Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the active constituent fluopicolide in the product Infinito SC Fungicide

APVMA Product Number 80625

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

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing, Department of Agriculture and Water Resources, and State Departments of Primary Industries.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for products containing new active constituents.

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

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

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

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

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

Making a submission

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

Submissions must be received by the APVMA by close of business on 12 December 2016 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

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

When making a submission please include:

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

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

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

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

Phone: +61 2 6210 4701
Fax: +61 2 6210 4721

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

Email: enquiries@apvma.gov.au

Further information

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

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

1 INTRODUCTION

1.1 Applicant

Bayer CropScience Pty Ltd.

1.2 Details of the product

It is proposed to register Infinito SC Fungicide, containing 62.5 g a.i./L of fluopicolide and 625 g a.i./L of propamocarb hydrochloride, as a suspension concentrate for the control of downy mildew and late blight in bulb vegetables (onions, spring onions and leeks), lettuce, poppies, cucurbits and potatoes. The proposed use for Infinito SC Fungicide will involve ground application at 1.6 L/ha and a maximum of 3 applications per crop at a minimum interval of 7 days.

Fluopicolide is a fungicide used in agriculture to control oomycetes (*Phycomycete*) caused diseases including downy mildews (*Plasmopara, Pseudoperonospora, Peronospora, Bremia*), late blight (*Phytophthora*), and some Pythium species. The mode of action of fluopicolide is unique and yet it is not well characterised. However, recent reports stated that it acts *via* inducing perturbation of a spectrin-like protein in the cytoskeleton of oomycetes. It affects the motility of zoospores, the germination of cysts, the growth of the mycelium and sporulation. Resistant oomycetes to phenylamides, strobilurin, dimethomorph and iprovalicarb are labile to fluopicolide. Since fluopicolide translocates toward the stem tips via the xylem, it has a systemic action but it does not translocate toward the roots. Chemically, it classed as an acylpicolide.

1.3 Overseas registrations

Infinito SC Fungicide (fluopicolide at 62.5 g a.i./L and propamocarb hydrochloride at 625 g a.i./L) as a suspension concentrate is currently registered for use on various crops in Algeria, Argentina, Austria, Azerbaijan, Belarus, Belgium, Brazil, Colombia, France, El Salvador, Germany, Guyana, Japan, Morocco, New Zealand, Nicaragua, Peru, Poland, Spain, Switzerland, Trinidad and Tobago, Tunisia, Ukraine and Uruguay.

Infinito SC Fungicide is registered in the United Kingdom and New Zealand for control of late blight (*Phytophthora infestans*) in potatoes and in other countries for the control of downy mildew in cucurbits.

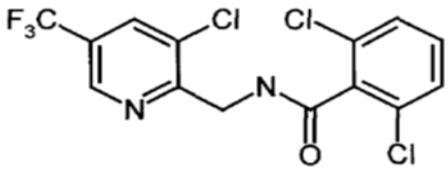
This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Infinito SC Fungicide, and approval of the new active constituent, fluopicolide.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The chemical active constituent fluopicolide is manufactured by Bayer CropScience. Tables 1 and 2 summarise key properties of this chemical.

Table 1: Nomenclature, chemistry and key identifiers of fluopicolide

COMMON NAME (ISO):	fluopicolide
IUPAC NAME:	2,6-dichloro-*N*-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl] benzamide
CAS REGISTRY NUMBER:	239110-15-7
MOLECULAR FORMULA:	$C_{14}H_8Cl_3F_3N_20$
MOLECULAR WEIGHT:	383.6 g/mol
STRUCTURAL FORMULA:	
CHEMICAL FAMILY:	Benzamide

Physico-chemical properties of the active constituent

Table 2: Summary of key physico-chemical properties of fluopicolide

PHYSICAL FORM:	Fine crystalline beige—coloured powder
ODOUR:	No characteristic odour
MOLECULAR WEIGHT:	383.59
PH:	6.5 at 22.0°C
MELTING POINT:	150°C
RELATIVE DENSITY AT 20°C:	1.65
WATER SOLUBILITY AT 20°C:	2.86 mg/l at pH 4 2.80 mg/L at pH 7 2.80 mg/L at pH 9
SOLVENT SOLUBILITY AT 20°C:	n-Hexane: 0.20 g/L Ethanol: 19.2 g/L Toluene: 20.5 g/L Ethyl acetate: 37.7 g/L Acetone: 74.7 g/L Dichloromethane: 126 g/L Dimethyl sulfoxide: 183 g/L
VAPOUR PRESSURE AT 25°C	8.3×10^{-7} Pa
DISSOCIATION CONSTANT ($_pK_A$):	No evidence of ionization in the pH range 1.9–9.8
SURFACE TENSION (90% SATURATED SOLUTION):	71.3 mN/M at 20°C
OCTANOL/WATER PARTITION CO-EFFICIENT LOG(K_{OW}):	Log K_{ow} = 3.26 at pH 7.8 and 22 ± 1°C Log K_{ow} = 2.9 at pH 4.0, 7.3 and 9.1 and 40°C
UV/VISIBLE ABSORPTION SPECTRUM:	Absorption maxima wavelengths (nm): In methanol: 203 and 271 In methanol/HCL: 202 and 270 In methanol/NaOH: 219 and 271
STABILITY:	Not degraded over 14 days at 54°C After 12 months at ambient temperature in polypropylene containers, no degradation was observed: the impurity profile did not change

2.2 Formulated product

The product, Infinito SC Fungicide will be manufactured in Australia and overseas and will be available in 1 L, 2.5 L, 3 L, 5 L, 7 L, 7.5 L, 10 L, 15 L, 20 L, 60 L and 110 L HDPE containers.

Table 3: Key aspects of the identity of the product Infinito SC Fungicide

DISTINGUISHING NAME:	Infinito SC Fungicide
FORMULATION TYPE:	Suspension Concentrate (SC)
ACTIVE CONSTITUENTS CONCENTRATION:	62.5 g/L fluopicolide and 625 g/L propamocarb hydrochloride

Physical and chemical properties of product

Table 4: Summary of key physico-chemical properties of the product Infinito SC Fungicide

PHYSICAL FORM:	beige suspension
PH VALUE:	7.0 @ 23ºC
RELATIVE DENSITY:	1.130 g/mL @ 20ºC
SURFACE TENSION:	31 mN/m @ 20ºC
VISCOSITY:	η (20°C, 20s^{-}) - 221 mPa.s η (20°C, 100s^{-}) - 100 mPa.s
FLASH POINT:	Not applicable.
OXIDISING PROPERTIES:	No oxidising properties
EXPLOSIVE PROPERTIES:	No explosive properties
FLAMMABILITY:	Auto-inflammable with a self-ignition temperature of 420 °C
CORROSIVE HAZARD:	Not corrosive to HDPE containers

2.3 Recommendations

The APVMA Chemistry and Manufacture Section has evaluated the chemistry aspects of fluopicolide and Infinito SC Fungicide (manufacturing process, quality control procedures, stability, batch analysis results and analytical methods) and found them to be acceptable.

On the basis of the data provided, and the toxicological assessment, it is proposed that the following APVMA active constituent standard be established for fluopicolide:

APVMA Active constituent standard for fluopicolide

Table 5: APVMA active constituent standard proposed for the active constituent fluopicolide

CONSTITUENT	SPECIFICATION	LEVEL
Fluopicolide	fluopicolide	Not less than 970 g/kg
	2,6-dichlorobenzamide	Not more than 4 g/kg

3 TOXICOLOGICAL ASSESSMENT

The product Infinito SC Fungicide contains a new active constituent, fluopicolide (62.5 g/L), and the existing active constituent propamocarb hydrochloride (625 g/L). The following summary focuses on the toxicity of fluopicolide with additional information on the toxicity of Infinito SC Fungicide.

The toxicity database of fluopicolide is extensive and consists primarily of toxicity studies conducted in laboratory animals. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified.

Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective, however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available.

Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur.

3.1 Chemical class

Fluopicolide is a fungicide of the benzamide and pyridine classes with an incompletely known mechanism of fungicidal action. The compound is effective against a wide range of Oomycete (Phycomycete) diseases including downy mildews (*Plasmopara, Pseudoperonospora, Peronospora, Bremia*), late blight (*Phytophthora*) and some *Pythium* species.

3.2 Toxicokinetics and metabolism

Toxicokinetic studies with fluopicolide have been performed in rats. It is well absorbed orally, with bioavailability $\geq$ 71%. The highest plasma concentration was reached 6 to 12 hours after a single oral dose, with a moderately rapid elimination via the faeces and urine. Low tissue residues were observed after the oral administration of fluopicolide and there was no potential for accumulation. The toxicokinetics for fluopicolide were qualitatively similar between sexes as was metabolism.

Fluopicolide is extensively metabolised via a number of different Phase I mechanisms including aromatic ring hydroxylation, hydrolysis, dealkylation, acetylation and oxidative N-dealkylation. Metabolites are conjugated with glucuronide sulphate and glutathione as part of Phase II processes.

3.3 Dermal absorption

The dermal absorption of fluopicolide in rats was less than 3% for the concentrate and approximately 22% from a dilution of Infinito SC Fungicide approximating that applicable to the in-use dilution of the product for spray application. In a direct comparison of absorption *in vitro* across human and rat skin, the absorption across rat skin was shown to be approximately 9.8 times greater than for human skin. Therefore, the dermal absorption factor for fluopicolide was considered to be 2.3% (22% ÷ 9.8 = 2.3%).

3.4 Toxicity of fluopicolide

The acute oral and dermal toxicities of fluopicolide in rats are low (oral LD_{50} > 5000 mg/kg bw; dermal LD_{50} > 5000 mg/kg bw), as is its acute inhalational toxicity (LC_{50} of 5.160 mg/L). Studies in rabbits show fluopicolide is non-irritating to the skin and a slight eye irritant. It is not a skin sensitiser in Guinea pigs. Fluopicolide has very low dermal repeat dose toxicity with a No Observed Effect Level (NOEL) in rats of 1000 mg/kg bw/d (4 week study).

Various animal studies in rats, mice and rabbits, as well as bacterial and mammalian cell assays, show fluopicolide is likely not genotoxic or a carcinogen, is not a reproductive toxicant and is not considered to be a teratogen or neurotoxin.

3.5 Toxicity of metabolites

An extensive range of toxicity studies has been submitted for a number of animal, plant and soil metabolites of fluopicolide which confirm the parent compound as the principal substance of toxicological concern but indicated that the metabolite 2,6 dichlorobenzamide (BAM), a residue in crop plants, was equally or slightly more toxic than fluopicolide. Consequently, an ADI and ARfD were established for both fluopicoloide and its metabolite, BAM.

3.6 Toxicity of Infinito SC Fungicide

Infinito SC Fungicide has low acute oral (LD_{50} > 2500 mg/kg bw), dermal (LD_{50} > 4000 mg/kg bw) and inhalational (LC_{50} > 3.195 mg/L) toxicity in rats with no deaths and no or only slight and transient, clinical signs. The product was mildly sensitising in mice by the local lymph node assay method, but non-sensitizing by the Buehler method in Guinea pigs. Eye irritation studies in rabbits demonstrated slight to moderate irritation resolving after 3 days with no permanent damage.

Like fluopicolide, the other active constituent of Infinito SC Fungicide, propamocarb hydrochloride, has a very low dermal repeat dose toxicity with a NOEL in rats of 717 mg/kg bw/d (3 week study). Also, propamocarb hydrochloride is not likely to present a genotoxic or carcinogenic risk to humans and is not considered a teratogen or neurotoxin.

As is common for relatively low toxicity compounds, the liver and kidneys were target organs of toxicity for fluopicolide and propamocarb hydrochloride at higher doses. Propamocarb hydrochloride also produced vacuolation in the ependymal cells of the choroid plexus in the brain of the rat. The toxicological significance

of this finding is uncertain, and it was not associated with any specific functional deficit even when described as moderate to severe histopathologically. Consequently, mild vacuolation was not considered adverse when determining NOELs. In dogs, vacuolation was observed in a wide range of tissues but again without any specific associated functional deficit. Also in dogs, the cells of the tapetum lucidum of the eye, a tissue that does not exist in primates including man, was a specific target of toxicity but in the absence of an analogous structure in humans was concluded not to be relevant to the human risk assessment.

3.7 Public health standards

Poisons scheduling of fluopicolide

On 12 May 2016, the Scheduling Delegate published an interim decision to create a new Appendix B entry for fluopicolide in the Poisons Standard (www.tga.gov.au/book-page/110-fluopicolide). The decision was implemented in October 2016. Fluopicolide was placed in Appendix B because of its low toxicity.

Infinito SC Fungicide contains the active constituent propamocarb hydrochloride as well as fluopicolide. As propamocarb hydrochloride is in Schedule 5 of the Poisons Standard with no cut-off, Infinito SC Fungicide will be a Schedule 5 product.

Acceptable Daily Intake (ADI)

The acceptable daily intake (ADI) for humans is the level of intake of an agricultural or veterinary chemical which can be ingested daily over an entire lifetime without appreciable risk to health. It is calculated by dividing the overall NOEL for the most sensitive toxicological endpoint from a suitable study (typically an animal study) by an appropriate safety factor. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans, intra-species variation, the completeness of the toxicological database and the nature of the potential toxicologically significant effects.

