queensland fruit fly and Mediterranean fruit fly) and overseas (against Mediterranean fruit fly) in stone fruit orchards.

For Mediterranean fruit fly (MFF), three studies conducted in Italy in peach, nectarine and apricot orchards were provided, with Trebon Insecticide applied at 50 mL/100 L. The climate and production systems in the area where the trials were conducted are comparable to stone fruit production areas in Western Australia, where MFF is a pest in Australia. Trials were conducted to a standard protocol which met or exceeded EPPO guidelines for evaluating efficacy against this pest with foliar application. In all three trials Trebon Insecticide gave good protection under moderate pest pressure, significantly reducing the number of fruit damaged by MFF in fruit on the trees and in wind-fallen fruit. Two studies conducted in peach orchards in the Perth Hills area of Western Australia provide partial support for efficacy under Australian conditions, but neither trial clearly demonstrated efficacy against MFF in stone fruit at the proposed rates of 50 mL/100 L or at 100 mL/100 L. Under low to moderate MFF pressure conditions, one trial demonstrated reduced incidence of MFF in wind-fallen fruit at the proposed rates, but not in fruit picked from the tree. The other trial was an extreme Mediterranean fruit fly pest situation undertaken opportunistically in an abandoned orchard. This trial clearly showed that Trebon Insecticide has efficacy against MFF at the proposed rates, but the pest pressure was too high for control of the pest to be achieved.

For Queensland fruit fly (QFF), three trials provided support for the proposed use of Trebon Insecticide at a rate of 50 or 100 mL/100 L to control QFF in peaches and nectarines. There was low pest pressure in trials conducted in peaches and in nectarines in an orchard in the Stanthorpe area, with moderate to good control of QFF obtained at the proposed rates. There was moderate QFF pressure in a trial in peaches in the Lockyer Valley, with suppression to moderate control obtained. These results all refer to fruit on the trees, as

in all three trials there were few or no wind-fallen fruit, in contrast to the results for all the MFF trials. Four other trials were established in Queensland, NSW and Victoria to evaluate efficacy against QFF, but they were only useful for crop safety evaluation due to inadequate pest levels or brown rot damage.

Considering both fruit fly species together, the results from five Australian trials (two with MFF and three with QFF) provide evidence for efficacy against both species, but this is limited by difficulties in obtaining trial sites with suitable fruit fly populations and undertaking trials on a sufficient scale to clearly show statistically significant differences in efficacy between treatments. However, this is supplemented by the three efficacy trials from Italy, which were larger and more readily demonstrated the efficacy of Trebon Insecticide against MFF. Trebon Insecticide is approved for the control of MFF in Spain and Italy and has been used there for many years. Data of similar quality to the Italian trials is not available for QFF, but the two species are similar and the Australian trials provide support for efficacy against QFF at the proposed Australian rates under low to moderate pest pressure.

Crop safety

Detailed assessments of phytotoxicity were made in a total of 16 trials with stone fruit, including the eight efficacy trials and eight other studies not suitable for evaluation of efficacy against MFF or QFF. These included seven cultivars of peach, four cultivars of nectarine, two cultivars of apricots and two cultivars of plums. No phytotoxic symptoms to the treated fruit trees or fruit were observed in any plots on any of the assessment occasions in any of the trials, despite application of Trebon Insecticide in various trials at 150 mL or 200 mL/100 L for apricots, peaches and nectarines and 50–75 mL/100 L for plums. These data demonstrate acceptable crop safety.

Resistance management

Etofenprox is a new synthetic pyrethroid-like insecticide. The Insecticide Resistance Action Committee (IRAC), has designated etofenprox as a Group 3A insecticide. Its mode of action is on the nervous system of insects disturbing the function of neurons by interaction with the sodium channel. Etofenprox has insecticide activity by contact and ingestion, has a broad spectrum of action on a wide variety of pests, with fast knockdown.

Insecticide resistance management strategies (RMS) have been developed for a number of crops and pests in Australia (see CropLife Australia 2019). Currently, there has not been a need to develop a specific RMS for stone fruits and/or fruit flies. Proposed label statements for Trebon Insecticide recommend that the product should be used alongside other control measures such as orchard hygiene, pest monitoring, mating disruption or lure and kill products to ensure effective season-long control. Label recommendations to limit applications of the product to no more than three per season, will also assist in reducing the likelihood of fruit flies developing resistance to Trebon Insecticide.

