The reconsideration of the active constituent azinphos-methyl, registrations of products containing azinphos-methyl and approvals of their associated labels

PRELIMINARY REVIEW FINDINGS

Volume 1: Review Summary

OCTOBER 2006

Canberra
Australia

The Australian Pesticides & Veterinary Medicines Authority publishes this preliminary review findings report for the active constituent azinphos-methyl and products containing azinphos-methyl. For further information about this review or the Pesticides Review Program, contact:

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FOREWORD

The Australian Pesticides & Veterinary Medicines Authority (APVMA) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals in Australia. Its statutory powers are provided in the Agvet Codes scheduled to the *Agricultural and Veterinary Chemicals Code Act 1994*.

The APVMA can reconsider the approval of an active constituent, the registration of a chemical product or the approval of a label for a container for a chemical product at any time. This is outlined in Part 2, Division 4 of the Agvet Codes.

The basis for the current reconsideration is whether the APVMA is satisfied that continued use of the active constituent azinphos-methyl and products containing azinphos-methyl in accordance with the instructions for their use:

- would not be an undue hazard to the safety of people exposed to it during its handling or people using anything containing its residues; and
- would not be likely to have an effect that is harmful to human beings; and
- would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment; and
- would not unduly prejudice trade or commerce between Australia and places outside Australia.

The APVMA also considered whether product labels carry adequate instructions and warning statements.

A reconsideration may be initiated when new research or evidence has raised concerns about the use or safety of a particular chemical, a product or its label.

The reconsideration process includes a call for information from a variety of sources, a review of that information and, following public consultation, a decision about the future use of the chemical or product.

In undertaking reconsiderations (hereafter referred to as reviews), the APVMA works in close cooperation with advisory agencies including the Office of Chemical Safety, the Department of the Environment and Heritage, and State departments of agriculture as well as other expert advisers as appropriate.

The APVMA has a policy of encouraging openness and transparency in its activities and community involvement in decision-making. The publication of review reports is a part of that process.

The APVMA also makes these reports available to the regulatory agencies of other countries as part of bilateral agreements. The APVMA recommends that countries receiving these reports will not utilise them for registration purposes unless they are also provided with the raw data from the relevant applicant.

This document sets out the preliminary review findings relating to the active constituent azinphos-methyl and products containing azinphos-methyl that have been nominated for review by the APVMA. The preliminary review findings and proposed recommendations are based on information collected from a variety of sources. The information and technical data required by the APVMA to review the safety of both new and existing chemical products must be derived according to accepted scientific principles, as must the methods of assessment undertaken.

The review summary (Volume 1) and the technical reports (Volume 2) for all registrations and approvals for azinphos-methyl are available from the APVMA web site: http://www.apvma.gov.au/chemrev/chemrev.html.

COMMENT FROM THE PUBLIC IS INVITED

This Preliminary Review Findings report:

- outlines the APVMA review process
- informs interested parties how to respond to the review
- summarises the technical assessments from the reviewing agencies
- outlines the proposed regulatory action to be taken in relation to the continued approval and registration of azinphos-methyl.

The APVMA invites persons and organisations to submit their comments and suggestions on PRF report directly to the APVMA. Your comments will assist the APVMA in preparing the Review Findings Report, which is the second report in the three-stage review reporting process. The final report is the Final Review Report and Regulatory Decision.

PREPARING YOUR COMMENTS FOR SUBMISSION

You may agree or disagree with or comment on as many elements of the Preliminary Review Findings as you wish.

When making your comments:

- clearly identify the issue and clearly state your point of view
- give reasons for your comments supporting them, if possible, with relevant information and indicate the source of the information you have used
- suggest to the APVMA any alternative solution you may have for the issue.

Please try to structure your comments in point form referring each point to the relevant section in the Preliminary Review Findings. This will help the APVMA assemble and analyse all of the comments it receives.

Finally please tell us whether the APVMA can quote your comments in part or in full.

THE CLOSING DATE FOR SUBMISSIONS IS 15 DECEMBER 2006

Your comments should be mailed to:
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ABBREVIATIONS AND ACRONYMS

µg	microgram
ADI	acceptable daily intake (for humans)
AC	Active constituent
ai	active ingredient
APVMA	Australian Pesticides & Veterinary Medicines Authority
ARfD	Acute Reference Dose
CDA	Controlled Droplet Applicators
ChE	cholinesterase
CODEX	FAO/WHO Codex Alimentarius Commission
CRP	Chemistry and Residues Program
DEF	*S, S, S*-tributylphosphorotrithioate
DEH	Department of Environment and Heritage (previously Environment Australia)
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DoC	Declaration of Composition
EC	emulsifiable concentrate
EC_{50}	concentration at which 50% of the test population are affected
ECG	electrocardiogram
EPN	*O*-ethyl *O*-4-nitrophenyl phenylphosphonothioate
FAISD	Handbook of First Aid Instructions, Safety Directions, Warning Statements and General Safety Precautions for Agricultural and Veterinary Chemicals
FAO	Food and Agriculture Organisation
FSANZ	Food Standards Australia and New Zealand
GAP	Good Agricultural Practice
h	hour
ha	hectare
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
IPM	integrated pest management
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	kilogram
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
MATC	maximum acceptable toxicant concentration
mg	milligram
mg/kg bw/day	mg/kg bodyweight/day
MIA	Murrumbidgee Irrigation Area
MOE	margin of exposure
MRL	maximum residue level
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Dietary Intake
NESTI	National Estimated Short-Term Intake
NHMRC	National Health and Medical Research Council
NOEL	no observable effect level
OCS	Office of Chemical Safety
OECD	Organisation for Economic Co-operation and Development
OHS	Occupational health and Safety

OP	organophosphate pesticide
PACC	Pesticides and Agricultural Chemicals Committee
PHED	Pesticides Handlers Exposure Database
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRF	Preliminary Review Findings report
REI	re-entry interval
SC	suspension concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
US EPA	United States Environment Protection Agency
USGS	United States Geological Survey
UV	Ultraviolet
WHP	withholding period
WP	Wettable Powder

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EXECUTIVE SUMMARY

INTRODUCTION

The APVMA has completed the assessment of data and information relating to the active constituent azinphos-methyl, registered products containing azinphos-methyl and their associated label approvals. This Preliminary Review Findings report summarises the data evaluated and the proposed recommendations arising from the review of the uses of azinphos-methyl.

Azinphos-methyl is a broad spectrum, non-systemic organophosphate insecticide. Products containing azinphos-methyl are used in pome and stone fruit orchards, citrus, macadamia nuts and grapes, with further minor uses in crops such as lychees, kiwifruit and blueberries. The main use is for the control of codling moth and light brown apple moth, predominately in pome and stone fruit orchards.

There are currently two active constituent approvals (Appendix 1 Table A) and four registered products containing azinphos-methyl as the active constituent (Appendix 1 Table B and Table C). All of the registered products are for uses in commercial situations and are not registered for use in the home garden

Azinphos-methyl product registrations and label approvals are under review as part of the APVMA's Review Program due to specific concerns about the safety to users of azinphos-methyl products, the impact of residues of azinphos-methyl on Australia's trade and the impact of azinphos-methyl on the environment. The review covered all aspects of the registration of azinphos-methyl. Assessments considered the approved use patterns of azinphos-methyl in terms of the impact on public health, occupational health and safety, the environment and trade.

ACTIVE CONSTITUENT

Based on the data provided the APVMA is satisfied that the active constituent azinphos-methyl meets requirements for continued approval. The APVMA proposes to affirm the active constituent approvals for azinphos-methyl.

TOXICOLOGICAL ASSESSMENT

The toxicological assessment for the review of azinphos-methyl was undertaken by the Office of Chemical Safety (OCS), which considered all the toxicological data and information submitted for the review.