Fluopicolide

The relevant NOEL for the establishment of an ADI for fluopicolide is 7.9 mg/kg bw/d from an 18 month mouse study based on organ weight increases and gross and microscopic changes in the liver and kidneys, supported by the NOEL from a 2 year dietary study in rats of 8.4 mg/kg bw/d based on histopathological changes in the liver and increased kidney weights. The toxicological database available for fluopicolide is extensive and of high quality. On this basis a safety factor of 100 is adequate and appropriate.

The ADI is therefore established as 0.08 mg/kg bw/d based on a NOEL of 7.9 mg/kg bw/d and applying a 100-fold safety factor.

2,6- Dichlorobenzamide

2,6-Dichlorobenzamide is a metabolite of fluopicolide found as a residue in crop plants with a toxicity similar or slightly greater than fluopicolide. Consequently, an ADI is established for this metabolite at 0.02 mg/kg bw/d from a NOEL of 2 mg/kg bw/d in the 2–year rat study based on the effects on body weight reductions, increased incidences of eosinophilic and basophilic foci in the livers and fat deposition and cellular degeneration in the liver at 3.5 mg/kg bw per day.

Acute Reference Dose (ARfD)

The acute reference dose (ARfD) is the estimate of the amount of a substance in food or drinking water, expressed on a milligram per kilogram body weight basis, that can be ingested over a short period of time, usually in one meal or during one day, without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation.

Fluopicolide

An ARfD for fluopicolide of 0.6 mg/kg bw/d was established from a NOEL of 60 mg/kg bw/d based on a marginally increased incidence of skeletal defects of the vertebrae and sternebrae, which might be attributable to a single exposure to fluopicolide at 700 mg/kg bw/d in a study of developmental toxicity in rats, and using a safety factor of 100. Since this ARfD is based on effects observed in a developmental study it only applies to women of child-bearing-age and not to the general population.

2,6-Dichlorobenzamide

In the absence of suitable data, an ARfD for the general population was established for 2,6-dichlorobenzamide based on the value of 0.6 mg/kg bw for the parent compound. This ARfD was derived from a study with fluopicolide and is sufficiently protective for application to 2,6- dichlorobenzamide, owing to the large dose spacing between the Lowest Observed Adverse Effect Level (LOAEL) and the No Observed Adverse Effect Level (NOAEL). Owing to the absence of suitable data the ARfD for 2,6- dichlorobenzamide applies to the whole population whereas the ARfD for fluopicolide applies only to women of child bearing age.

4 RESIDUES ASSESSMENT

4.1 Introduction

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

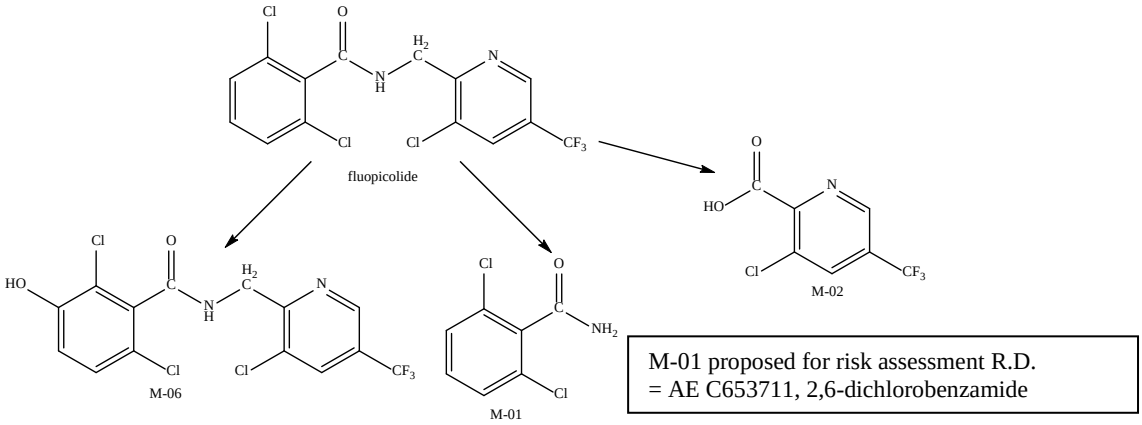
4.2 Metabolism

Fluopicolide—plants

Metabolism of fluopicolide has been studied using both [phenyl-UL-^{14}C]-labelled and [pyridyl-2,6-^{14}C]-labelled fluopicolide in representatives of four crop groupings for metabolism data generation: leafy crops (lettuce, treated with either 2 × 200 g ai/ha foliar applications or 1 × 200 g ai/ha soil drench application), root crops (potatoes, 2 × foliar applications at 200 or 2000 g ai/ha), fruits and fruiting vegetables (grapes, treated with a 167 + 116 g ai/ha foliar applications), and pulses and oilseeds (rapeseed, after seed treatment at 20 g ai/kg seed, equivalent to 120 g ai/ha for a typical 6 kg/ha sowing rate).

The metabolism of fluopicolide in plants after direct foliar, seed treatment or soil application involves two pathways: hydroxylation at the 3-position on the phenyl ring giving M-06 (2,6-dichloro-N-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]-3-hydroxybenzamide), and cleavage at the amide nitrogen – methyl bond to yield M-01 (2,6-dichlorobenzamide) and, after oxidation, M-02 (3-chloro-5-trifluoromethylpyridine-2-carboxylic acid).

Metabolism in plants is not extensive, especially after foliar application. Parent compound was generally the major component of the residue (40-96% of the TRR). The most significant metabolite was M-01 at 0.1-37% of the TRR, followed by M-02 at 0.6-26% of TRR and M-06 at 0.1-2.8% of TRR. Higher proportions of M-01 were observed after soil application to lettuce compared with foliar application, seed treatment application to rapeseeds, and in potatoes, as M-01 is also a soil metabolite subsequently taken up by the plant. The



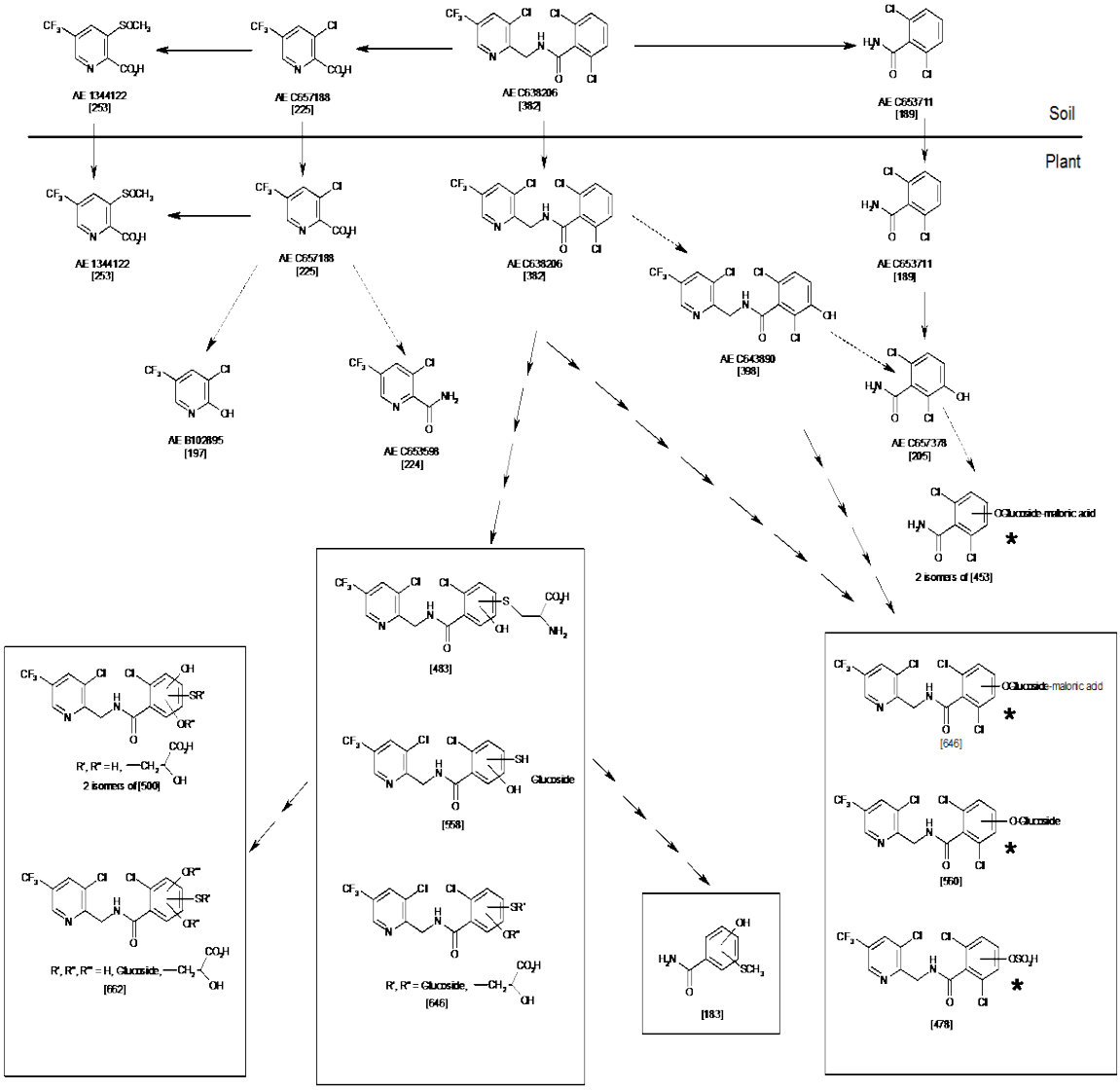
proposed metabolic pathway of fluopicolide in plants is shown below:

Figure 1: Metabolic pathway for fluopicolide in plants

Rotational cropping metabolism studies were carried out for lettuce, radish, and wheat planted out at intervals of 29, 133 and 365 days after application of either [phenyl-UL-^{14}C]-labelled or [pyridyl-2,6-^{14}C]-labelled fluopicolide to bare soil at 400 g ai/ha.

The principal compounds identified in phenyl-labelled experiments were parent fluopicolide (2.1–48% of TRR), M-01 (3.4–81% of TRR), and in wheat only, M-04 (3-hydroxy- M-01, at 14-59% of TRR). M-06, which is the 3–hydroxy derivative of fluopicolide, was detected at a quantifiable level only in 29 day wheat grain and forage (13%, 0.021 mg equiv/kg and < 1.0%, < 0.049 mg equiv/kg, respectively).

The principal compounds identified in pyridyl-labelled experiments included parent fluopicolide (1.8–80% of TRR), M-02 (2.1–70% of TRR), and M-05 (2.9-65% of TRR). In addition M-06, M-08 and M-09 were detected at low levels only occasionally exceeding either 10% or 0.05 mg equiv/kg in crops used for animal fodder and not exceeding either 10% or 0.01 mg equiv/kg in commodities considered as human



foods. The proposed metabolic pathway of fluopicolide in rotational crops is shown below:

Figure 2: Metabolic pathway for fluopicolide in confined rotational crops

Fluopicolide—animals

Metabolism data has been provided for fluopicolide in rats, lactating cattle and laying hens.

The major metabolic pathways observed in animals are hydroxylation at the 3 and/or 4 positions in the phenyl ring, sulphate, glucuronide or glutathione (the last observed in rats only) conjugation of the hydroxyl groups, and cleavage of the amide linkage yielding the phenyl and pyridyl fragments 2,6-dichlorobenzamide and 3-chloro-5-trifluoromethylpyridine-2-carboxylic acid (with conjugation of cleavage products only verified in rats). The cleavage pathway was not observed in cattle. The proposed metabolic pathways for fluopicolide in cattle and hens are shown below:

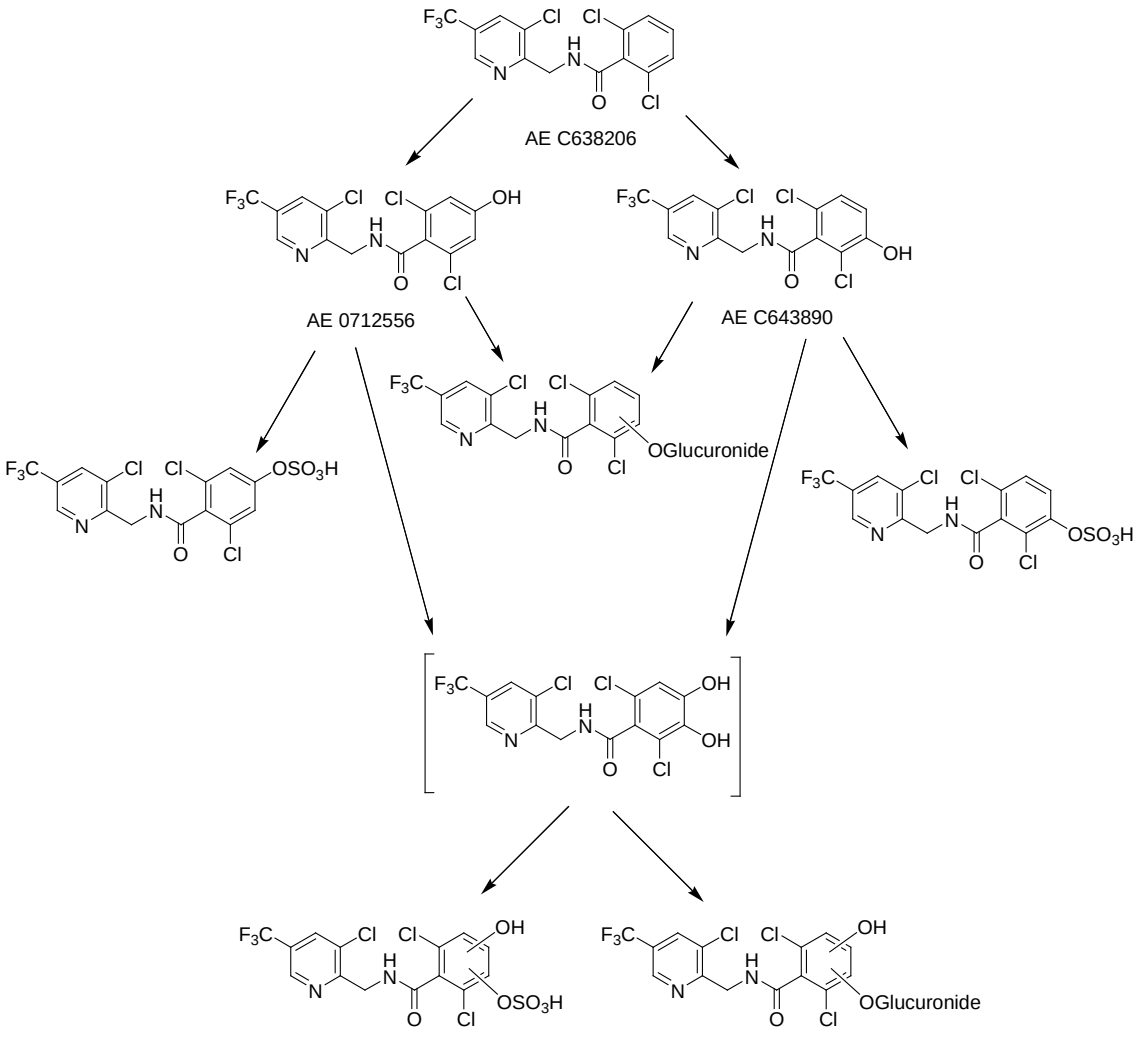


Figure 3: Metabolic pathway for fluopicolide in lactating cows

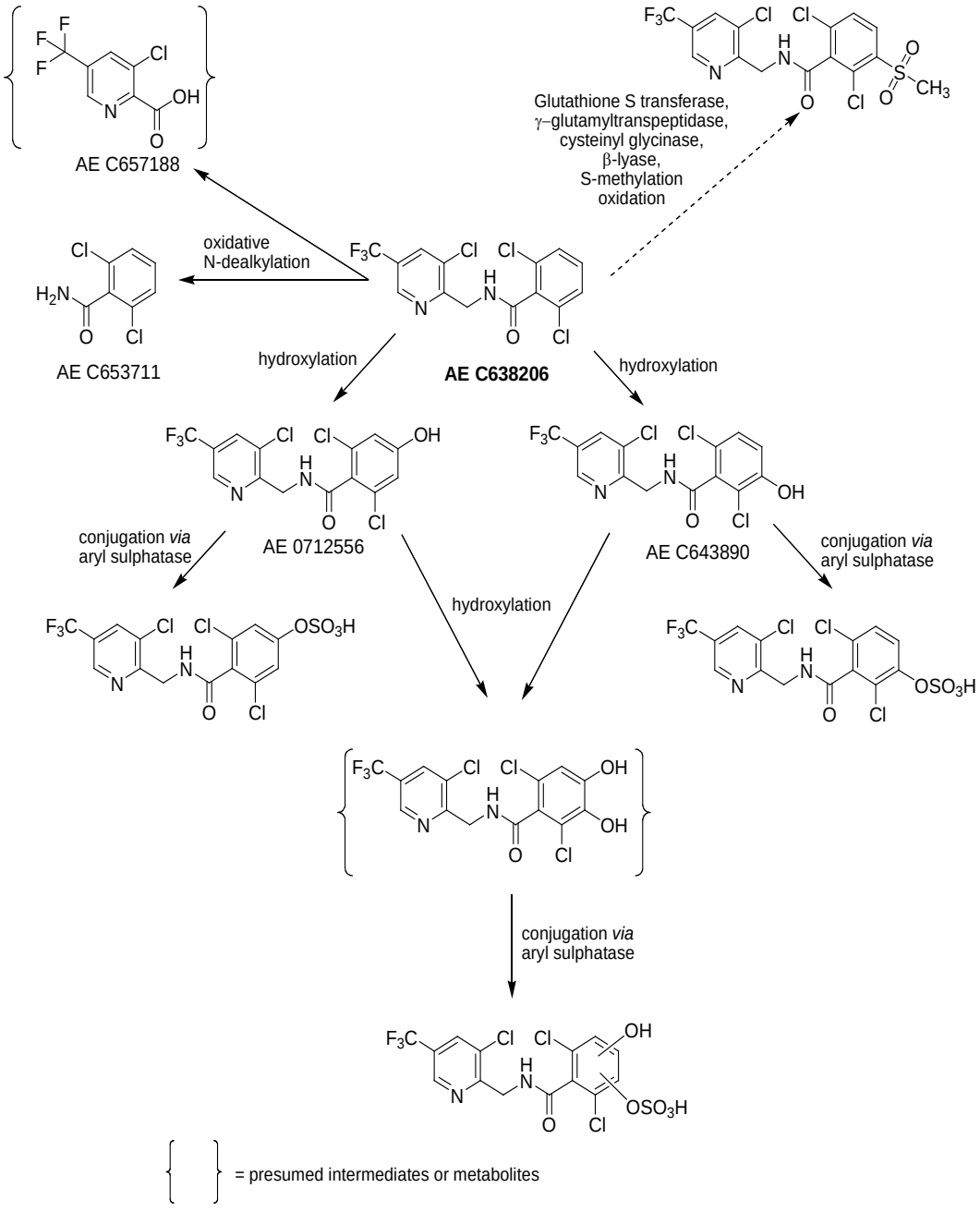


Figure 4: Metabolic pathway of fluopicolide in laying hens

Propamocarb—plants

Metabolic studies for propamocarb have been conducted in spinach (foliar application), lettuce (foliar and soil application studies), tomatoes (both foliar and soil application), cucumbers (soil application and treatment of the nutrient solution in hydroponic cucumbers), and potatoes (foliar and soil application). These experiments cover the leafy crop, root crop and fruit/fruiting vegetable groups for the purposes of collection of metabolism data.

In crops treated by foliar application, parent compound was the major component of the residue, at 75-89% of the TRR in lettuce, spinach, and tomatoes. After soil application, or foliar application to potatoes, levels of parent compound were much lower, ranging from not detected to 17% of the TRR. Identified metabolites in plants included propamocarb-N-oxide, 2-hydroxy propamocarb, N-desmethyl propamocarb, and propamocarb oxazolidin-2-one. A large proportion of the radioactive residue in plants after soil application, particularly in potatoes, appeared to be the result of incorporation of radiocarbon into natural plant components.

The major pathway for metabolism of propamocarb in plants is mineralisation in the soil, leading ultimately to formation of carbon dioxide. Minor pathways include oxidation of the amine moiety to give propamocarb-N-oxide, N-demethylation of one of the amine methyl groups, and hydroxylation of the alcohol propyl moiety at the 2 position, followed by cyclisation. The proposed metabolic pathway for propamocarb in plants is shown below.

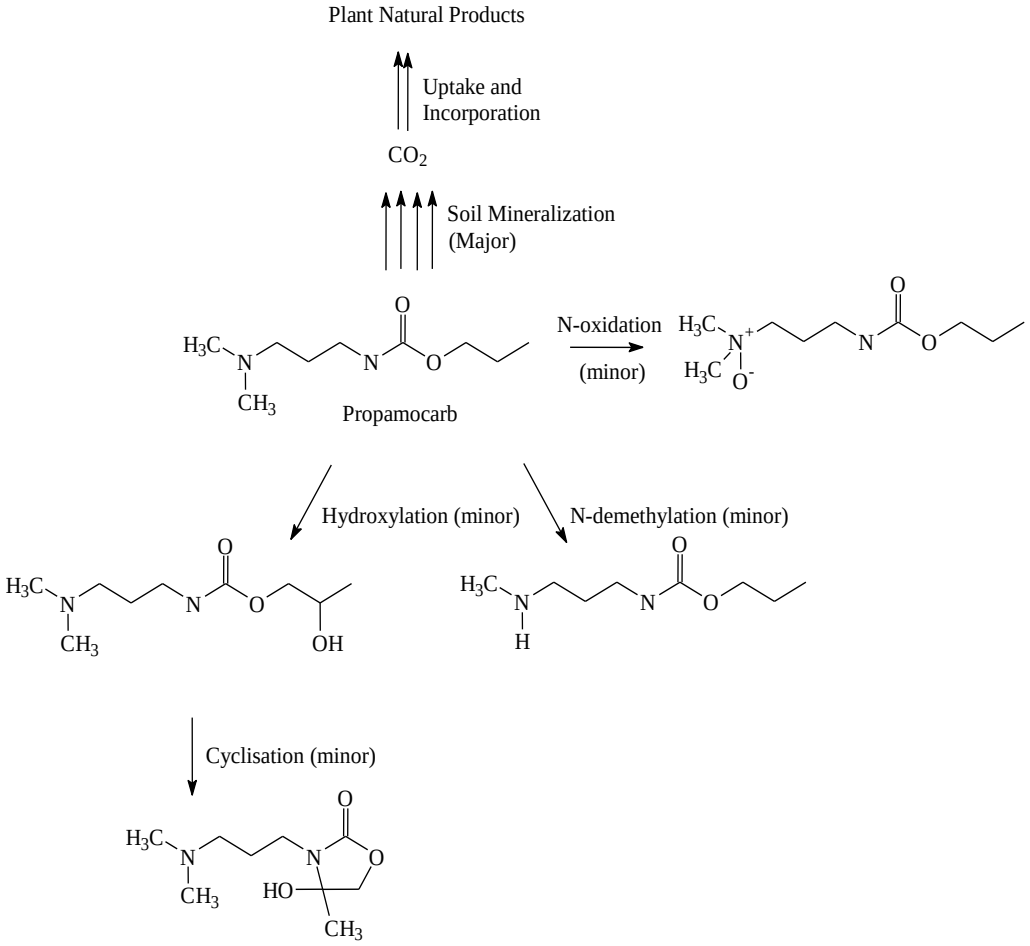


Figure 5: Metabolic pathway of propamocarb in plants

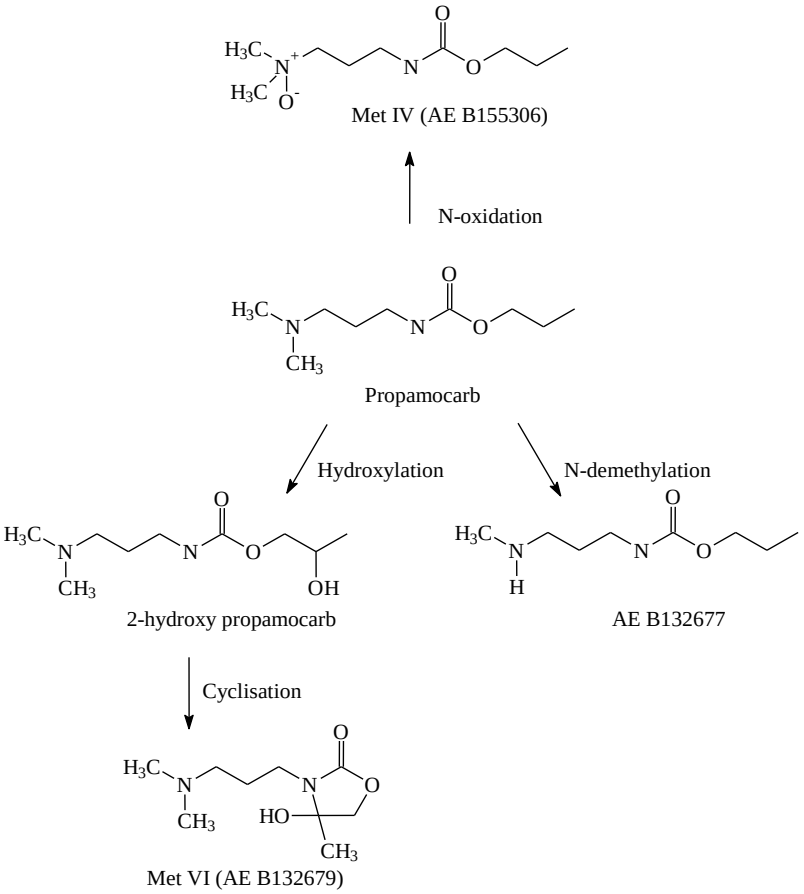
No hydrolysis products of propamocarb hydrochloride were found in test solutions simulation of food industry processes using radiolabelled propamocarb. Propamocarb hydrochloride is stable to processing conditions simulating pasteurisation, baking, boiling, brewing and sterilisation.

In rotational cropping studies for propamocarb, leafy lettuce, radishes and wheat were planted at 30 days, 120 days and 365 days after treatment of bare soil with radiolabelled compound at approximately 6 kg ai/ha.