8.3 Recommendations

Trial data support that Trebon Insecticide will provide acceptable control against Queensland fruit fly and Mediterranean fruit fly in stone fruit (except cherries) when used as directed. Acceptable crop safety is

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

There are no objections on efficacy or target-crop safety grounds to the registration of the product Trebon Insecticide, containing 287.5 g/L of etofenprox.

9 LABELLING REQUIREMENTS

POISON

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

TREBON®

Insecticide

ACTIVE CONSTITUENT: 287.5 g/L ETOFENPROX
SOLVENT: 591 g/L LIQUID HYDROCARBONS

GROUP	3A	INSECTICIDE

For the control of Queensland fruit fly and Mediterranean fruit fly on stone fruit (except cherries) as indicated in the DIRECTIONS FOR USE

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE

CONTENTS: 1 - 1000 LITRES

SIPCAM

SIPCAM PACIFIC AUSTRALIA PTY LIMITED
Level 1, 191 Malop Street Geelong VIC 3220

® Registered Trademark of Mitsui Chemicals Agro Japan

Batch No.:
Date of Manufacture:

Not subject to the ADG Code when transported in Australia by Road or Rail in packages 500L or less; or IBCs (refer to SP AU01). However if transported by Air or Sea, this provision does not apply. Then the product is classed as Dangerous (Class 9 Environmentally Hazardous) by IATA and IMDG/IMSBC respectively.
For specialist advice in emergency only, call 1800 033 111 all hours, Australia wide

DIRECTIONS FOR USE

Restraints
DO NOT apply if heavy rain 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 more than 3 applications of Trebon per season in any crop.
DO NOT apply with aircraft.
DO NOT apply by a boom sprayer.

Spray Drift Restraints:
DO NOT allow bystanders to come into contact with the spray cloud.

DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The advisory buffer zones in the relevant buffer zone table below provide guidance but many 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 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	Natural aquatic areas	Livestock areas
2 metres tall and smaller, maximum dilute water rate of 1000 L/ha	20 metres	Not required
Taller than 2 metres (not fully-foliated), maximum dilute water rate of 1500 L/ha	55 metres	20 metres
Taller than 2 metres (fully foliated), maximum dilute water rate of 1500 L/ha	45 metres	15 metres

CROP	INSECT PEST	RATE	WHP	CRITICAL COMMENTS
Stone fruit (except cherries)	Queensland fruit fly and Mediterranean fruit fly	50-100 mL/100L	3 days	Spray to wet foliage to near the point of run-off. Thorough coverage and penetration into plant canopy is essential. Use the higher rate for heavy infestations and longer residual control. Apply first application as maturity approaches (fruit turning colour) and the target pest numbers are at critical thresholds. Continue to monitor pest pressure and if re-application is needed, a minimum of 7 days is required between treatments. Do not apply more than 3 applications per season.

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

WITHHOLDING PERIODS:
STONE FRUIT: DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION
DO NOT GRAZE ANY TREATED AREA OR CUT FOR STOCKFOOD

EXPORT TRADE ADVICE
Treated crop commodities destined for export may require extra time being allowed between application and harvest, as some export markets have either no Maximum Residue Limit (MRL) or different MRL to those of Australia. Details of overseas standards and export interval can be obtained by contacting Sipcam before using this product.

GENERAL INSTRUCTIONS
TREBON Insecticide is a contact and residual insecticide. For both fruit fly, cultural control methods (e.g. removal or destruction of fallen fruit by mulching) should be used to prevent excessive build-up of the pests.

MIXING
Add the required quantity of TREBON Insecticide to water in the spray tank and mix thoroughly. Maintain agitation during mixing and application.

APPLICATION
Use a sprayer designed to apply high volumes of water up to the point of run-off and matched to the stage of growth of crop being sprayed. Calibrate and operate the sprayer to achieve even coverage throughout the crop canopy.

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

INSECTICIDE RESISTANCE WARNING

GROUP	3A	INSECTICIDE

For insecticide resistance management TREBON Insecticide is a Group 3A insecticide. Some naturally occurring insect biotypes resistant to TREBON Insecticide and other Group 3A insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if TREBON Insecticide or other Group 3A Insecticides are used repeatedly. The effectiveness of TREBON Insecticide on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Sipcam Pacific Australia Pty Ltd accepts no liability for any losses that may result from the failure of TREBON Insecticide to control resistant insects. TREBON Insecticide may be subject to specific resistance management strategies. For further information, contact your local supplier, Sipcam Pacific Australia Pty Ltd representative or local department of agriculture agronomist.