The OCS considered the health intake standards for azinphos-methyl products. The Acceptable Daily Intake (ADI) was amended, an Acute Reference Dose (ARfD) was established and changes to the water quality guidelines have been recommended, these standards were used in the assessment of dietary intake from residues. Toxicology hazard assessments form the basis of the occupational health and safety risk assessment. The toxicological assessment found that product labels do not carry adequate instructions and warning statements.

The APVMA has considered the advice received from the OCS and recommends that product labels are varied to include new warning statements and safety directions.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

The occupational health and safety assessment for the review of azinphos-methyl was undertaken by the OCS, which considered all the occupational health and safety data and information submitted for the review. The APVMA has considered the advice received from the OCS and makes the following recommendations relating to the continued use of products containing azinphos -methyl.

The APVMA is not satisfied that mixing and loading by operators of azinphos -methyl suspension concentrate (SC) products would not be an undue hazard to the safety of people exposed to it during its handling. However, the APVMA can be satisfied containers can be changed to wide neck containers which would address identified risks.

The APVMA is not satisfied that product labels carry adequate instruction for re-entry intervals (REI) to prevent post application exposure that would not have an effect that is harmful to human beings. However, the APVMA can be satisfied that post application exposure would not have an effect that is harmful to human beings if REI are varied. Therefore, it is recommended that labels be varied to change the re-entry intervals.

RESIDUES ASSESSMENT

The residue assessment for the review of azinphos-methyl was undertaken by the APVMA Chemistry and Residues Program (CRP), which considered all the residue data and information submitted for the review. The APVMA makes the following recommendations relating to the continued use of products containing azinphos -methyl.

The APVMA is not satisfied that the continued use of azinphos-methyl for use on apricots and kiwi fruit would not be an undue hazard to the safety of people using anything containing its residues. Therefore, it is recommended that instructions for use for these crops are to be deleted from labels.

The APVMA is satisfied that continued use of registered azinphos-methyl products on, pome fruit (apples, pears, quinces) macadamias, stone fruit (except apricots), citrus, blueberries, lychees and grapes would not be an undue hazard to the safety of people using anything containing its residues. It is recommended that these use patterns be affirmed.

TRADE ASSESSMENT

The APVMA is satisfied that continued use of registered azinphos-methyl products would not unduly prejudice trade between Australia and places outside Australia. It is recommended that the use of azinphos-methyl on product to be exported from Australia be affirmed.

ENVIRONMENTAL ASSESSMENT

The environmental assessment for the review of azinphos-methyl was undertaken by the Department of the Environment and Heritage (DEH). The DEH considered all the environmental data and information submitted for the review. The APVMA makes the following recommendations relating to the continued use of products containing azinphos - methyl.

The APVMA is not satisfied that the continued use of azinphos-methyl for use on citrus would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment due to spray drift. Therefore, instructions for use on citrus are to be deleted from labels. It is recommended that product labels be varied.

The APVMA is not satisfied that the use of azinphos-methyl would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment, as product labels do not contain adequate instructions. The APVMA being satisfied that the risk can be mitigated by adding restraint and protection statements to the label that would result in products not being likely to have an unintended effect that is harmful to animals, plants or things or to the environment. Therefore, it is recommended that that product labels be varied.

PUBLIC SUBMISSIONS

Two public submissions were received regarding the use of azinphos-methyl (Section 5). The submissions did not contain data that required evaluation.

PROPOSED REGULATORY OUTCOMES

a) Affirm active constituent approval (Appendix 1, Table A).

b) Vary label approvals (Appendix 1, Tables B and C).

To satisfy the requirements for continued registration of products, the APVMA proposes the following label variations:

- The use on apricots, kiwi fruit and citrus is to be deleted.
- Restraint statements are to be added.
- Statements for the protection of wildlife, fish, crustaceans and environment are to be added.
- A statement for the protection of bees is to be added.
- Withholding Period for blueberries is to be amended.
- Re-entry periods to be amended.
- Warning Statements and Safety Directions are to be amended.
- It is also recommended that old approved labels are deemed not to contain adequate instructions and are to be cancelled.

c) Vary registration conditions (Appendix 1, Tables B and C).

To satisfy the requirements for continued registration of products, the APVMA proposes the following variations to registration conditions:

- Containers are to be changed to have a wide neck for all SC products.

d) Affirm product registrations.

If the proposed label variations and changes to registration conditions are made then the product registrations and label approvals of four products (Appendix 1, Tables B and C) can be affirmed

1. INTRODUCTION

The APVMA has completed the assessment of data and information for the review of the approval of the active constituent azinphos-methyl, registered products containing azinphos-methyl and the associated label approvals. This document summarises the data evaluated and the proposed recommendations from the review of the active constituent azinphos-methyl and products containing azinphos-methyl and associated label approvals.

1.1 REGULATORY STATUS OF AZINPHOS-METHYL IN AUSTRALIA

Azinphos-methyl was first registered in Australia in the late 1960's. Originally it was commonly used as part of a spray program for the prevention and control of various insect pests of fruit. However, the use of azinphos-methyl has now generally been incorporated into Integrated Pest Management (IPM) programs, where it is used to control breakouts in the IPM program, or as a preparation chemical for the introduction of IPM programs.

Azinphos-methyl is a systemic pesticide (contact and stomach action). Exposure of pests affects the nervous system by inhibiting the activity of acetyl cholinesterase. Contact of the enzyme in insects with the pesticide is thought to result in irreversible phosphorylation of cholinesterase, leading to the accumulation of acetylcholine at the neuron/neuron and neuron/muscle (neuromuscular) junctions or synapses.

As at August 2006, there were two active constituent approvals for azinphos-methyl (Appendix 1 Table A), four registered products containing the active constituent azinphos-methyl and three registrants (Appendix 1 Table B and C). All product formulations of azinphos-methyl are suspension concentrates (Table 1). Information on the uses of azinphos-methyl products can be found in Section 2 of this Preliminary Review Findings (PRF) report.

Table 1: Registered formulations of azinphos-methyl considered in the review.

Formulation Type	Level of active constituent	Product Type
Suspension concentrate	350g/L	Agricultural Insecticide
Suspension concentrate	200g/L	Agricultural Insecticide

1.2 REASONS FOR AZINPHOS-METHYL REVIEW

The active constituent azinphos-methyl, all products containing azinphos-methyl and their associated labels were placed under review as part of the third cycle of the existing chemical review program because of concerns over toxicological, occupational health and safety, environmental, residue and trade issues.

1.3 SCOPE OF THE REVIEW

When the extent of the review was scoped the reasons for the nomination of azinphos-methyl, the information already available on this chemical, and the approved uses of the product in Australia were taken into account.

The basis for a reconsideration of the registration and approvals for a chemical is whether the APVMA is satisfied that the requirements prescribed by the Agvet Codes for continued registration and approval are being met. In the case of azinphos-methyl, these requirements are that the use of the product in accordance with the instructions for its use would not be likely to:

- be an undue hazard to the safety of people exposed to it during its handling or people using anything containing its residues
- have an effect that is harmful to human beings
- have an unintended effect that is harmful to animals, plants or things or to the environment
- would not unduly prejudice trade or commerce between Australia and places outside Australia.

The APVMA reviewed the toxicological, occupational health and safety, residues and environmental aspects of azinphos-methyl, including

- the potential for high toxicity to fish, birds and bees
- the potential for run-off and spray drift to enter aquatic environments
- the potential for exposure to users of products
- the potential chronic and moderate acute toxicity risk

The APVMA also considered whether product labels carry adequate instructions and warning statements. Such instructions include:

- the circumstances in which the product should be used
- how the product should be used
- times when the product should be used
- frequency of the use of the product
- the withholding period after the use of the product
- disposal of the product and its container
- safe handling of the product.

On the basis of the human health, occupational health and safety, environment and residues concerns, it was decided that the active constituent, product registrations and label approvals for azinphos-methyl should be reviewed under the provisions of Part 2, Division 4, of the Agvet Codes.