Analysis of the extracts at 30 days and also from a wheat sample at 365 days showed a similar profile in all crops at both time points. Propamocarb was found consistently in all samples and was frequently the major component (1.3–67% of TRR at the 30 day plant back interval; not detected in wheat straw at the 365 day PBI). The remaining components identified comprised 2-hydroxy propamocarb (lettuce and wheat, 2.3–5.7% of TRR) and the oxazolidine (Met VI, 3.0–20% of TRR) with traces of N-oxide (Met IV, 1.2–6.1% of TRR) and desmethyl propamocarb (30 days wheat only). The remaining radioactivity was composed by a complex mixture of highly polar components, which eluted at the solvent front on HPLC and at, or close to the origin on TLC. Residues released after acid and base hydrolysis indicated a similar pattern of metabolites to those in the extracted residues, albeit with generally a higher proportion of the very polar components.

Propamocarb—animals

Metabolism of propamocarb has been investigated in rats, lactating cattle and laying hens. Metabolism in the three animal species was largely similar, with the major pathways being hydroxylation at the 2- and 3-positions in the alcohol propyl group followed by cyclisation to give 3-(3-dimethylaminopropyl)-4-hydroxy-4-methyloxazolidin-2-one, demethylation of the tertiary amine group to yield N-desmethyl propamocarb, and ultimately bis N,N-desmethyl propamocarb, and oxidation of the tertiary amine group to yield propamocarb-



N-oxide. The proposed metabolic pathways of propamocarb in cattle and hens are shown below:

Figure 6: Metabolic pathway of propamocarb in the cow

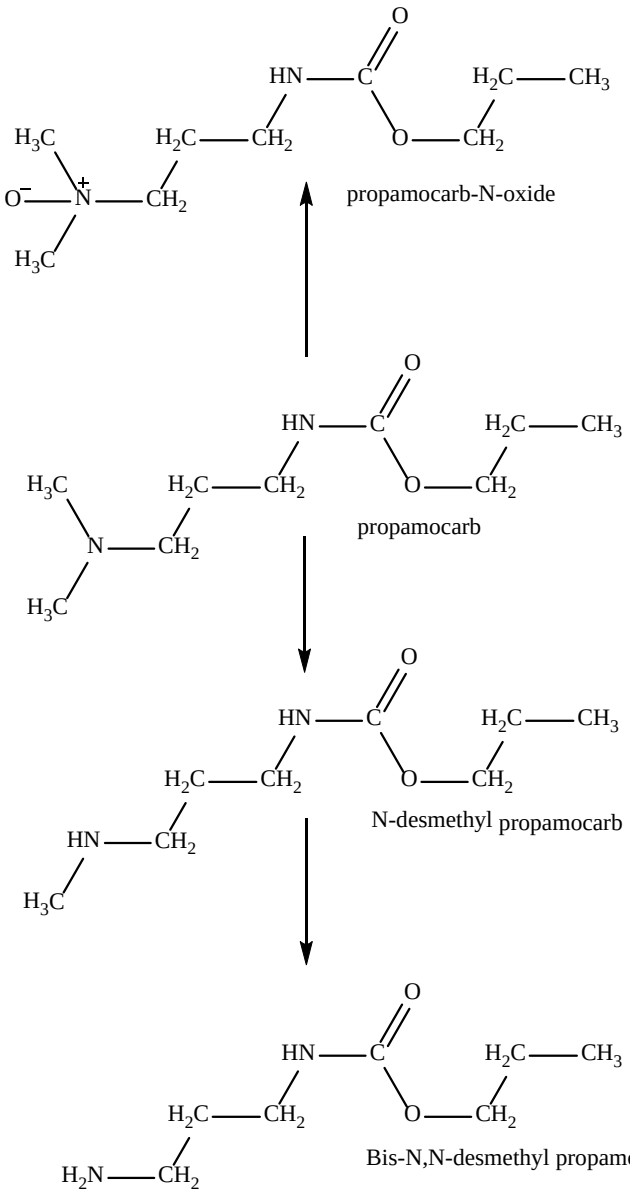


Figure 7: Metabolic pathway of propamocarb in laying hens

4.3 Analytical methods

Fluopicolide

A number of methods for determination of fluopicolide and its metabolites, particularly 2,6-dichlorobenzamide (M-01) and 3-chloro-5-trifluoromethylpyridine-2-carboxylic acid (M-02). Some variations of the method were also able to quantify the metabolites (M-04) and 3-methylsulfinyl-5-trifluoromethylpyridine-2-carboxylic acid (M-05). The basis of the methods (e.g. method number 00782) used for most of the residue trials was extraction of samples using acetone and formic acid or dilute sulfuric acid, followed by partition of the residues into methyl tert-butyl ether (MTBE). Analyses were conducted by LC-MS/MS. Some variations of the method involved derivatising M-02 to the methyl ester prior to analysis. The methods were validated in a range of plant matrices, covering oily, dry, high acid and high water content sample types, with an LOQ of 0.01 mg/kg achieved for each analyte, and acceptable recovery, precision and linearity data.

A QuEChERS-type method (for concurrent determination of fluopicolide parent compound, M-01, and propamocarb), and a multi-residue method (DFG S19, for fluopicolide parent compound only), were also validated for determination of fluopicolide residues in plant commodities.

The key animal commodities method for fluopicolide (parent compound) was a multi-residue method (DFG S19). Meat, liver, egg and milk samples were extracted with acetone/water, and cleaned up by partitioning into cyclohexane/ethyl acetate after addition of sodium chloride. An aliquot of the organic phase was filtered, and further cleaned up by partitioning into cyclohexane after evaporation to an aqueous residue, followed by final cleanup steps with gel permeation chromatography and silica gel column chromatography before analysis by GC-MS. Cream samples were mixed with sand and sodium sulphate, then placed in a column and extracted with hexane/actone before cleanup with gel permeation chromatography and silica gel column chromatography prior to GC-MS analysis. An LOQ of 0.01 mg/kg was validated for fluopicolide in all matrices. Acceptable method linearity, recovery (mean values all within the range 70–120% at 0.01 and 0.10 mg/kg fortification in all matrices), and precision (RSD <20%) were demonstrated.

Propamocarb

The key method for determination of propamocarb (which was either quantified as the base or as the hydrochloride) in plant matrices was method number 00880 and its variations. The basic method is extraction of samples with dilute acetic acid, with cleanup by solid phase extraction (C18 column), followed by LC-MS/MS analysis. Some matrices (e.g. brassicas, alliums and avocado) required the use of matrix matched standards. Validation data was provided for a range of plant matrices, covering oily, dry, high water content and high acid content samples, with an LOQ of 0.01 mg/kg, and acceptable recovery, precision and linearity being achieved. A QuEChERS-based multi-residues method (see discussion under fluopicolide) was validated for concurrent determination of propamocarb with fluopicolide and its metabolite M-01. Validation of the multiresidue method DFG S19 for determination of propamocarb in plant matrices was not successful.

For determination of propamocarb in animal commodities, three different methods were evaluated.

In the cattle feeding study, for determination of propamocarb and the metabolites 2-hydroxypropamocarb, propamocarb-N-oxide, and propamocarb oxazolidin-2-one, milk and homogenised tissue samples were extracted twice by blending with acetonitrile, while for determination of propamocarb glucucronide, samples were extracted with acetic acid/methanol. The extracts were cleaned up by partition with hexane, and residues in the aqueous phase were finally reconstituted in dilute HCl prior to LC-MS/MS analysis. An LOQ of 0.01 mg/kg was confirmed for each analyte.

In the poultry feeding study, residues of propamocarb parent and desmethyl propamocarb were extracted from tissue and egg samples using acetonitrile in the presence of diatomaceous earth. Analyses were completed by LC-MS/MS. The method LOQ was 0.01 mg/kg for each analyte (as the free bases). All recoveries were within the range 70–120%.

A QuEChERS-based multiresidue method was developed and validated for determination of propamocarb parent compound in eggs, milk, meat, fat and kidney. An LOQ of 0.01 mg/kg (as the free base) was verified, with acceptable recoveries, precision and linearity being demonstrated.

4.4 Stability of the pesticides in stored analytical samples

Residues of fluopicolide parent compound and its metabolites M-01 and M-02 were stable for at least 30 months of frozen storage in a range of plant matrices (wheat grain, cabbage, potato, grapes, refined sugar, molasses, dried sugar beet pulp, tomato puree and paste, and wheat flour, bran and shorts), covering high water and acid content, and dry matrices, and for at least 24 months in sunflower seed (high oil content).

In storage stability studies for propamocarb parent compound, residues were determined to be stable on frozen storage for at least 26 months in potatoes and tomatoes, at least 30 months in cabbage, and 3 months in canola seed.

4.5 Residue definition

Fluopicolide

Given that fluopicolide parent compound is a marker residue found in nearly all plant and animal matrices in the metabolism studies, and was often the largest component of the residue, it is suitable for use as the enforcement definition. The proposed residue definition for enforcement of MRLs in both plant and animal commodities is therefore: *fluopicolide*.

M-01 (2,6-dichlorobenzamide) has been determined to be of equal or slightly greater toxicological significance than fluopicolide, with separate health standards being established, and therefore it needs to be accounted for in the risk assessment definition. Noting that 2,6-dichlorobenzamide is also a metabolite of the herbicide dichlobenil, as well as its separate health standards, 2,6-dichlorobenzamide will need to be considered separately from fluopicolide in dietary exposure estimation.

The proposed residue definition of fluopicolide for dietary risk assessment is therefore: *fluopicolide and 2,6-dichlorobenzamide, measured separately.*

Propamocarb

In the plant metabolism studies involving foliar application to lettuce, spinach and tomato, parent compound formed the major component of the residue, typically >75% of the TRR. Where propamocarb was applied to the soil in metabolism studies in lettuce, cucumber or tomato, and in the potato metabolism studies, parent was generally a minor component of the residue, being <30% of the TRR. A significant proportion of the radioactive residue in the soil treatment studies was present as radiocarbon incorporated into natural plant components. Surprisingly, a higher proportion of parent compound was found in the rotational crop metabolism studies, where it comprised 15–67% of TRR in lettuce, radish and wheat forage and straw when planted at a 30–day plant back interval after application to bare soil. It is noted that the currently proposed use patterns involve foliar rather than soil application.

In the cattle metabolism study, parent compound was found in all matrices, at 6–25% of the TRR. However, the major residue component was propamocarb-N-oxide in muscle, kidney and liver, at 41–49% of the TRR, and 2-hydroxy propamocarb in milk, at 38% of the TRR. In hens, parent was likewise found in all matrices, at 2–12% of the TRR. Desmethyl propamocarb was the largest component of the residue in hen matrices, at 6–45% of the TRR. Given the proposed use patterns, which do not involve use in crops that are significant livestock feeds, the dietary burden of propamocarb in livestock is expected to be low.

The residue definition for propamocarb is therefore proposed to remain as: *propamocarb (base)*, for both enforcement and dietary risk assessment.

4.6 Residue trials

Bulb vegetables

The proposed GAP in bulb vegetables is 3 × 1000 g propamocarb hydrochloride + 100 g fluopicolide per hectare applications at 7–day intervals, with a 7–day harvest withholding period.

Residue trials in bulb onions, spring onions, and leeks were conducted in Australia, Europe and the USA.

Residues of fluopicolide in bulb onions at 7 days after 3 × 100 g ai/ha applications (1× GAP) were <0.01 (7), 0.01 (4), 0.02 (3), 0.03 (4), 0.04, and *0.054* mg/kg, where values in italics indicate results scaled to the proposed GAP.

Residues of 2,6-dichlorobenzamide in bulb onions at 7 days after 3 × 100 g ai/ha applications of fluopicolide were <0.01 (20) mg/kg.

An MRL of 0.1 mg/kg is proposed for fluopicolide in bulb onions (compared with the OECD calculator recommendation of 0.07 mg/kg which was not adopted as it was not considered to provide a sufficient margin above the 0.054 mg/kg HR).

The combined fluopicolide residue data sets matching GAP for spring onions and leeks are:

Fluopicolide: 0.19, 0.23, 0.42, 0.46, 0.52, 0.62, 0.63, 0.94, and 1.6 mg/kg.

2,6-dichlorobenzamide: <0.01 (7), 0.01, and 0.016 mg/kg.

An MRL of 3 mg/kg is proposed for fluopicolide in bulb vegetables, other than bulb onions (3 mg/kg was the value determined using the OECD calculator).

Residues of propamocarb (base) in bulb onions at 7 days after 3 × 1000 g ai/ha propamocarb HCl applications (1× GAP) were <0.01 (2), 0.01, 0.02 (4), 0.03, 0.04, 0.05 (5), 0.07, 0.09, 0.16, 0.21, and 0.27 mg/kg.

The OECD MRL calculator determined a figure of 0.4 mg/kg, and an MRL of 0.5 mg/kg (rounding up to the next standard MRL step) is proposed for propamocarb in bulb onions, together with an STMR of 0.05 mg/kg.

The combined propamocarb residue data set matching GAP for spring onions and leeks is:

1.3, 1.8, 1.9, 2.0, 4.1, 4.9, 5.8 and 15 mg/kg.

An MRL of 30 mg/kg (the OECD calculator value) is proposed for propamocarb in bulb vegetables other than bulb onions, together with an STMR of 3.1 mg/kg.

Fruiting vegetables, cucurbits

The proposed GAP in cucurbits is 2 × 1000 g propamocarb hydrochloride + 100 g fluopicolide per hectare applications at 7–day intervals, with a 3–day harvest withholding period, except for cucumbers which have a 1-day harvest withholding period.

Residue data in accordance with the proposed GAP is available for fluopicolide and propamocarb in field grown and protected cucumbers, zucchini and melons.