PROTECTION OF HONEY BEES AND OTHER INSECT POLLINATORS
Highly toxic to bees. Harmful to bee brood. DO NOT spray while bees are actively foraging. DO NOT apply to crops 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 is reduced by spraying in the early morning or late evening when bees are not foraging.

INTEGRATED PEST MANAGEMENT
Toxic to beneficial arthropods. Not compatible with integrated pest management (IPM) programs utilising beneficial arthropods. Minimise spray drift to reduce harmful effects on beneficial arthropods in non-crop areas.

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

STORAGE AND DISPOSAL
Store in the closed, original container, in a cool, well-ventilated area. Do NOT store for prolonged periods in direct sunlight. Triple rinse containers before disposal. Add rinsings to spray tank. Do NOT dispose of undiluted chemicals on site. If recycling, replace cap and return clean container to recycler or designated collection point. If not recycling, break, crush or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose, clear of waterways, desirable vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

SAFETY DIRECTIONS
Will irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container and

preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length chemical resistant gloves and a face shield or goggles. Wash hands after use. After each day's use, wash gloves, face shield or goggles and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre (Phone Australia: 13 11 26; New Zealand 0800 764 766). If swallowed, do NOT induce vomiting.

SAFETY DATA SHEET
For further information, refer to the Safety Data Sheet (SDS) which is available from the supplier or from our web site, www.sipcam.com.au

NOTICE TO BUYER
This product must be used in accordance with the directions for use. Where this product is not a good of a kind ordinarily acquired for personal, domestic or household use or consumption under the Australian Consumer Law, Sipcam's liability for any direct, indirect or consequential loss which you incur, including, without limitation, loss or damage to crop, loss of equipment, property damage, personal injury or death is limited, at Sipcam's option, to the replacement of the product or the supply of an equivalent product. By opening this package, you agree to be bound by these terms. If you do not agree to these terms, please return the entire unopened package intact to Sipcam or the place in which you purchased this product for a full refund.

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
ARfD	Acute Reference Dose
bw	bodyweight
d	day
DT_{50}	Time taken for 50% of the concentration to dissipate
DT_{90}	Time taken for 90% of the concentration to dissipate
EC	Emulsifiable concentrate pesticide formulation
EC_{50}	concentration at which 50% of the test population are immobilised
EFSA	European Food Safety Authority
EPHC	Environment Protection and Heritage Council
EPPO	European and Mediterranean Plant Protection Organization
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
g	gram
GAP	Good Agricultural Practice
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
ISO	International Organization for Standardization
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_d	Distribution coefficient to measure the mobility of a compound in soil
kg	kilogram

K_{OC}	Organic carbon partitioning coefficient
kPa	kilopascal
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
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
mg	milligram
mL	millilitre
mPa	megapascal
MRL	Maximum Residue Limit
n	Number of samples
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NOAEL	No Observed Adverse Effect Level
Pa	Pascal
PEC	Predicted environmental concentration
PH	Acidity or alkalinity of a solution
PPE	Personal Protective Equipment
ppm	parts per million
RAL	Regulatory acceptable level
S.D.	Standard deviation of a mean
STMR	Supervised Trial Median Residue
TRR	Total radioactive residue
µg	microgram
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
CAS number	Unique numerical identifier assigned by the Chemical Abstracts Service (CAS) to every chemical substance
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
De-ethylation	The chemical process resulting in the removal of a methyl group from a molecule
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Henry's law constant	A gas law that states that the amount of dissolved gas in a liquid is proportional to its partial pressure above the liquid
IUPAC name	International Union of Pure and Applied Chemistry naming scheme for organic compounds
Leaching	Removal of a compound by use of a solvent
Mesocosm	Outdoor experimental system that examines the natural environment under controlled conditions
Metabolism	The chemical processes that maintain living organisms
Oxidation	The chemical process in which a substance gains oxygen
Photodegradation	Breakdown of chemicals due to the action of light
QuEChERS multi-residue method	Extraction method for the detection of pesticide residues in food samples (Quick, easy, cheap, effective, rugged and safe)
Toxicology	The study of the nature and effects of poisons
Toxicokinetics	The study of the rate a substance enters the body and what occurs to excrete and metabolize the substance once it is in the body

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