1.4 REGULATORY OPTIONS

There can be three possible outcomes to the reconsideration of the registration of products containing azinphos-methyl and their labels. Based on the information reviewed the APVMA may be:

- satisfied that the products and their labels continue to meet the prescribed requirements for registration and approval and therefore confirms the registrations and approvals.
- satisfied that the conditions to which the registration or approval is currently subject can be varied in such a way that the requirements for continued registration and approval will be complied with and therefore varies the conditions of registration or approval.
- not satisfied that the requirements for continued registration and approval continue to be met and suspends or cancels the registration and/or approval.

2. APPROVED AZINPHOS-METHYL USE PATTERNS

Azinphos-methyl is a broad spectrum, non-systemic organothiophosphate insecticide. Products containing azinphos-methyl are used in pome and stone fruit orchards, citrus, macadamia nuts and grapes, with further minor uses in crops such as lychees, kiwifruit and blueberries (Table 2). The main use is for the control of codling moth and light brown apple moth, predominately in pome and fruit orchards. In Australia there are currently four registered products containing azinphos-methyl that are used in commercial situations.

Azinphos-methyl was originally used as part of a broad spraying strategy, but has now generally been incorporated into IPM programs. In IPM programs azinphos-methyl is used either as a clean-up chemical (i.e. a one off spray to control escapes), or as a preparation chemical for the introduction of the IPM programs (i.e. to reduce pest numbers to a level where they can be controlled by pest management methods). The maximum use rates stated on the labels (tree butt and soil drench) correspond to 98g ai/100L, but most orchard rates correspond to 36-49 g ai/100L. Normal practice in orchards situations is to spray to run-off. Use in pome and stone fruit orchards accounts for approximately 80% of azinphos-methyl used, 10% used on macadamias, with other registered crops accounting for the remaining 10%

Table 2: Approved uses of products containing azinphos-methyl.

Crop	Insect Pest Species	Rate/100L	Application methods	Comments
Pome fruit (Apples, Pears, Quinces)	Codling moth, lightbrown apple moth, spring beetle, apple leaf hopper, bryobia mite, pear and cherry slug, woolly aphid,	**200 SC**: 190-245 mL/100 L water (~0.04-0.05%) for high volume spray; may be mixed with **350 SC**: 110-140 mL/100 L water (~0.04-0.05%); first spray at 210 mL/100 L (~0.07%) for wooly aphid infestations	Mainly applied by airblast or air shear (using low volume spray: 250 – 600 L /ha) equipment, with fewer applications by controlled droplet applicator (CDA) equipment (using low volume spray: less than by air shear or airblast) and fewer still by vertical oscillating boom sprayers (using high volume spray: 10000 L/ha) Butt spray (using high volume spray)	Apply as a full cover spray at intervals of 2 to 3 weeks commencing with the emergence of the of the first codling moths in late October/early November
	San Jose scale, oystershell scale	**200 SC**: 245ml **350 SC**: 140ml + summer oil 1.2L		Apply late November to early March. 1-3 applications may be necessary depending on the severity of infestation. Apply as a soil drench or overall cover spray
	Root borer	**200 SC**: 245ml **350 SC**: 140ml		Apply as a soil drench or all over cover spray

Crop	Insect Pest Species	Rate/100L	Application methods	Comments
	Curculio beetle, Fuller's rose weevil	**200 SC**: 245 – 490ml **350 SC**: 140 – 280ml		Apply lower rate as a high volume spray to foliage, butt and soil when weevils are first seen in October/November. Apply a second spray 3 to 4 weeks later
Stone fruit (Peaches, Apricots Nectarines, Plums)	Oriental fruit moth, lightbrown apple moth, bryobia mite, pear and cherry slug	**200 SC**: 245ml **350 SC**: 140ml	Mainly applied by airblast or air shear (using low volume spray: 250 – 600 L /ha) equipment, with fewer applications by CDA equipment (using low volume spray: less than by air shear or airblast) Where high volume equipment is used, the rates vary between 38 – 49 g ai/100 L of water. Where concentrate or semi-concentrate sprayers are used, up to five times the high volume rate can be applied Butt spray (using high volume spray)	Apply as a full cover spray at intervals of 3 -4 weeks at times of infestation
	San Jose scale	**200 SC**: 245ml **350 SC**: 140ml + winter oil 1.2		Apply at early budswell
	Root borer	**200 SC**: 245ml **350 SC**: 140ml		Apply as a soil drench or all over cover spray
	Curculio beetle, Fuller's rose weevil	**200 SC**: 245ml – 490ml **350 SC**: 140ml – 280ml		Apply lower rate as a high volume spray to foliage, butt and soil when weevils are first seen in October/November. Apply a second spray 3 to 4 weeks later
Blueberries	Lightbrown apple moth	**200 SC**: 245ml	Applied using orchard airblast equipment applying approximately 300 L/ha spray mixture	Apply at 14 day intervals after flowering
Cherries	Oriental fruit moth, lightbrown apple, moth, bryobia mite	**200 SC**: 245ml	Mainly applied by airblast or air shear (using low volume spray: 250 – 600 L /ha) equipment, with fewer applications by CDA equipment (using low volume spray: less than by air shear or airblast) Where high volume equipment is used, the rates vary between 38 – 49 g ai/100 L of water. Where concentrate or semi-concentrate sprayers are used, up to five times the high volume rate can be applied Butt spray (using high volume spray)	Apply as a full cover spray at intervals of 3 -4 weeks at times of infestation
	Pear and cherry slug	**200 SC**: 245ml		Apply as a full cover spray when slugs appear in late November/early December. Repeat spray as necessary
Citrus	Red scale, soft brown	**200 SC**: 245ml	Main methods of application are airblast,	Apply as a full cover spray at intervals of 3-4 weeks in

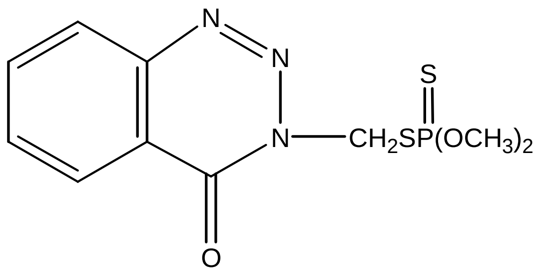
Crop	Insect Pest Species	Rate/100L	Application methods	Comments
	scale, black or olive scale, white wax scale, tortrix, aphids, yellow scale, lightbrown apple moth	**350 SC**: 140ml + white or summer oil 1L	vertical booms and CDA	December and February
Grapes	Grapevine scale	**200 SC**: 245ml **350 SC**: 140ml + winter oil 2 L	Applied by airblast using modification of air stream for overall coverage; sometimes applied as a spot spray to scale infested vines	Spot spray infested vines
	Grapevine hawk moth (*Hippotion celerio*) grapevine moth (*Phalaenoides glycinae*)	**200 SC**: 245ml **350 SC**: 140ml		Spray as required
	lightbrown apple moth	**200 SC**: 245ml **350 SC**: 140ml		Apply 3-4 weeks after flowering and later as required
	Fig longicorn, elephant weevil	**200 SC**: 245ml		Apply insecticide thoroughly to trunk and arms ensuring that all bark areas are drenched. Apply to foliage to assist in the control of adults. Apply monthly between November and April.
Kiwifruit	Scale insects, lightbrown apple moth	**200 SC**: 245ml	Applied mainly by orchard airblast with some directional modification of air stream to enable spray to reach overhead foliage (kiwis grown on overhead trellises)	Apply as a cover spray during December to March or apply at first sign of pest. Repeat at 3-4 week interval while activity continues.
Lychees Macadamias	Macadamia nutborer, fruitspotting bug	**350 SC**: 190ml	Main methods of application are airblast followed by air shear (using low volume spray: 250 – 600 L /ha) equipment, with fewer applications by CDA equipment (using low volume spray: less than by air shear or airblast) or electrostatic sprayers	Spray to thoroughly cover nuts or fruit when pest numbers indicate or on a 2 to 3 weekly schedule during the period when pests are normally active.