Residues of fluopicolide in cucumbers at 1 day after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were 0.02 (P, 3), 0.03 (2), 0.03 (P, 2), 0.04 (2), 0.04 (P, 2), 0.08 (P), 0.09 (P), 0.11, and 0.27 (P) mg/kg (where P indicates a result from a protected cropping trial; STMR = 0.04 mg/kg).

Residues of 2,6-dichlorobenzamide in cucumbers at 1 day after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were <0.01 (5), and <0.01 (P, 10) mg/kg (where P indicates a result from a protected cropping trial; STMR = 0.01 mg/kg).

Residues of fluopicolide in zucchini at 3 days after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were 0.01, 0.02, 0.03 (2), and 0.08 mg/kg.

Residues of 2,6-dichlorobenzamide in zucchini at 3 days after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were <0.01 (5) mg/kg.

Residues of fluopicolide in melons at 3 days after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were 0.01 (P), 0.02 (3), 0.03 (4), 0.03 (P, 2), 0.04 (2), 0.04 (P), 0.05 (P), 0.07, 0.08, 0.08 (P, 3), 0.09, and 0.10 mg/kg (where P indicates a result from a protected cropping trial).

Residues of 2,6-dichlorobenzamide in melons at 3 days after 2 or 3 × 100 g ai/ha applications in the Australian and European trials were <0.01 (13), and <0.01 (P, 8) mg/kg (where P indicates a result from a protected cropping trial).

A group MRL based on the 1–day cucumber data set is recommended. An MRL of 0.5 mg/kg (noting OECD MRL calculator value of 0.4 mg/kg, to account for variation over group) is proposed for fluopicolide in fruiting vegetables, cucurbits, in conjunction with a 1–day harvest withholding period for cucumbers and a 3–day harvest withholding period for the other crops in the group.

Residues of propamocarb (base) in cucumbers at 1 day after 2 or 3 × 1000 g propamocarb hydrochloride per hectare applications in the Australian and European trials were 0.13, 0.17, 0.21, 0.26 (P), 0.27 (P), 0.34 (P), 0.35 (P), 0.35 (P), 0.37 (P), 0.40, 0.41 (P), 0.44, 0.59 (P), 0.64 (P), and 2.5 (P) mg/kg (where P indicates a result from a protected cropping trial; STMR = 0.035 mg/kg).

Residues of propamocarb (base) in zucchini at 3 days after 2 or 3 × 1000 g propamocarb hydrochloride per hectare applications in the Australian and European trials were 0.19, 0.25, 0.34, 0.43, and 0.49 mg/kg.

Residues of propamocarb (base) in melons at 3 days after 2 or 3× 1000 g propamocarb hydrochloride per hectare applications in the Australian and European trials were 0.074, 0.10, 0.12 (3), 0.13 (P), 0.14 (2), 0.15, 0.17, 0.20, 0.21 (P), 0.24, 0.24 (P), 0.26, 0.28 (P), 0.29, 0.43 (P), 0.45 (P), 0.48, and 0.64 (P) mg/kg (where P indicates a result from a protected cropping trial).

A group MRL based on the 1-day cucumber data set is recommended. An MRL of 5 mg/kg (noting the OECD calculator recommendation of 3 mg/kg, which was not considered to provide a sufficient margin over the 2.5 mg/kg HR value and to account for variation over the group) is proposed for propamocarb in fruiting vegetables, cucurbits, in conjunction with a 1-day harvest withholding period for cucumbers and a 3–day harvest withholding period for the other crops in the group.

Lettuce

The proposed GAP in lettuce is 3 × 1000 g propamocarb hydrochloride + 100 g fluopicolide per hectare applications at 7–day intervals, with a 7–day harvest withholding period.

Residue data from trials conducted in Australia and Europe in field and protected head and leafy lettuce were provided. MRLs will be established on the basis of the leafy lettuce data as limited protected cropping data are available for head lettuce.

Residues of fluopicolide in leafy lettuce at 7 days after the last of 3 × 100 g ai/ha applications were 0.07, 0.14, 0.22, 0.28, 0.29 (P), 0.35, 0.36 (2), 0.41, 0.54, 0.54 (P, 2), 0.55 (2), 0.61 (P), 0.74 (P), 0.78, 0.91, 1.4 (P), 1.8 (2), 2.6 (P), 3.4, 4.1 (P), 5.8 (P), and 14.5 (P) mg/kg (where P indicates a result from a protected cropping trial; STMR = 0.55 mg/kg).

Residues of 2,6-dichlorobenzamide in leafy lettuce were <0.01 (4), <0.01 (P, 3), 0.01 (P), 0.01 (2), 0.012, 0.012 (P), 0.014 (2), 0.015, 0.016, 0.018, 0.02 (3), 0.022 (P, 2), 0.024 (P), 0.028 (P), 0.04, and 0.05 (P) mg/kg (where P indicates a result from a protected cropping trial; STMR = 0.014 mg/kg).

MRLs of 30 mg/kg are proposed for fluopicolide in head and leafy lettuce, in conjunction with a 7–day harvest withholding period (the OECD calculator value of 15 mg/kg was not considered to provide a sufficient margin over the HR of 14.5 mg/kg owing to potential variance across crop group).

Residues of propamocarb (base) in leafy lettuce at 7 days after 3 × 1000 g propamocarb hydrochloride per hectare applications were 1.6, 4.0, 4.1, 4.9, 5.9 (P), 6.0, 6.4, 6.7, 6.8, 6.9, 7.4 (P), 7.5, 7.9, 8.2 (P), 8.6, 10 (P), 11, 11.6 (P), 12 (P), 13, 16, 26.2 (P), 34 (P), 37, 37 (P), and 42 (P) mg/kg (where P indicates a result from a protected cropping trial; STMR = 8.1 mg/kg).

MRLs of 70 mg/kg (rounding up from the OECD MRL calculator recommendation of 60 mg/kg to account for variation within types of lettuce) are proposed for propamocarb in head and leafy lettuce, in conjunction with a 7–day harvest withholding period.

Potatoes

The proposed GAP in potatoes is 2 × 1000 g propamocarb hydrochloride + 100 g fluopicolide per hectare applications at 7–day intervals, with a 14–day harvest withholding period.

Residue data from trials conducted in Australia, the USA and Europe is available for potatoes.

Residues of fluopicolide in potatoes 14 days after 2–4 × 100-135 g ai/ha applications were <0.01 (20), 0.01 (2), 0.013, and 0.02 mg/kg (STMR = 0.01 mg/kg).

Residues of 2,6-dichlorobenzamide in potatoes 14 days after 2 or 3 × 100 g ai/ha fluopicolide applications were <0.01 (24) mg/kg (STMR = 0.01 mg/kg).

An MRL of 0.05 mg/kg is proposed for fluopicolide in potatoes, in conjunction with a 14–day harvest withholding period.

Residues of propamocarb (base) in potatoes 14 days after 2–4 × 1000 g propamocarb hydrochloride per hectare applications were <0.01 (9), 0.01 (2), and 0.03 mg/kg (STMR = 0.01 mg/kg).

An MRL of 0.05 mg/kg is proposed for propamocarb in potatoes, in conjunction with a 14–day harvest withholding period (rounding up from the OECD calculator estimate of 0.04 mg/kg).

Poppies

The proposed GAP in poppies is 3 × 1000 g propamocarb hydrochloride + 100 g fluopicolide per hectare applications, at 7–day intervals, with application from ground cover stage until the start of flowering (approximately BBCH stage 61). A harvest withholding period is not required when the product is used as directed.

A package of six residue trials in poppies was conducted over two seasons in Victoria and Tasmania.

After application in accordance with GAP (3 × 100 g ai/ha applications, with the last at BBCH stage 41–81 (or 41–61 days before harvest)), residues of fluopicolide in poppy seed at harvest were 0.02, 0.03, 0.04, 0.07, 0.11, and 0.25 mg/kg (STMR = 0.055 mg/kg).

Residues of 2,6-dichlorobenzamide at harvest were <0.01 (2), and 0.02 (4) mg/kg (STMR = 0.02 mg/kg).

An MRL of 0.5 mg/kg, as calculated by the OECD MRL calculator, is proposed for fluopicolide in poppy seed, with a harvest withholding period not required when used as directed.

After application of propamocarb hydrochloride in accordance with the proposed GAP (3 × 1000 g propamocarb hydrochloride per hectare applications, with the last at BBCH stage 41–81 (or 41–61 days before harvest)), residues of propamocarb (base) in poppy seed were 0.44, 0.69, 0.80, 0.90, and 2.3 (2) mg/kg (STMR = 0.85 mg/kg).

An MRL of 5 mg/kg, as calculated by the OECD MRL calculator, is proposed for propamocarb in poppy seed, with a harvest withholding period not required when used as directed.

4.7 Rotational crops

Fluopicolide

Details of field rotational crop studies conducted in Europe and the USA have been provided. In each case applications were made to a primary potato crop. In the European studies, 4 × 100 g ai/ha applications of fluopicolide were made at each site, while in the US studies, 3 × 133 g ai/ha applications were made, giving in both cases a total rate of 400 g ai/ha, which is 1.3× the proposed maximum rate per crop in Australia (3 × 100 g ai/ha = 300 g ai/ha).

In all edible matrices from rotational crops in the European and US studies (wheat grain, faba bean seed, and cabbage) residues of parent fluopicolide were below the LOQ, although it is noted that some residues below the LOQ (at 0.006–0.009 mg/kg) were found in wheat grain at some of the US sites. After scaling for the proposed total application rate, the expected maximum residue is 0.007 mg/kg.

It is therefore proposed to include an MRL at the LOQ (0.01 mg/kg) for fluopicolide in ‘all other foods’.

In animal feed matrices from the European rotational studies, the highest observed residue of parent fluopicolide was 0.07 mg/kg in wheat stalks (forage), 0.12 mg/kg in wheat straw, and 0.03 mg/kg in faba bean shoots (forage). On a dry weight basis, this gives maximum residues of 0.28 mg/kg in wheat forage, 0.14 mg/kg in wheat straw, and 0.09 mg/kg in bean forage. Residues of M-01 in feed matrices from the European studies reached maximum levels of 0.02 mg/kg in wheat shoots/stalks (forage), 0.03 mg/kg in wheat straw, and 0.10 mg/kg in faba bean shoots (forage). On a dry weight basis, this gives maximum levels of 0.08 mg/kg in wheat forage, 0.034 mg/kg in wheat straw and 0.29 mg/kg in bean forage.

Residue levels in feed matrices from the US studies were significantly higher, with fluopicolide reaching a maximum of 0.86 mg/kg in wheat forage, 0.69 mg/kg in wheat hay, and 0.35 mg/kg in wheat straw, while M-01 reached a maximum of 0.48 mg/kg in forage, 0.15 mg/kg in hay and 0.05 mg/kg in straw, with all results on a dry weight basis.

Noting that in the US and European field rotational trials the total application rate to each crop was 400 g ai/ha, compared with a maximum total of 300 g ai/ha per crop proposed for the Australian use pattern, it is proposed to establish an MRL in Table 4 of the Standard at 1 mg/kg for fluopicolide in primary feed commodities as a limit for residues in feeds resulting from application to a preceding crop.

Propamocarb

Details of field rotational crop studies conducted in Europe and the USA have been provided. In the USA bare soil at 11 sites was treated with 4 × 1.68 kg ai/ha propamocarb hydrochloride applications (total per crop rate of 6.72 kg ai/ha, compared with a maximum of 3 kg ai/ha propamocarb hydrochloride per crop as proposed for the Australian use pattern). Crops (winter or spring wheat, sugar beet, table beet, soybean or dry beans) were planted 30 days, 60 days or 365 days after the final soil treatment. In a series of studies in Europe application was made to a primary cabbage or lettuce crop at 2 × 3.6 kg ai/ha or 3 × 1.3 kg ai/ha with leafy vegetables, cereals or root and tuber vegetables sown after various plant back intervals.

Given that no residues above the LOQ were found in any of the food matrices from the European or US field rotational cropping trials (sugar or table beet roots, carrot roots, wheat or barley grain, soybean, dry beans, or lettuce), it is not proposed to establish any Table 1 entries in relation to propamocarb in rotational crops.

As finite residues were observed in wheat forage (up to 0.41 mg/kg dry weight, scaled) and hay (up to 0.12 mg/kg dry weight, scaled) in the US field rotational cropping trials, it is proposed to establish a primary feed commodities MRL for propamocarb in Table 4 at 0.7 mg/kg.

4.8 Animal commodity MRLs

Fluopicolide

The livestock dietary burdens for beef and dairy cattle are summarised below:

Beef Cattle—for MRL estimation.

COMMODITY	CC	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	DIET CONTENT (%)	RESIDUE CONTRIBUTION (ppm)
Potato process waste	AB	0.15	STMR-P	12	1.25	5	0.063
Primary feed commodities (wheat forage—scaled)		0.65	HR	100	0.65	95	0.61
Total						100	0.68

Dairy Cattle—for MRL estimation.

COMMODITY	CC	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	DIET CONTENT (%)	RESIDUE CONTRIBUTION (ppm)
Potato culls	VR	0.02	HR	20	0.10	10	0.01
Primary feed commodities (oat forage—scaled)		0.65	HR	100	0.65	90	0.59
Total						100	0.60

The maximum dietary burden for fluopicolide in mammalian meat animals (beef cattle) is 0.68 ppm and 0.60 ppm in dairy animals (cattle). In a dairy cattle animal transfer study, no residues of fluopicolide, M-01 or M-02 were found above the LOQ in milk at feeding levels of 0.5 or 1.7 ppm, or in tissues at a 5.7 ppm feeding level. Detectable residues of fluopicolide or its metabolites are not expected in any mammalian matrices as a result of the proposed use pattern. MRLs at the method LOQ are therefore proposed for fluopicolide in mammalian commodities, using the LOQ of 0.01 mg/kg in milk, cream, muscle, liver, and egg from the multi-residue method (DFG S19).

There are no poultry feed commodities commonly used in Australia derived from any of the crops in which Infinito SC Fungicide is proposed for use. A poultry feeding study was not provided for fluopicolide. However, given the nil dietary burden in poultry, detectable residues of fluopicolide or its metabolites are not expected in eggs or poultry meat or offal. It is therefore proposed to establish poultry commodity MRLs for fluopicolide at the LOQ. Given that the multi-residue method DFG S19 has been validated at an LOQ of 0.01 mg/kg in cattle meat and liver, and in eggs, MRLs of *0.01 mg/kg are proposed for eggs, poultry meat and poultry edible offal.

Considering the $\log_{10}K_{OW}$, the preferential partitioning of fluopicolide parent compound into fatty matrices, and noting that JMPR consider residues of fluopicolide to be fat soluble, it is proposed that MRLs of fluopicolide in mammalian and poultry meat will be established ‘in the fat’.

Propamocarb

The livestock dietary burdens for beef and dairy cattle are summarised below:

Beef Cattle—for MRL estimation

COMMODITY	CC	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	DIET CONTENT (%)	RESIDUE CONTRIBUTION (ppm)
Primary feed commodities (wheat or oat forage)		0.41	HR	100	0.41	100	0.41
Total						100	0.385

Dairy Cattle—for MRL estimation

COMMODITY	CC	RESIDUE (mg/kg)	BASIS	DM (%)	RESIDUE DW (mg/kg)	DIET CONTENT (%)	RESIDUE CONTRIBUTION (ppm)
Potato culls	VR	0.03	HR	20	0.15	10	0.015
Primary feed commodities (wheat or oat forage)		0.41	HR	100	0.41	90	0.37
Total						100	0.385

The maximum dietary burden for propamocarb in mammalian meat animals (beef cattle) is 0.41 ppm and 0.39 ppm in dairy animals (cattle).

In a dairy cattle animal transfer study, no residues of propamocarb parent compound were detected in any milk sample at any of the feeding levels, and none of the metabolites were found at levels above the LOQ for either the 0.78 or 2.4 ppm dose groups. In tissues, no residues of propamocarb parent compound were found above the LOQ in any of the 8.1 ppm dose group samples (the lower dose group samples were not analysed). The metabolites 2-hydroxypropamocarb, propamocarb-N-oxide and propamocarb oxazolidin-2-one were not detected in any of the 8.1 ppm dose group tissue samples, while the remaining metabolite, propamocarb glucuronide, was only found above the LOQ in liver from the 2.4 and 8.1 ppm groups (it was <LOQ in 0.78 ppm liver).

Given the very low dietary burden for propamocarb in mammalian meat and dairy animals (maximum of 0.41 ppm in beef cattle, and a maximum of 0.39 ppm in dairy cattle), detectable residues of propamocarb are not expected in milk, meat or offal of mammalian livestock. It is therefore proposed to establish MRLs at the LOQ. MRLs of *0.01 mg/kg are therefore proposed for propamocarb in milk and mammalian meat and offal.

Given the nil dietary burden in poultry, detectable residues of propamocarb or desmethyl propamocarb are not expected in eggs or poultry meat or offal. It is therefore proposed to establish poultry commodity MRLs for propamocarb at the LOQ. Given that an LC-MS/MS method has been validated at an LOQ of 0.01 mg/kg in cattle meat, liver and kidney, and in eggs, MRLs of *0.01 mg/kg are proposed for eggs, poultry meat and poultry edible offal.

4.9 Estimated dietary intake

The chronic dietary exposure to fluopicolide and propamocarb is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived primarily from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with WHO Guidelines[2] and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for fluopicolide is equivalent to <10% of the ADI. The NEDI for the fluopicolide metabolite 2,6-dichlorobenzamide is equivalent to <2% of the ADI. The NEDI for propamocarb is equivalent to <5% of the ADI.

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 1995 National Nutrition Survey of Australia. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. The highest acute dietary intake was estimated at <50%, <1%, and <35% of the ARfDs for fluopicolide, 2,6-dichlorobenzamide and propamocarb respectively. It is concluded that the acute dietary exposure is acceptable.

4.10 Bioaccumulation potential

The $\log_{10}K_{OW}$ value (octanol-water partition coefficient) for fluopicolide is 2.9–3.3 at pHs between 4.0 and 9.0, indicating borderline fat solubility.

It is noted that in the lactating cattle feeding study, where whole milk samples from the high dose group animals were separated into skim milk and cream, residues of fluopicolide parent compound in skim milk were <0.01 mg/kg, while residues in cream were 0.012–0.018 mg/kg. Residues of M-01 and M-02 were <0.01 mg/kg in both skim milk and cream. In fat and muscle samples, even in the high dose group, residues of parent and metabolites were all <LOQ.

Considering the $\log_{10}K_{OW}$, the preferential partitioning of fluopicolide parent compound into fatty matrices, and noting that JMPR consider residues of fluopicolide to be fat soluble, it is proposed that MRLs of fluopicolide in mammalian and poultry meat will be established ‘in the fat’.

The $\log_{10}K_{OW}$ value (octanol-water partition coefficient) for propamocarb is 0.84, while that for propamocarb hydrochloride is -1.21 (at pH 7). In the cattle feeding study, no residues of parent compound were found above the LOQ in skim milk, milk fat, muscle or body fat. In the poultry feeding study, residues of propamocarb parent compound were slightly higher in muscle than in fat. Residues of propamocarb are not considered to be fat soluble and mammalian and poultry meat MRLs will not be established ‘in the fat’.

[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.

4.11 Spray drift

Application will be by ground application only. For propamocarb, no residues of parent compound were detected in milk, muscle or liver of animals fed at the highest dose level in the cattle feeding study (8.1 ppm as propamocarb base), however detectable residues, but below the LOQ (0.05 mg/kg) were found in fat and kidney at this feeding level. A feeding level of 8.1 ppm corresponds to an acceptable drift of 12.15 g ai/ha, assuming pasture consists of 1500 kg DM/ha. As a fraction of the field rate this is 0.01×.

Using the APVMA's standard scenario for ground application / high boom/ medium droplets the average drift over a 300 m field is 0.0047× the field rate. A mandatory no-spray zone is not required for ground application of propamocarb for protection of international trade.

For fluopicolide, at a feeding level of 5.7 ppm in the cattle feeding study, no residues above LOQ were found in tissues, while only two low level detections of parent compound above LOQ were made in milk. A feeding level of 5.7 ppm corresponds to an acceptable drift of 8.55 g ai/ha, assuming pasture consists of 1500 kg DM/ha. As a fraction of the field rate this is 0.09×. A mandatory no-spray zone is also not required for ground application of fluopicolide for protection of international trade.

4.12 Recommendations

In considering the application, and section 5A(3)(b)(iii) of the schedule to the Code Act, the following amendments will be made to the APVMA MRL Standard should the application be approved:

Table 1

COMPOUND		FOOD	MRL (mg/kg)
ADD:			
Fluopicolide			
		All other foods	0.01
VA	0035	Bulb vegetables [except Onion, Bulb]	3
MO	0105	Edible offal (Mammalian)	*0.01
PE	0112	Eggs	*0.01
VC	0045	Fruiting vegetables, Cucurbits	0.5
VL	0482	Lettuce, Head	30
VL	0483	Lettuce, Leaf	30
MM	0095	Meat (mammalian) [in the fat]	*0.01
ML	0106	Milks	*0.01
VA	0385	Onion, Bulb	0.1
SO	0698	Poppy seed	0.5
VR	0589	Potato	0.05

COMPOUND		FOOD	MRL (mg/kg)
PO	0111	Poultry, Edible offal of	*0.01
PM	0110	Poultry meat [in the fat]	*0.01
Propamocarb			
DELETE:			
VL	0053	Leafy vegetables	T20
ADD:			
VA	0035	Bulb vegetables [except Onion, Bulb]	30
MO	0105	Edible offal (Mammalian)	*0.01
PE	0112	Eggs	*0.01
VC	0045	Fruiting vegetables, Cucurbits	5
VL	0053	Leafy vegetables [except Lettuce, Head and Lettuce, Leaf]	T20
VL	0482	Lettuce, Head	70
VL	0483	Lettuce, Leaf	70
MM	0095	Meat (mammalian)	*0.01
ML	0106	Milks	*0.01
VA	0385	Onion, Bulb	0.5
SO	0698	Poppy seed	5
VR	0589	Potato	0.05
PO	0111	Poultry, Edible offal of	*0.01
PM	0110	Poultry meat	*0.01

Table 3

COMPOUND	RESIDUE
ADD:	
Fluopicolide	Commodities of plant and animal origin for enforcement: fluopicolide
	Commodities of plant and animal origin for dietary exposure assessment: fluopicolide and 2,6-dichlorobenzamide, measured separately

Table 4

COMPOUND	FOOD	MRL (mg/kg)
ADD:		
Fluopicolide		
	Primary feed commodities	1
ADD:		
Propamocarb		
	Primary feed commodities	0.7

MRL amendments recommended for Tables 1 and 3 above will be considered for inclusion in Schedule 20 of the Australia New Zealand Food Standards Code.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

The proposed use does not involve treatment of major trade commodities and significant residues are not expected to arise in livestock feeds as a result of the proposed use. Animal commodity MRLs for fluopicolide and propamocarb hydrochloride are proposed at the respective LOQs for the analytical methods. The risk to trade in animal commodities is low.

For crops, the applicant has proposed the following risk mitigation statement which is considered appropriate and acceptable:

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

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Use pattern

The product is intended to be applied via ground application to bulb vegetables, including bulb onions, leeks and spring onions, and to cucurbits, lettuce, potatoes and poppies.

The maximum recommended dose rate per application of product is 1.6 L/ha, corresponding to 0.1 kg fluopicolide/ha and 1.0 kg propamocarb hydrochloride/ha. The proposed label stipulates a maximum number of three applications per crop for bulb vegetables, lettuce and poppies, and a maximum number of two applications per crop for cucurbits and potatoes. An interval of 7–10 days is recommended between applications.

6.2 Exposure during use and recommended Safety Directions/First Aid Instructions

Farmers and their employees, as well as contract sprayers will be the main users of Infinito SC Fungicide. Workers may be exposed to the product when opening containers, mixing/loading/application, cleaning up spills, maintaining equipment and entering treated crops. The main routes of potential exposure to the product will be dermal, inhalational and ocular.

As the general public are unlikely to be exposed to the product under normal conditions of use, the risk to the public is negligible.

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

The toxic endpoint of concern and identified NOEL for risk assessment is derived from a repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account both potential inter-species extrapolation and intra-species variability.

The exposure assessment determined that worker exposure to the active constituents is acceptable (MOE ≥100) when workers wear overalls and gloves during mixing/loading of the product.

In addition to the likely exposure workers may have to the active constituents, the hazard of the overall formulation was taken into account for the development of Safety Directions and First Aid Instructions. Undiluted Infinito SC Fungicide has low acute oral, dermal and inhalational toxicity. It may cause mild skin sensitisation and slight to moderate eye irritation. It is not a skin irritant. Therefore, the following Safety Directions and First Aid Instructions for the label are:

Will irritate the eyes. Avoid contact with the eyes. If product in eyes wash it out immediately with water. Repeated exposure may cause allergic disorders. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length chemical resistant

gloves and face shield. Wash hands after use. After each day's use, wash gloves and face shield and contaminated clothing.

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

6.3 Post-application exposure

Re-entry risks associated with conducting activities after the product has been applied are expected to be by the dermal route, and exposure to the active constituents is expected to occur at specific periods of time after application to a crop. However, it has been estimated that there is no need to wear Personal Protective Equipment (PPE) during spray application. Therefore, exposure from re-entry into sprayed areas is unlikely to present a significant risk requiring a specific label statement.

Similarly, exposure from the washing of equipment is not anticipated to add significantly to the overall exposure derived from mixing/loading and spraying.

Warning Statements and General Safety Precautions

No warning statements or general safety precautions are indicated for Infinito SC Fungicide.

Recommendations for safe use

Users should follow the first aid instructions and safety directions on the product label.

6.4 Conclusion

The registration of Infinito SC Fungicide, containing fluopicolide (62.5 g/L) and propamocarb hydrochloride (625 g/L) for the control of fungi in specified vegetables and poppies is supported.

Infinito SC Fungicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above.

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

It is proposed to register Infinito SC Fungicide for the for the control of downy mildew and late blight in bulb vegetables (onions, spring onions and leeks), lettuce, poppies, cucurbits, and potatoes. Section 1 describes the proposed use in greater detail.

7.2 Environmental fate and behaviour

No new environmental studies of propamocarb hydrochloride were considered in this risk assessment, therefore the environmental fate of fluopicolide was assessed as described below.

Hydrolysis

Fluopicolide and its metabolites are stable to hydrolysis under typical environmental pH and temperature conditions.