3. ACTIVE CONSTITUENT ASSESSMENT

The active constituent assessment for the review of azinphos-methyl was undertaken by the APVMA Chemistry and Residues Program. The active constituent assessment is summarised below.

3.1 CHEMICAL IDENTITY

IUPAC name:	*S*-(3,4-dihydro-4-oxobenzo[*d*]-[1,2,3]-triazin-3-ylmethyl) *O*,*O*-dimethyl phosphorodithioate
Chemical name:	*O*,*O*-dimethyl *S*-[(4-oxo-1,2,3-benzotriazin-3(4*H*)-yl)methyl] phosphorodithioate
Common name:	Azinphos-methyl
Manufacturer's code:	Bayer 17147; R 1582
CAS Registry number:	86-50-0
Molecular formula:	$C_{10}H_{12}N_3O_3PS_2$
Structural formula:	



Molecular weight:	317.33

3.2 PHYSICO-CHEMICAL PROPERTIES

Appearance:	Colourless; Active Constituent (AC) is a yellow solid
Odour:	None; AC described as mercaptan like
Melting Point:	72.4 ° C
Boiling Point:	Decomposes
Specific Gravity/Density	1.518 @ 21 ˚C
Vapour Pressure:	1.8×10^{-4} Pa @ 20 ˚C 5×10^{-4} mPa @ 20 ˚C (Tomlin, 1997) 1×10^{-3} mPa @ 25 ˚C (Tomlin, 1997))
Solubility in Water	33 mg/L @ 20 ˚C
Octanol-Water Coefficient.	Log P_{ow} = 2.96
Henry's Constant	1.73×10^{-3} atm m^3/mol (calculated) 5.70×10^{-6} Pa m^3/mol (Tomlin, 1997) 3.66×10^{-9} m^3/mol (US EPA, 1999)
Dissociation Constant:	Not applicable

3.2.1 Henry's Law Constant

The calculation of the Henry's Law constant for azinphos-methyl was conducted by Department of Environment and Heritage and was based on the above data for vapour pressure and water solubility. The constant, H, was determined to be 1.73 x 10^{-3} atm.m^3/mol and indicates that azinphos-methyl has low volatility from water.

3.2.2 Summary of Physico-Chemical Data

From the physico-chemical properties, azinphos-methyl is moderately soluble in water and highly soluble in organic solvents. It has a moderate partition coefficient and moderate binding to sediment/soil is expected. It is slightly volatile but has low volatility from water.

3.3 COMPOSITION OF AZINPHOS-METHYL ACTIVE CONSTITUENT

3.3.1 Declaration of Composition (DoC)

FAO Specification: The Food and Agricultural Organisation (FAO) Specification Limit for technical azinphos-methyl states that the material should consist of azinphos-methyl together with related manufacturing impurities, and should be yellow crystalline flakes free from visible extraneous matter and added modifying agents. The azinphos-methyl content should be not less than 870 g/kg.

Azinphos-methyl content:		not less tan 870 g/kg
Impurities:	Water	2 g/kg maximum acetone insoluble 5 g/kg maximum

Australian Specification: The Minimum Compositional Standard for azinphos-methyl states that the active content of the technical material should be not less than 900 g/kg. The two approved sources of technical azinphos-methyl meet the Australian requirements.

Toxic Impurities: The toxicological impurity O,O,S-trimethylphosphorodi thioate can be present in the active constituent azinphos-methyl (at a maximum concentration of 40 g/kg).

4. SUMMARY OF DATA ASSESSMENTS

4.1 TOXICOLOGY

The toxicological assessment for the review of azinphos-methyl was undertaken by the OCS. The OCS considered all the toxicological data and information submitted for the review. The toxicological findings are summarised below.

4.1.1 Toxicology hazard profile

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of absorption	PO: almost complete absorption. Maximum plasma concentration 2-3 h after PO dosing. Majority of dermal absorption in the first h after application; 21-54% after 10 h in rats, 22-29% in humans
Distribution	Similar distribution following PO or iv administration; target organs include the kidneys, liver and lungs.
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	95% excreted in urine, bile and expired air within 48 h of PO or iv administration.
Metabolism	2 major urinary metabolites and 6 other products. 5 faecal metabolites (10-12% of administered dose).
Toxicologically significant compounds (animals, plants and environment)	Parent compound and benzazimide

Acute toxicity

Rat oral LD_{50} (mg/kg bw)	4.4
Worst oral LD_{50} in other species	15 (ICR/SIM mice)
Rat dermal LD_{50} (mg/kg bw)	72.5
Worst dermal LD_{50} in other species	1380 (NZW rabbits)
Rat inhalation LC_{50} (mg/m^3)	132 (females)
Worst inhalation LC_{50} in other species	40 (CF mice; 1h exposure)
Skin irritation	Non irritant
Eye irritation	Irritant
Skin sensitization	Sensitiser
T-value	0.4

Degradation products

Benzazimide

Rat oral LD_{50} (mg/kg bw)	None reported
Rat dermal LD_{50} (mg/kg bw)	2000
Rat inhalation LC_{50} (mg/m^3)	1760

Short-term toxicity

Target/critical effect	Plasma cholinesterase (ChE) inhibition
Lowest relevant oral NOEL (mg/kg bw/d)	0.25 (28-d human study)
Lowest relevant dermal NOEL	2.0 (3-wk rabbit study)

(mg/kg bw/d)	
Lowest relevant inhalation NOEL (mg/m^3)	1.24 (12-wk rat study)

Genotoxicity	Non-genotoxic

Long-term toxicity and carcinogenicity

Target/critical effect	Plasma ChE inhibition
Lowest relevant NOEL (mg/kg bw/d)	0.125 (52-wk and 2-y dietary dog studies)
Carcinogenicity	No evidence of oncogenic potential

Reproductive toxicity

Reproduction target/critical effect	Reduced pup viability and retardation of growth at maternally toxic doses
Developmental target/critical effect	Minor variations (skeletal development) at maternotoxic doses
Lowest relevant developmental NOEL (mg/kg bw/d)	1.2 (rats)

Delayed neurotoxicity	No evidence of delayed neurotoxicity
Immunotoxicity	No adequate evidence of immunotoxicity

Summary	*NOEL* (mg/kg bw/d)	**Study**	**Safety factor**
Current ADI (0.001 mg/kg bw/d) [Plasma ChE inhibition]	0.125	2-y feeding dog	100
New ADI (0.025 mg/kg bw/d) [Plasma ChE inhibition]	0.25	28-d repeat-dose human	10
ARfD	0.075 mg/kg bw/d		

4.1.2 Public Health Aspects

Azinphos-methyl is an organophosphorus pesticide (OP). Like other OPs, azinphos-methyl kills insects by inhibiting the acetylcholinesterase enzyme (AChE) in the nervous system. This interference causes overstimulation of the nervous system, resulting in rapid twitching and paralysis of muscles, leading to death.

Because it also inhibits AChE in vertebrates, azinphos-methyl is highly toxic to animals and humans. Poisoning can occur by oral ingestion (swallowing), dermal absorption (via the skin) or inhalation (breathing) of the spray. The extent of poisoning is directly related to the quantity ingested, absorbed or inhaled. The toxicological effects of azinphos-methyl in mammals are typical of other OPs and include increased swallowing, salivation, lacrimation (secretion of tears), vomiting, diarrhoea, anorexia, reduced locomotor activity (movement), piloerection (stiffening of the body hair), loss of coordination (staggering), muscle and generalised body tremors, convulsions, rapid breathing, respiratory failure and death. Atropine is an effective antidote for the immediate poisoning effects of azinphos-methyl if administered promptly.