Photolysis/photodegradation

Aqueous photolysis of fluopicolide is negligible under environmental conditions.

Mobility

Laboratory studies on nine soil types indicate that fluopicolide has low to medium mobility in top soils when the organic content ≥ 0.5%. In such soils Kfoc values were found to be in the range 172–580 mL/g (mean 321 mL/g, medium mobility). In sub-soils, with organic content ≤ 0.2%, fluopicolide was highly mobile (Kfoc = 83–106 mL/g). The metabolite M-03 is also highly mobile (Kfoc = 82–133 mL/g; mean = 109 mL/g). The metabolites M-01 (Koc = 31-51 mL/g), M-05 (mean Koc = 26 mL/g), M-02 (mean Koc = 6.0 mL/g), and M-10 (mean Koc = 6.3 mL/g) are very highly mobile.

The average annual concentrations of fluopicolide and the metabolite M-02 were less than 0.1 µg a.c./L at depths below 85 cm and 30 cm respectively. However, the metabolite M-01 reached average annual concentrations up to 2.93 µg a.c./L at 120 cm during the third year of the study.

Bioaccumulation

Fluopicolide has a bio-concentration factor (BCF) of 121 L/kg and a log K_{ow} of 2.9 indicating it does not have a potential for bioaccumulation.

Atmospheric fate

The theoretical half-life of fluopicolide in air is 2.2–3.4 days, so volatilised fluopicolide will degrade slowly and does have the potential to be transported over long distances in the atmosphere, albeit at very low concentrations.

Biodegradation

Aerobic soil metabolism

Fluopicolide is very slightly degradable in aerobic soils under laboratory conditions with the DT50 values of 194–411 d (geometric mean = 271 d).

Fluopicolide initially degrades to the compound M-03 which is a short-lived intermediate (DT50 = 2.2-5.0 d) that breaks down to the compounds M-01 and M-02. The latter compound readily degrades (DT50 = 3.2-4.6 d) to various pyridine derivatives, some of which may be moderately persistent depending on the soil type. The metabolite M-01 is the major toxic degradation product from the aerobic soil metabolism.

Anaerobic soil metabolism

In anaerobic soils, the degradation of fluopicolide is even slower with a mean DT50 = 424 d (very slightly degradable). The extent of degradation of fluopicolide in sterilised and non-sterilised soil was in the same range, which suggests that microbes do not play a major role in the degradation of this compound.

Aerobic aqueous metabolism

The degradation of fluopicolide is very slow in whole water/sediment systems. Dissipation of fluopicolide from the water phase in whole water-sediment system is rapid (DT50 = 8.9 d) in systems with high organic content and cation exchange capacity but slow (DT50 = 263 d) in systems with low organic content. It is very slightly degradable in both abiotic and biotic water/sediment systems, which indicates that microbial degradation is not a significant factor. The calculated DT50 for the whole system was 873–1428 d (mean = 1116.5 d). M-01 and M-02 were identified as degradation metabolites and both tended to partition to water phase (M-01 max 18.2% in water, 3.9% in sediment and M-02 max 7.4% in water, 0.8% in sediment).

Biodegradability studies indicate that fluopicolide and the metabolite M-01 are not readily biodegradable.

7.3 Environmental effects

No new effects studies of propamocarb hydrochloride were considered in this risk assessment, therefore the environmental effects of fluopicolide were assessed as described below.

Terrestrial organisms

The toxicity of fluopicolide and its metabolites (M-01, M-02, M-03 to a number of terrestrial organisms based on the results (Table 12) from submitted studies, can be summarised as:

- to mammals—practically non-toxic to rats, with no evidence of reproductive toxicity to rabbits or rats
- to birds—practically non-toxic to birds, with no significant adverse effects observed for two species, while metabolite M-01 has slight short-term dietary toxicity
- to bees—very slight oral and contact toxicity

- to two standard non-target arthropod species (for example, *Aphidius rhopalosiphi,* and *Typhlodromus pyri*)
- to earthworms in soil—fluopicolide and metabolites M-01 and M-03 have at worst moderate acute toxicity and M-02 has low acute toxicity (Table 13).

Soil micro-organisms

Laboratory tests demonstrate that fluopicolide has an insignificant effect (≤ 25%) on soil microbial respiration and nitrogen transformation. In these tests fluopicolide was applied to the soils at rates equivalent to 0.133 and 1.33 kg ac/ha (equivalent to 0.184 and 1.84 mg ac/kg dws respectively). During the tests the maximum effect on respiration rate was -8% (relative to control), whilst the maximum effect on nitrogen transformation rate was -9%.

The effects of the metabolite M-01 on soil microbial respiration and nitrogen transformation have also been reported. The results demonstrated that the metabolite M-01 had an insignificant effect (≤ 25%) on soil respiration and nitrogen transformation at 0.92 mg M-01/kg dws.

Studies on the effects of fluopicolide on the growth of pure soil fungal cultures (5 species) indicate that only the soil oomycete *Phytophthora nicotianae* was significantly inhibited by fluopicolide. The studies were conducted at rates in the range 0.3–30.0 mg ac/kg dws and determined a NOEC for *P. nicotianae* of 0.3 mg ac/kg dws. It is not surprising that fluopicolide exhibited significant inhibition of this species because oomycete fungi are particularly sensitive to this compound and are the major target taxa.

Aquatic organisms

Effects on fish

Fluopicolide is moderately to highly toxic to most of the commonly tested fish species except the fathead minnow (*Pimephales promelas*) to which it was slightly toxic. The metabolite M-01 is practically non-toxic to rainbow trout (*Oncorhynchus mykiss*) (Table 13).

Effects on aquatic invertebrates

The toxicity of fluopicolide to aquatic invertebrates can be summarised as:

- at worst, moderate acute toxicity to aquatic invertebrates
- slightly (reproduction)to moderately (chronic) toxic to *Daphnia magna* and metabolite M-01 was practically non-toxic
- moderately toxic to marine oysters (*Crassostrea virginica*) and mysid shrimp (*Americamysis bahia*)
- very slightly toxic to *Chironomus riparius*.

Effects on algae and aquatic plants

The toxicity of fluopicolide to algae and aquatic plants can be summarised as:

- most sensitive algal species tested was the freshwater diatom *Navicula pelliculosa*, to which fluopicolide was highly toxic.
- moderately-highly toxic to the marine diatom *Skeletonema costatum*
- moderately-highly toxic to the freshwater green algae species *Scenedesmus subspicatus,* a second species (*Pseudokirchneriella subcapitata*) was less sensitive.
- metabolite M-01 is slightly toxic to *N. pelliculosa* and very slightly toxic to *P. subcapitata*
- aquatic plant *Lemna gibba* showed little sensitivity to fluopicolide, and less to its metabolite M-01 (Table 13).

Table 13: Toxicity of active constituent fluopicolide (and its metabolites M-01, and/or M-02, M-03) for various organisms

ORGANISM		MEASURE OF TOXICITY OR EFFECT	PARAMETER (TEST PERIOD)	TOXICITY (UNIT)
Terrestrial species				
Mammals:	Rats	Acute toxicity (oral)	>5000 LD_{50}	mg ac/kg bw/d
	Rats, rabbits	Reproduction	103.4, 20 NOAEL	mg ac/kg bw/d
Bird	Bobwhite quail	Acute toxicity (oral)	>2250 LD_{50}	mg ac/kg bw
	Bobwhite quail, mallard duck *Bobwhite quail*	Short term dietary exposure ***M-01***	>5620 LC_{50} (5 d) ***3867 LC_{50} (5 d)***	mg ac/kg feed
	Bobwhite quail, mallard duck	Reproduction	88.9, 140.8 NOEC 2060, 200 NOAEL	mg ac/kg bw/d mg ac/kg feed/d
	Honeybee (*Apis mellifera*)	Oral toxicity Contact toxicity	>241 LD_{50} (48 h) >100 LD_{50} (48 h)	µg/bee
Non-target arthropods	parasitoid (*Aphidius rhopalosiphi*)	Tier 1 dose/response	>419 LR_{50} (48 h)	g ac/ha
	predatory mite (*Typhlodromus pyri*)		312 LR_{50} (48 h)	
	Earthworm	Acute toxicity ***M-01, M-02 M-03***	>500 LC_{50} >750, >1000, >500 LC_{50}	mg/kg
		Reproduction	250 NOEC	mg/kg

ORGANISM		MEASURE OF TOXICITY OR EFFECT	PARAMETER (TEST PERIOD)	TOXICITY (UNIT)
Plants	5 crop species, 11 broad-leaved weed species, 9 grass weeds, 2 sedges ***M-01 (9 crop species)***	Seedling emergence test Pre- and post-emergence	Not herbicidal at rates up to 1280 >12.01 EC_{50}	g ac/kg µg/kg dws
Aquatic species				
Fish	Rainbow trout (*Oncorhynchus mykiss*), sheepshead minnow (*Cyprinodon variegatus*), zebra fish (*Brachydanio rerio*)	Acute toxicity ***M-01***	0.360, 0.410, 1.80 LD_{50} (96 h) ***240 LD_{50} (96 h)***	mg ac/L
	Fathead minnow (*Pimephales promelas*)	Early life stage toxicity	0.155 NOEC (33 d)	mg ac/L
Marine organisms	Marine oysters (*Crassostrea virginica*)	Acute toxicity	>2.6 EC_{50} (96 h)	mg ac/L
	Mysid shrimp (*Americamysis bahia*)	Acute toxicity	3.2 EC_{50} (96 h)	mg ac/L
Aquatic invertebrate	*Daphnia magna*	Acute toxicity	1.8 LC_{50} 180 LC_{50}	mg ac/L
	Daphnia magna	Reproduction	0.37 NOEC (21 d)	mg ac/L
	Chironomus riparius	Chronic exposure	49 NOEC (28 d)	mg/L
Aquatic plants	*Lemna gibba*	Growth inhibition ***M-01***	>3.2 E_rC_{50} (72 h) >80 E_rC_{50} (72 h)	mg ac/L
Algae	*Pseudokirchneriella subcapitata* *Scenedesmus subspicatus* Diatoms: *Navicula pelliculosa* ***M-01*** *Skeletonema costatum* (marine) ***M-01***	Growth inhibition	>4.3 E_rC_{50} (72 h) 1.6 E_rC_{50} (72 h) 0.069 E_rC_{50} (72 h) >10.0 E_rC_{50} (72 h) 0.066 E_rC_{50} (72 h) 120 E_rC_{50} (72 h)	mg/L

Terrestrial plants

A glasshouse pre-emergent and post-emergent screening trial on 5 crop, 11 broad-leaved weed, 9 grass weed and 2 sedge species indicate that fluopicolide is not herbicidal at application rates up to 1280 g ac/ha.

The metabolite M-01 was tested for pre- and post-emergent herbicidal effects on 9 crop species at soil concentrations in the range 0.011–12.1 µg/kg dws. Pea seedling survival and onion seedling emergence were the most sensitive with decreases of 12% and 23% respectively at the highest concentration. However, the effects were inconsistent in all tests and were not correlated with concentration. The maximum effects were less than 50%, with an EC50 of > 12.01 µg as/kg dws for all species tested.

7.4 Risk assessment

The product is applied by ground spraying at a maximum application rate of 1.6 L/ha (= 100 g fluopicolide + 1000 g/ha propamocarb hydrochloride)/ha. A maximum of 3 applications per crop is proposed at a minimum interval of 7 d with medium quality spray. Based on the submitted data, the risk to birds, mammals, plants, honeybees, earthworms and other non-target terrestrial invertebrates was found acceptable, and no harmful impact on soil nitrogen and carbon metabolism is expected from the proposed uses. The risk to aquatic and sediment-dwelling organisms from spray drift, run-off or groundwater were found to be acceptable. The risk to non-target vegetation is acceptable.

7.5 Conclusion

The risk assessment has included assessment and considered the risks of fluopicolide alone, propamocarb hydrochloride alone and the combination product, Infinito SC Fungicide. In considering the submitted data, particular attention has been given to the potential risk to organisms in aquatic, benthic and terrestrial environments.

The APVMA is satisfied that risk resulting from use of Infintio SC Fungicide will be acceptable.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

It is proposed to register Infinito SC Fungicide, containing 62.5 g a.i./L of fluopicolide and 625g a.i./L of propamocarb hydrochloride, as a suspension concentrate for the control of downy mildew and late blight in bulb vegetables (onions, spring onions and leeks), lettuce, poppies, cucurbits and potatoes. The proposed use for Infinito SC Fungicide will involve ground application at 1.6 L/ha and a maximum of, 2 applications in potatoes and cucurbits and 3 applications in bulb vegetables, lettuce and poppies, at a minimum interval of 7 days.

8.2 Summary of evaluation of efficacy and crop safety

Efficacy

Data were supplied from thirty-eight field trials conducted in Australia and New Zealand comparing the efficacy and crop safety of Infinito SC Fungicide with industry standard fungicides for control of late blight (*Phytophthora infestans*) in potatoes and the following species of downy mildews on crops:

- Bremia lactucae on lettuce
- Peronospora destructor on onions
- Pseudoperonospora cubensis on cucurbits, and
- Peronospora cristata (and P. meconopsidis) on oilseed poppies.

Infinito SC Fungicide (infinito) was applied at rates of 0.8 to 3.2 L/ha as a foliar broadcast spray with multiple applications and repeat sprays 7–10 days apart. The field trials were based on randomised, complete block designs, with at least three or four replicates. The trials were conducted on commercial crops in a range of different soil types in New Zealand or a number of different Australian states, under conditions of natural disease infections. Disease pressure varied during the trials from high to low levels.

Data from five trials were submitted on efficacy against downy mildew (*Bremia lactucae*) in lettuce. Infinito at rates of 1.2 to 1.6 L/ha was effective in controlling downy mildew and as effective as an industry standard. Infinito was safe to use on lettuce up to rates of 3.2 L/ha and 3 spray applications at 7 to 10 day intervals.

Data from nine trials were submitted on efficacy against downy mildew (*Peronospora destructor*) in various onions varieties. Infinito at rates of 1.2 L/ha and above (with the addition of an non-ionic wetter) were as effective as an industry standard in controlling downy mildew in onions. Infinito was safe to use on a number of varieties of onion at rates of up to 3.2 L/ha and 4 applications.

Data from five trials were submitted on efficacy against downy mildew (*Pseudoperonospora cubensis*) in cucurbits (rockmelon and zucchini). Infinito at 1.2 to 1.6 L/ha was as effective at controlling downy mildew as an industry standard. Infinito was safe to use on cucurbits at rates of up to 3.2 L/ha and 3 spray applications.

Data from six trials were submitted on efficacy against downy mildew (*Peronospora cristata* and *P. meconopsidis*) in oilseed poppies. In the trials on poppies, Infinito at rates of 0.8 to 2.4 L/ha and with 5 spray applications was effective in controlling downy mildew in poppies and was safe to use on opium poppies.

Data from five trials were submitted on efficacy against late blight (*Phytophthora infestans*) in potatoes. In the potato trials Infinito at 1.2 to 1.6 L/ha was as effective as an industry standard in controlling late blight. Infinito was safe to use on potatoes.

The trial data supplied demonstrates the efficacy of Infinito SC Fungicide to control downy mildews in bulb vegetables, cucurbits, lettuce and poppies and late blight in potatoes when used as a foliar application at rates of 1.2–1.6 L/ha and 2-3 applications per crop (depending on the crop).

Crop safety

Crop safety assessments were conducted in the efficacy trials submitted in this application. In addition, the Applicant submitted data from eight crop safety- specific trials.

Lettuce: Replicated field trials conducted in NSW and Victoria in 2013 and 2104, respectively, compared fungicides for crop safety to head lettuce. Up to four fungicide application were made at between 7 and 10 day intervals. No phytotoxic effects were evident with Infinito shown to be safe to use on lettuce at rates up to 2.4 L/ha and with 4 spray applications.

Onions: A replicated field trial was conducted in NSW in 2014 comparing fungicides for crop safety to onion. No phytotoxic effects were evident and Infinito, at rates up to 2.4 L/ha and with 4 spray applications was safe to use on onions.

Squash: A replicated field trial was conducted in, QLD in 2013 comparing fungicides for crop safety to squash. Three applications of fungicides were made at 8 to 13 day intervals. No phytotoxicity was observed in the trial and Infinito at rates of up to 2.4 L/ha and 3 sprays was safe to use on squash.

Watermelon: A replicated field trial was conducted in WA in 2014 comparing fungicides for crop safety in watermelon. Four applications of fungicides were made at 6–10 day intervals. No phytotoxicity was observed in the trial and Infinito at rates of up to 2.4 L/ha and with 4 spray applications was safe to use on watermelon.

Zucchini: Two replicated field trials were conducted in QLD in 2013–2014 comparing fungicides for crop safety to zucchini. Two or four fungicide applications were made at 8 to 10 day intervals. No phytotoxicity was observed and Infinito at rates of up to 2.4 L/ha and 3 sprays was safe to use on zucchini.

Potatoes: A replicated field trial was conducted NZ in 2010 comparing crop safety of fungicides in potatoes. Fungicides were applied with a maximum of 10 applications at 10 day intervals. No phytotoxicity was observed and Infinito was safe to use on potatoes at rates of up to 1.6 L/ha and with10 spray applications at 10 days apart.

The trial data evaluated demonstrates that Infinito SC Fungicide is safe to use at rates up to 3.2 L/ha at 7 to 14 day intervals.

Resistance management

The Fungicide Resistance Action Committee (a specialist technical group of Crop Life International) has designated fluopicolide as a Group 43 fungicide and propamocarb hydrochloride as a Group 28 fungicide. Fluopicolide and propamocarb hydrochloride are effective against oomycete pathogens. The use of the Infinito SC Fungicide is therefore subject to a fungicide resistance management strategy.

8.3 Conclusions

The claims on the proposed label that Infinito SC Fungicide provides acceptable control of late blight of potatoes, downy mildew on lettuce, onions, cucurbits and against P. cristata and P. meconopsidis on oilseed poppies when used as directed are supported by the results from the Australian and New Zealand trials.

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

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

9 LABELLING REQUIREMENTS

LABEL

CAUTION

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

Infinito®

SC FUNGICIDE

ACTIVE CONSTITUENTS: **625 g/L PROPAMOCARB HYRDOCHLORIDE**
62.5 g/L FLUOPICOLIDE

GROUP	43 28	FUNGICIDE

For the control of downy mildew and late blight in various crops as specified in the DIRECTIONS FOR USE table

*** L**

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

* 1 L, 2.5 L, 3 L, 5 L, 7 L, 7.5 L, 10 L, 15 L, 20 L, 60 L, 110 L

INFINITO SC FUNGICIDE

STORAGE AND DISPOSAL

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

(1 L, 2.5 L, 3 L, 5 L, 7 L, 7.5 L, 10 L, 15 L, 20 L, 60 L, 110 L non returnable containers only)

Triple rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product. Do not re-use empty container for any other purpose.

(110 L returnable containers 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.

SAFETY DIRECTIONS

Will irritate the eyes. Avoid contact with eyes. If product in eyes wash it out immediately with water. Repeated exposure may cause allergic disorders. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow length chemical resistant gloves and face shield. Wash hands after each use. After each day's use, wash gloves and faceshield and contaminated clothing.

FIRST AID

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

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.

Infinito® is a Registered Trademark of the Bayer Group.

APVMA Approval No.: 80625/101299

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

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FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY PHONE 1800 033 111

Batch Number: DOM: Barcode

Bayer

BOOKLET / LEAFLET

CAUTION

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

INFINITO SC FUNGICIDE

ACTIVE CONSTITUENTS: 625 g/L PROPAMOCARB HYDROCHLORIDE
62.5 g/L FLUOPICOLIDE

For the control of downy mildew and late blight in various crops as specified in the DIRECTIONS FOR USE table

DIRECTIONS FOR USE

RESTRAINTS
Do not apply by aircraft

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a **MEDIUM** spray droplet category as defined by the ASABE S572 Standard. Users **MUST ONLY USE** nozzles classified as suitable for delivering a **MEDIUM** spray droplet category according to the nozzle manufacturer's specifications.
DO NOT apply when wind speed is less than 3 or more than 20 km/h as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.
Users of this product **MUST make an accurate written record** of the details of each spray application within 24 hours following application and **KEEP** this record for a minimum of 2 years. The spray application details that must be recorded are: **1.**date and start and finish times of application; **2.**location address and paddock/s sprayed; **3.**full name of this product; **4.**amount used per hectare and number of hectares applied to; **5.**crop/situation and weed/pest; **6.**wind speed and direction during application; **7.**air temperature; **8.**nozzle brand, model and type and spray system pressure measured during application; **9.**name and address of person applying this product. (Additional record details may be required by the State or Territory where this product is used.)

CROP	DISEASE	RATE	WHP	CRITICAL COMMENTS
Bulb vegetables, including bulb onions, leeks and spring onions	Downy mildew (*Peronospora destructor*)	1.2–1.6 L/ha	7 days (H)	Apply as a protectant program with a maximum of 3 applications per crop. Commence when conditions favour disease development—humid or wet conditions. Apply before first sign of infection according to mildew infection periods or local warnings and repeat at 7–10 day intervals. Apply the high rate under conditions of high infection pressure. A non-ionic wetter e.g. Agral 600 should be added at 10 mL/100 L of spray solution. **Resistance Management** This use pattern is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at http://www.croplife.org.au/industry-stewardship/resistance-management/ before using the product
Cucumber (field and protected cropping systems)	Downy mildew (*Pseudoperonospora cubensis*)		1 day (H)	Apply in a protectant program with a maximum of 2 applications per crop. Commence when conditions favour disease development - when humid or wet conditions favour infection. Apply before first sign of infection according to mildew infection periods or local warnings and repeat at 7–10 day intervals. Apply the high rate under conditions of high infection pressure. No wetter is required. **Resistance Management** This use pattern is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at http://www.croplife.org.au/industry-stewardship/resistance-management/ before using the product.
Cucurbits except cucumber (field and protected cropping systems)			3 days (H)	
Lettuce (field and protected cropping systems)	Downy mildew (*Bremia lactucae)*		7 days (H)	Apply as a protectant program with a maximum of 3 applications per crop. Commence when conditions favour disease development—humid or wet conditions. Apply before the first sign of infection according to mildew infection periods or local warnings, repeat at 7–10 day intervals. Apply the high rate under conditions of high infection pressure. No wetter is required. **Resistance Management** This use pattern is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at http://www.croplife.org.au/industry-stewardship/resistance-management/ before using the product.

CROP	DISEASE	RATE	WHP	CRITICAL COMMENTS
Poppies	Downy mildew (*Peronospora cristata, Peronospora meconopsidis*)	1.2–1.6 L/ha	Nil (H)	Apply as a protectant program with a maximum of 3 applications per crop. Commence when conditions favour disease development—humid or wet conditions. Apply before first sign of infection according to mildew infection periods or local warnings and repeat at 7–10 day intervals. Apply from ground cover crop stage until the start of flowering. Apply the high rate under conditions of high infection pressure. No wetter is required. **Resistance Management** This use pattern is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at http://www.croplife.org.au/industry-stewardship/resistance-management/ before using the product.
Potatoes	Late blight (*Phytophthora infestans*)		14 days (H)	Apply as a protectant program with a maximum of 2 applications per crop. Commence when conditions favour disease development—when humid or wet conditions favour infection. Apply according to late blight infection periods or local warnings and before first sign of infection and repeat at 7–10 day intervals. In the absence of any warnings, applications should commence when the crop meets along the row. Apply the high rate under conditions of high infection pressure. **Resistance Management** This use pattern is subject to a CropLife Australia resistance management strategy. Please refer to this strategy at www.croplife.org.au/industry-stewardship/resistance-management/ before using the product.

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

WITHHOLDING PERIODS

Harvest -
Cucumbers: DO NOT HARVEST FOR 1 DAY AFTER LAST APPLICATION
Cucurbits (except cucumber): DO NOT HARVEST FOR 3 DAYS AFTER LAST APPLICATION
Bulb vegetables and lettuce: DO NOT HARVEST FOR 7 DAYS AFTER LAST APPLICATION
Potatoes: DO NOT HARVEST FOR 14 DAYS AFTER LAST APPLICATION:
Poppies: NOT REQUIRED WHEN USED AS DIRECTED

BOOKLET / LEAFLET

GENERAL INSTRUCTIONS

Infinito SC Fungicide is a member of the **43 and 28** group of fungicides. Infinito is a co-formulation of two complimentary active ingredients - fluopicolide and propamocarb hydrochloride—which together provide anti-sporulant, protectant, translaminar and systemic activity.

Fungicide Resistance Warning

GROUP	43	28	FUNGICIDE

For fungicide resistance management Infinito is a Group **43 and 28** fungicide. Some naturally occurring fungal populations resistant to the product and other Group **43 and 28** fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungal population if these fungicides are used repeatedly. These resistant fungi will not be controlled by this product or other Group **43 and 28** fungicides, thus resulting in a reduction in efficacy and possible yield loss. Since the occurrence of resistant fungi is difficult to detect prior to use, Bayer CropScience Pty Ltd accepts no liability for any losses that result from failure of Infinito to control resistant fungi.

Export of treated produce

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

Application

Application should be by ground spray equipment only. Thorough coverage of the target area is essential. Apply as a high volume, medium droplet spectra spray at a water volume appropriate to the crop stage to ensure good coverage e.g. 200–600 L/ha. Apply in sufficient water, and using suitable application parameters (nozzles, pressure, speed, etc.) to ensure thorough and even coverage. Adjust water volumes according to the crop growth stage. Use only a medium spray droplet size classification according to ASAE S572 definition for standard nozzles.

Dilute Spraying

- Use a sprayer designed to apply high spray volumes, 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. e.g. 200–600 L/ha.
- The required spray volume may be determined by applying different test volumes, using different settings on the sprayer, or from industry guidelines or expert advice.
- Add the amount of product specified in the Direction for Use table for each hectare volume of water.
- The required dilute spray volume will change and the sprayer set up and operation may also need to be changed, as the crop grows.

Compatibility

For the latest compatibility recommendations contact the Bayer Crop Science Technical Enquiry Hotline 1800 804479 or your local Bayer Crop Science representative.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Very toxic to aquatic life. **DO NOT** contaminate streams, rivers, drains or waterways with the chemical or used containers.

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ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EI	Export Interval
EGI	Export Grazing Interval
ESI	Export Slaughter Interval
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour

ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection—level at which residues can be detected
LOQ	Limit of Quantitation—level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NHMRC	National Health and Medical Research Council

NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	repels water
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

REFERENCES

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

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

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

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

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

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

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

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