In mammals, azinphos-methyl is rapidly absorbed, metabolised and excreted, mainly in urine. Long-term exposure to low concentrations of azinphos-methyl in the diet caused inhibition of cholinesterase activity and clinical signs consistent with other OPs. Azinphos-methyl does not interact with genetic material. Long term studies in animals gave no indication that it would be likely to cause cancer in humans. Similarly, exposure to low doses of azinphos-methyl had no adverse effects on reproduction or on the development of the foetus in experimental animals.

4.1.3 Evaluation of toxicology

The toxicological database for azinphos-methyl, which consists primarily of toxicity tests conducted using animals, is quite extensive. 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. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes ADI and ARfD at which no adverse health effects in humans would be expected.

4.1.3.1 Toxicokinetics and Metabolism

Studies conducted in rats showed that azinphos-methyl, given orally, was rapidly and almost completely absorbed from the gastrointestinal tract. Dermal absorption of azinphos-methyl in rats was approximately 21-54% after 10 hours, with the majority of absorption occurring within the first hour of application. In a recent study, the dermal absorption of a single dose of azinphos-methyl in human volunteers was approximately 22-29%, while earlier published studies reported dermal absorption of 16%. Azinphos-methyl was distributed predominantly to the adrenals and those organs associated with its excretion or metabolism, namely the kidneys and liver. Over 95% of orally absorbed azinphos-methyl was excreted in the urine, bile and expired air within 48 hours, with the majority excreted via the urine (60-70%).

In rats, the initial steps of the metabolism of orally administered azinphos-methyl appear to be sulfoxidation, hydroxylation of the ester bond or conjugation with glutathione. *In vitro* studies utilising various subcellular fractions suggested that azinphos-methyl metabolism is mediated by glutathione-S-transferase and cytochrome P-450. At least two major urinary metabolites (cysteinylmethylbenzazimide sulfone and methylsulfonylmethyl-benzazimide) and up to six other products (formed at low concentrations) have been identified in rats. Five faecal metabolites, accounting for approximately 10% of the administered dose, have also been characterised. Generally, the toxicokinetic characteristics of a major metabolite of azinphos-methyl, benzazimide, were similar to the parent compound.

4.1.3.2 Acute Studies

Azinphos-methyl was highly acutely toxic and its profile of clinical signs was consistent with other OPs. Clinical signs commonly observed in experimental animals following acute exposure were salivation, lacrimation, vomiting, diarrhoea, anorexia, reduced locomotor activity, piloerection, staggering gait and muscular tremors. These signs were qualitatively similar, irrespective of the route of administration. They were generally evident within 5-20 minutes after treatment in the lethal dose range, except after dermal exposure, where the signs occurred between 1-24 hours after application.

The acute oral LD_{50} in rats ranged from 4.4 to 26 mg/kg bw, while single studies in mice, guinea pigs and dogs reported LD_{50} values of 15, 80 and > 10 mg/kg bw, respectively. The lowest dermal LD_{50} in rats was 72.5 mg/kg bw but was much higher in rabbits (1380 mg/kg bw). The lowest acute 1-h and 4-h inhalational LC_{50} values in rats were 310 and 132 mg/m^3, respectively. Acute toxicity was slightly increased by intraperitoneal administration, with LD_{50} values in rats ranging from 3.4 to 11.6 mg/kg bw. Azinphos-methyl was not a skin irritant in rabbits, but was a slight eye irritant and skin sensitiser. Reported LD_{50} values for products containing azinphos-methyl were generally representative of the percentage of active ingredient present in the formulation.

The acute toxicity of one of the metabolites of azinphos-methyl, benzazimide, was tested in a limited number of experiments conducted in laboratory animals. While there were no acute oral toxicity studies in the database, an acute inhalational study in rats indicated that the 4-h inhalational LC_{50} of benzazimide was in excess of 1760 mg/m^3. The acute dermal toxicity of benzazimide in rabbits was low (LD_{50} > 2000 mg/kg bw).

In rats, acute azinphos-methyl toxicity was potentiated by ethion or DEF (defoliant *S*, *S*, *S*-tributylphosphorotrithioate), while EPN (*O*-ethyl *O*-4-nitrophenyl phenylphosphonothioate) or malathion had no effect. A number of other compounds were found to have an additive effect in rats and dogs, as well as in an *in vitro* study using human cells.

While atropine is a known antidote for immediate poisoning effects of azinphos-methyl, other compounds, individually or in combination with atropine, have shown antidotal potential in rodents. Such compounds included toxogonin, compound 30 [4-hydroxyiminomethyl-1(3-*N*, *N*-dimethylaminopropyl) pyridium chloride hydrochloride], scopolamine, propantheline, 2-PAM (pyridine-2-aldoxime) and BH6 (obidoxime chloride).

4.1.3.3 Short-Term Studies

Regardless of the route of exposure, cholinesterase inhibition was the most sensitive indicator of toxicity in a number of short-term repeat-dose studies conducted predominantly in rats for periods ranging from 6 days to 9 weeks. Following oral dosing (diet or gavage), the lowest NOEL in rats for the inhibition of plasma, red blood cell and brain cholinesterase activities was 0.8 mg/kg bw/d. At higher doses (> 2.5 mg/kg bw/d), decreased body weight and food consumption were observed. Dietary studies conducted in cattle and horses also reported inhibition of cholinesterase activity, with clinical signs also observed in one study conducted in heifers. Rabbits exposed to azinphos-methyl dermally showed reduced body weight (females) and inhibition of plasma and red blood cell cholinesterase activity at 20 mg/kg bw/d, while brain cholinesterase activity was unaffected. Inhibition of cholinesterase activity was also detected in rats exposed to aerosols of azinphos-methyl (NOEL = 1.24 mg/m^3).

The inhibition of cholinesterase activity was also a common toxicological effect in a number of subchronic toxicity studies conducted in rats and dogs. A 16-week dietary study conducted in rats found inhibition of plasma and red blood cell cholinesterase at 1 mg/kg bw/d. When azinphos-methyl was given to rats by oral gavage for 13 weeks, inhibition of red blood cell cholinesterase activity and salivation in males occurred at and above 0.86 mg/kg bw/d. At 3.44 mg/kg bw/d, inhibition of brain and plasma cholinesterase activities and the presence of a viscous yellow fluid in the small intestine of males were observed. A 19-week dietary study conducted in dogs did not establish a NOEL as whole blood cholinesterase activity was inhibited at all doses (lowest dose of 0.5 mg/kg bw/d). The general condition of the animals was impaired at 1.25 mg/kg bw/d and above, with cholinergic signs seen at and above 2.5 mg/kg bw/d. Doses of 1.25 mg/kg bw/d and above caused weight loss, and at 10 mg/kg bw/d dogs frequently refused to eat. At 10 mg/kg bw/d, one dog (female) died after 9 weeks.

4.1.3.4 Long-Term Studies

As with other OPs, the typical toxicological effects of azinphos-methyl during chronic studies in mice, rats and dogs included dose-related cholinesterase inhibition (plasma, red blood cell and brain) and classic cholinergic signs (body tremors, convulsions, muscle weakness, reduced weight gain) and mortality. Cholinesterase inhibition was observed at and above 3.49, 0.75 and 0.5 mg/kg bw/d in mice, rats and dogs, respectively (inhibition of plasma, red blood cell and brain cholinesterase activities in mice and rats, inhibition of plasma and red blood cell cholinesterase activities in dogs). Other effects including decreased body weight gain were seen at higher doses. There have been no reported effects of azinphos-methyl on gross pathology, histopathology or tumour incidences in mice, rats or dogs. Thus there is no evidence of any carcinogenic potential.

4.1.3.5 Reproduction and Developmental Studies

There was no evidence that azinphos-methyl affected reproductive parameters in mice, rats or rabbits. Observations of toxicity in offspring (reduced pup weight, reduced viability during lactation) occurred at doses that were also toxic to maternal animals. Therefore these effects may have been the consequence of reduced maternal care or lactation.

In developmental studies, no major malformations were observed in mice, rats or rabbits. In mice, malaligned sternebrae, reduced foetal weight and supernumerary ribs were observed at doses that caused frank toxicity in maternal animals. The majority of developmental studies conducted in rats found no developmental effects or evidence of foetotoxicity, while cholinergic signs and/or inhibition of cholinesterase activity were commonly observed in maternal animals. A single rat study did observe an increased incidence of supernumerary ribs and some retarded ossification at an apparently non-maternally toxic dose (3.6 mg/kg bw/d), however no maternal cholinesterase activity was measured in this study. Results from other studies indicated that inhibition of cholinesterase activity occurred in rats at approximately 1 mg/kg bw/d and therefore it was likely that cholinesterase inhibition would have occurred in this study at the dose where developmental variations were observed. In rabbits, the majority of studies reported no maternotoxicity or teratogenicity. In a single rabbit study, retarded ossification of the long bones, asymmetric pelvic articulation and reduced foetal size were observed at doses that caused significant inhibition of red blood cell cholinesterase activity. The minor developmental variations observed in these single rat and rabbit studies were not considered to be toxicologically significant as they fell within or just outside the historical control range of the performing laboratory. The weight-of-evidence indicates that minor developmental variations can occur in laboratory animals at maternotoxic doses of azinphos-methyl.

4.1.3.6 Genotoxicity Studies

Consistent with the absence of any detectable carcinogenicity during long term feeding studies, azinphos-methyl did not show any genotoxic potential in a variety of *in vivo* genotoxicity assays (mouse micronucleus test, mammalian bone marrow cytogenetic test, mouse dominant lethal assay, recessive lethal test in *Drosophila melanogaster*). Azinphos-methyl was negative in the *Ames* test and in the majority of other *in vitro* genotoxicity assays. Findings of clastogenicity or unscheduled deoxyribonucleic acid (DNA) synthesis occurred at cytotoxic concentrations or were not corroborated in other studies using the same cells. On the weight of evidence, azinphos-methyl was not considered to be genotoxic.

4.1.3.7 Neurotoxicity

The delayed neurotoxic potential of azinphos-methyl was studied in a series of experiments conducted in hens. Although these studies provided limited methodological information and/or data, the findings suggested that azinphos-methyl does not induce delayed neurotoxicity in hens after single or repeated oral administration.

4.1.3.8 Effects in Humans

In recent human studies, a single oral dose of azinphos-methyl was well tolerated by male volunteers up to 1 mg/kg bw and in female volunteers at 0.75 mg/kg bw, the highest doses tested. No effect on any vital signs, electrocardiogram (ECG), haematology, clinical chemistry, urinalysis, plasma and red blood cell cholinesterase activities were detected. In a subsequent 28-day repeat dose study, no effects were observed in male volunteers who were given daily oral doses of azinphos-methyl at 0.25 mg/kg bw/d. Although these experiments indicated that azinphos-methyl could be tolerated by males, either as a single oral dose up to 1 mg/kg bw, or as a 28-day repeat oral dose at 0.25 mg/kg bw, neither study addressed the acute or short term effects in females, or the long term or cumulative effects of azinphos-methyl in humans.

In general, no adverse health effects have been observed in male or female workers involved in azinphos-methyl production and formulation under normal safety precautions. A small number of occupational studies conducted in agricultural workers demonstrated greater than 20% inhibition of plasma and/or red blood cell cholinesterase activity, which was probably attributable to azinphos-methyl exposure. A number of other studies detected azinphos-methyl and/or its metabolites in the urine of orchardists, with only one study reporting the inhibition of plasma and red blood cell cholinesterase activities.

4.1.3.9 Bystander exposure

Issues relating to bystander exposure, especially for households adjacent to orchards, have not specifically been considered in this PRF. While the APVMA notes that some State/Territory jurisdictions require buffer zones when spraying, and the APVMA is developing spray drift guidelines, the possible risk to bystanders will be further considered during the period when the PRF is released for public comment.

4.1.3.10 Conclusion

Compound	**Dietary Standard, mg/kg bw**		**No Observable Effect Level (NOEL), mg/kg bw**	**Safety Factor**	**Reference (OCS/ JMPR, date)**
Azinphos-methyl	ADI[1]	0.025	0.25	10	28/02/05
	ARfD[2]	0.075	0.75	10	28/02/05

In Australia, there are four registered products containing azinphos-methyl. All four are registered for use in commercial horticultural situations. Based on an assessment of the toxicology, it is considered that there should be no harmful effects to human beings from the continued registration of products containing azinphos-methyl if used in accordance with label instructions.

4.2 OCCUPATIONAL HEALTH AND SAFETY (OHS)

Azinphos-methyl products are applied by mechanized sprayers (air blast, air shear) or by hand-held sprayers. Workers may be occupationally exposed to azinphos-methyl during mixing, loading, and applying the pesticide, or to foliar residues during harvesting or pruning some days or weeks after application.

Biomonitoring and dislodgeable foliar residue (DFR) studies were conducted to investigate the extent of worker exposure during various agricultural tasks. The exposure data in the studies were used to determine the occupational risk to workers during mixing/loading, application and post-application activities. The risk is determined by a margin of exposure (MOE), which is a measure of how close the likely occupational exposure comes to the NOEL observed in an appropriate animal or human study. The risk assessment used an internal (NOEL) dose of 0.25 mg/kg bw/day from a 4-week human dietary study. A MOE of 100 or more was considered to be acceptable.

As determined by OCS the most appropriate measure of exposure is ChE inhibition. In all cases evaluated in this review, plasma ChE is used as the critical indicator of exposure. An oral NOEL was used in the absence of dermal NOEL for humans. A correction factor of 30% dermal absorption was applied to calculate absorbed amounts for the German model and Pesticides Handlers Exposure database (PHED) used in the risk assessment. No correction was made for inhalation absorption, as 100% absorption was assumed. The two risks were added together to give a measure of total risk.

In estimating the risk to workers handling azinphos-methyl products, it is assumed that workers wear appropriate personal protective equipment (PPE) as specified on product labels. Consistent with the cholinergic effects of organophosphates, the signs of acute azinphos-methyl exposure include diarrhoea, salivation, lacrimation, vomiting, muscle tremors, paralysis, ataxis and convulsions. The toxicity end point was compared with the standard exposure estimates to give MOE for each Australian use scenario (eight in all). As a human toxicity end point was used, MOE of approximately 100 or more were considered to be acceptable to account for intra-species variability. The overall risk of adverse health effects to workers decreases as the MOE increases.

[1] http://www.tga.gov.au/docs/pdf/adi.pdf
[2] http://www.tga.gov.au/docs/pdf/arfd.pdf

Owing to the high percutaneous absorption rate in humans (30%) and the low oral NOEL (0.25 mg/kg bw/day) no acceptable MOEs could be achieved for mixing, loading and applying azinphos methyl products while wearing conventionial PPE of cotton overalls and gloves. However, for mixer/loaders, suitable MOEs were attained when water-proof clothing and footwear are worn. For applicators, PPE alone was able to provide adequate protection from exposure. However, engineering controls, such as the use of an enclosed tractor cab fitted with charcoal filter (to filter incoming air), could provide acceptable MOEs. No other modes of application, such as a hand-held apparatus, are considered safe for use with azinphos methyl products.

Post-application activities (thinning and harvesting) in blueberry crops and in orchards resulted in low worker exposures indicating low risk to workers during these activities. When adjusted for the application rates and treatment schedules recommended for Australian azinphos-methyl products, the MOEs for workers re-entering blueberry, macadamia and citrus, pome-, stone-fruit crops have been assessed as acceptable. Re-entry intervals have been set at one day for these crops. However, a relatively prolonged re-entry interval of 14 days has been recommended for kiwi fruit and grapes (applying to all activities except grape girdling and cane turning, for which a 44-day re-entry interval is required). This is due to the lack of reliable data on exposure of persons tending and harvesting vine crops, and the high default transfer coefficients associated with these activities. The re-entry intervals applying to vine crops could be re-considered if additional information on use pattern, foliar residues or worker exposure becomes available.

4.3 RESIDUES

The residues aspects of the use of azinphos-methyl on crops were reviewed by the Chemistry and Residues Program who examined the metabolism, analytical methods and residues data. This has included plant and animal metabolism studies, animal transfer data and Australian and overseas crop residue data. Additional information that had been submitted to the Pesticides and Agricultural Chemicals Committee (PACC) in support of the establishment of maximum residue levels (MRL), is also included. Recent data reviewed by Joint FAO/WHO Meeting on Pesticide Residues (JMPR), were also incorporated into the assessment where relevant.

4.3.1 Residues Evaluation

4.3.1.1 Metabolism

Metabolism data for plants, laboratory and food animals were considered. Studies in plants demonstrated that the main residue present in plant material was the parent compound azinphos-methyl. Small quantities of mercaptomethylbenzazimide and desmethyl azinphos-methyl were also found in apples, while small quantities of benzazimide and anthranilic acid were found in oranges.

When azinphos-methyl was fed to cows and goats, no parent compound was found in tissues or milk other than in fat, where 5% of the total residue was found as parent. The major metabolite found in liver, kidney, muscle and fat was methylsulfonylmethylbenzazimide. A major portion of the residue (up to 83% of the radioactivity in the liver) was found conjugated with the protein fraction. Essentially the same metabolites as in the tissues are found in milk, but these are different to those found in plant commodities.

From a residues definition perspective, consideration could be given to separate definitions for plant and animal commodities, as the parent azinphos-methyl is not a suitable measure of good agricultural practice (GAP) when feeding treated plant commodities to animals. However, FAO/WHO Codex Alimentarius Commission (Codex) and overseas regulatory authorities all use the parent only as the residue definition and harmonisation with these bodies is appropriate.

4.3.1.2 Analytical methods

Submitted methods

There were 12 analytical methods submitted for plant materials, including colorimetric and gas chromatographic methods. There were also photofluorometric, gas chromatographic or liquid chromatographic methods submitted in support of animal tissues and milk. The methods currently listed by the US EPA for determination of azinphos-methyl in crops and animal tissues and milk are acceptable for analysing azinphos-methyl and are listed in Table 3.

Table 3: Currently methods listed by the US EPA for determination of azinphos-methyl in crops and animal tissues and milk

Method reference.	Sample matrix	Technique		LOQ, mg/kg
		Extraction	Instrument	
Gas Chromatographic Method For Determination Of Guthion Residues In Plant Material. (Westburg & Becker 1981	Moist crops containing chlorophyll and oilseed crops	Crops: acetone Oilseed: Pet ether	Gas chromatography	Not given
A Method For The Determination Of Guthion And Guthion Oxygen Analog In Bovine Tissues And Milk Utilizing Gas Chromatography And High Pressure Liquid Chromatography. (Wargo *et al* 1978)	Tissues and milk	Soxhlet extraction with pet ether	Gas chromatography and also HPLC.	0.001-0.01

The method for animal tissues and milk was validated satisfactorily.

Stability of pesticide residues in stored analytical samples

Data were presented for stability of azinphos-methyl residues in apples, pears, blueberries, milk and liver that demonstrated that azinphos-methyl was reasonably stable when stored frozen at –18°C to –24°C. Data were also presented that demonstrated that azinphos-methyl was stable in orange and peach juices when stored at 0-20°C, but was unstable at 40°C, with a half-life of 7 days.

4.3.1.3 Residue definition

The data presented support the present residue definition of the parent azinphos-methyl *per se*. However, when azinphos-methyl is fed to animals, the residues found in tissues and milk were not the parent, except in fat, where it formed about 5% of the total residue. After three days, the major metabolite found in liver, kidney, muscle and fat was methylsulfonylmethylbenzazimide. A great portion of the residue (up to 83% of the radioactivity in the liver) was found conjugated with the protein fraction. However, to maintain harmony with other regulatory agencies throughout the world, and because there are no registered uses in major animal feed commodities, the current residue definition of azinphos-methyl should be maintained for both the plant and animal material.

4.3.1.4 Residues in foods and animal feeds

Plant commodities

Residues data for pome fruit, stone fruit, citrus fruit, grapes, litchis, blueberries and macadamias were considered and are summarised in Table 4.

Table 4: Residues of azinphos-methyl in fruit commodities at the withholding period.

	Application rate	**WHP**	**Retreatment**	**Azinphos-methyl residues (mg/kg)**	
Commodity	**(kg ai/100L)**	**(Days)**	**Interval (Days)**	**HR**	**STMR**
Pome fruit	0.044-0.100	14	14-21	1.1	0.225
Citrus fruit	0.029-0.034	14	21-29	0.85	0.45
Stone fruit	0.025-0.050	14	7-25	2.6	0.33
Grape	0.042-0.050	14	7	0.767	?
Macadamia	0.049, 0.098	7	14-16	<0.01	?
Litchis	0.049-0.098	1	6-13	1.0	?
Blueberry	840g ai/ha	14	?	1.0	?

Not all data presented addressed the GAP for Australia. Most of the data were generated overseas. No data were presented to support the use in kiwifruit. All residues data indicated compliance with the Australian MRLs, except for peach, where a maximum residue of 2.6 mg/kg occurred in fruit in one trial, and where an increase of the MRL to 5 mg/kg will be required. An increase in the MRL for blueberry from 1 mg/kg to 2 mg/kg will also be required, due to the uncertainty of the available data.

4.3.1.5 Animal transfer studies and required animal commodity MRLs

Three levels of azinphos-methyl (11, 33 and 77 ppm) were fed to cattle in alfalfa pellets for 28.5 days. Tissue samples were analysed for the presence of azinphos-methyl and its oxygen analogue. Residues were <0.01 mg/kg in all tissues, including muscle, fat, liver and kidney. Residues in all milk samples were <0.001 mg/kg.

4.3.1.6 Effect of processing on residues

The data demonstrate that residues of azinphos-methyl can be reduced during processing. Overall, the data indicate that for citrus and apple, most of the residues are on the skin and are removed with the skin. Residues in peaches are reduced to LOQ during the canning process. Highest residues to occur on minor animal feed commodities were 6.4 mg/kg in apple pomace, 2.3 mg/kg in grape pomace, and 2.4 mg/kg in citrus peel/rind. However, these feeds form no more than 20% of the diet of cattle or sheep. Should continued registration of azinphos-methyl products be supported, the following MRLs will need to be established in Table 4 of the *MRL Standard*:

Apple pomace, dry	8 mg/kg;
Grape pomace, dry	3 mg/kg,
Citrus peel/rind	3 mg/kg.

4.3.1.7 Crop rotation

Three separate studies on crop rotation were presented. However, the crops for which registration is current are not broadacre crops that are replanted or are at risk from carryover of residues.

4.3.2 Dietary risk assessment

The following health standards (Table 5) have been recommended by the Office of Chemical Safety, Department of Health and Ageing.

Table 5: Health standards for azinphos-methyl

Compound	Dietary Standard, mg/kg bw		No Observable Effect Level (NOEL), mg/kg bw	Safety Factor	Reference (OCS/ JMPR, date)
Azinphos-methyl	ADI[3]	0.025	0.25	10	28/02/05
	ARfD[4]	0.075	0.75	10	28/02/05

The end-points for the ADI and the ARfD were based on the level at which there was no inhibition of cholinesterase activity.

4.3.2.1 Chronic dietary exposure assessment

The chronic dietary exposure to azinphos-methyl is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all uses of the chemical and the mean daily dietary consumption data derived from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with international guidelines[5] and is a conservative estimate of the dietary exposure to chemical residues in food. The NEDI for azinphos-methyl is 14.7% of the ADI.

It is concluded that the chronic dietary exposure of azinphos-methyl is acceptable.

4.3.2.2 Acute dietary exposure assessment

The acute dietary exposure was estimated using the National Estimated Short Term Intake (NESTI) calculations, in accordance with the deterministic method used by the JMPR, with 97.5th percentile food consumption data derived from the 1995 Australian National Nutrition Survey. NESTI calculations are conservative estimates of acute exposure (24-hour period) to chemical residues in food. The NESTIs for all relevant commodities for azinphos-methyl are summarised in Table 6.

The highest acute dietary intake was estimated at 104% of the ARfD for apricots, in 2-6 year old children. The APVMA found that the acute dietary exposure of azinphos-methyl is not acceptable for apricots. Consequently, the MRL for stone fruit will need to be amended. All other acute exposures were considered to be acceptable.

[3] http://www.tga.gov.au/docs/pdf/adi.pdf
[4] http://www.tga.gov.au/docs/pdf/arfd.pdf
5. Food and Agriculture Organization of the United Nations, Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed, 2002, Rome.

Table 6: NESTI calculations for commodities for azinphos-methyl

Code	Food	NESTI (%ARfD)		Code	Food	NESTI (%ARfD)	
		2 years +	2-6 years			2 years +	2-6 years
FB 0020	Blueberries	21.7	63.2	MM 0095	Meat [mammalian]	0.5	0.9
FC004	Oranges, raw (including peeling)	9.8	31.6	ML 0106	Milks	2.0	5.1
FC 0203	Grapefruit (raw)	9.5	0.0	FP 0226	Apple, raw, unpeeled	14.8	45.2
FC 0204	Lemon, raw (including peel)	2.5	0.0	FP 0230	Pear, raw, unpeeled	16.1	60.7
FC 0206	Mandarin, raw	10.1	36.0	FS 0240	Apricot, raw	25.2	103.7
MO 0105	Edible offal (mammalian)	0.2	0.1	FS 0245	Nectarine, raw, unpeeled	34.0	77.5
FB 0269	Grapes	7.9	18.5	FS 0247	Peach, raw, unpeeled	36.7	90.2
FI 0341	Kiwifruit	14.9	10.7	FS 0248	Plum, raw	21.3	36.5
FI 0343	Litchi	3.9	12.6	FS 0244	Cherry, raw	7.0	24.6
TN 0669	Macadamia nut	0.0	0.0				

4.3.3 Residue related aspects of trade

Blueberries, kiwifruit, lychees (*Litchi*) and macadamia nuts are not major export commodities[6] and the overall risk to Australia's export trade is considered to be small. However, use of azinphos-methyl may result in detectable residues in these commodities other than macadamias, and the growers/ producers/ stakeholders should become aware of any potential trade risks to their industry.

4.3.3.1 Commodities exported

Citrus, stone and pome fruits, and grapes are all exported and are listed in Part 5B[6], and require consideration of trade issues.

4.3.3.2 Destination and Value of Exports

The three largest export markets for individual commodities by value for the season 2002/2003 are shown in Table 7 below (*The Australian Horticultural Statistics Handbook 2004*).

Table 7: Export markets for individual commodities by value for the season 2002/2003

Commodity	Destinations	Value, $ million
Apples	UK, Malaysia, India	41.4
Pears	Singapore, Malaysia, Indonesia	22.0
Apricots	Singapore, Bahrain, France	0.8
Cherries	Hong Kong, Taiwan, Singapore	13.7
Nectarines	Taiwan, Hong Kong, Singapore	22.7
Peaches	Taiwan, Singapore, UAE	5.5
Plums	Hong Kong, Taiwan, Singapore	26.2
Oranges	USA, Hong Kong, Malaysia	146.4
Lemons/limes	Japan, Hong Kong, Singapore	6.1
Grapes	Hong Kong, Malaysia, Indonesia	95.4

[6] Part 5B, Volume 3 of the Manual Of Requirements and Guidelines, Ag MORAG, Overseas Trade Aspects of Residues in Food Commodities. http://www.apvma.gov.au/MORAG_ag/MORAG_ag_home.shtml

4.3.3.3 Comparison of Australian MRLs with Codex Alimentarius Commission (Codex) and overseas MRLs.

The Codex Alimentarius Commission is responsible for establishing Codex MRLs for pesticides. Codex MRLs are primarily intended to facilitate international trade, and accommodate differences in GAP employed by various member countries. Some countries may accept Codex MRLs when importing foods. Azinphos-methyl has been considered by Codex. The relevant Codex and international MRLs have been established for azinphos-methyl can be seen in Table 8.

Table 8: Comparison of overseas MRLs and tolerances that have been established

Commodity	Tolerance, mg/kg			
	Australia	Taiwan	Codex	EU
Apple	2	2	2	0.5
Pear	2	2	2	0.5
Apricot	2	2	1	0.5
Cherry	2	2	2	0.5
Nectarine	2	2	2	0.5
Peach	2	2	2	0.5
Plum	2	2	2	0.5
Orange	2	2	1	1
Lemon	2	2	1	1
Grape	2	0.5	1	1

Furthermore, Hong Kong and Singapore adopt the standards of Codex for azinphos-methyl.

Animal commodities

Animal commodities have MRLs set at or about the limit of analytical quantification, so that any animal eating treated produce should not produce any quantifiable residues in its tissues, so that there is no trade risk associated with animals consuming azinphos-methyl treated feeds. The data indicate that residues of 77 ppm azinphos-methyl in feed will not produce residues in animal tissues and milk. The maximum residues to occur in animal feeds (6.4 ppm) are well below this, so that compliance with the MRLs for animal tissues should occur.

4.3.3.4 Potential risk to trade

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

Australian MRLs tend to be the same as Codex for pome and stone fruit, except for apricots, where the Australian MRL is double that of Codex. Australia's MRLs for grapes and citrus are also double that of Codex. However, when comparison is made with the monitoring data found in Section 1.7, there have been no reported violations of the MRL, nor have there been residues that have exceed half MRL. Furthermore, to the evaluator's knowledge, there have been no trade incidents involving this chemical in pome, stone or citrus fruits, or in grapes.

4.3.4 Conclusions

The APVMA has assessed that there is no undue hazard to the health of consumers, except from apricots, for which the acute dietary exposure calculations indicated an unacceptable level of risk in children. No data were available to support the ongoing use in kiwifruit. Changes and additions to the *MRL Standard* will need to be made.

When treated commodities are fed to animals, there are no residues found in the animal tissues or in milk. Additions to Table 4 the *MRL Standard* will need to be made for fruit processing wastes identified in the review for the minor animal feeds of apple pomace, grape pomace and citrus peel/rind.

The current residue definition of azinphos-methyl *per se* was considered adequate. Analytical methods are available which address this residue definition.

Therefore, the potential for prejudice to Australia's trade is acceptable and there is unlikely to be any 'undue' risk to Australia's trade.

4.4 ENVIRONMENT

4.4.1 Environmental Fate And Degradation

4.4.1.1 Hydrolysis

Azinphos-methyl is reported from four experiments to be relatively stable in low pH aqueous buffers but more rapid hydrolysis occurs at higher pH (half-lives: ~39-42 days @ pH 4; ~23-25 days @ pH 7; ~2-2.5 days @ pH 9). A number of hydrolysis products are formed, largely a series of benzazimides that eventually lead to anthranilic acid. Hydrolysis could be a significant contributor to the overall degradation of azinphos-methyl in the environment, particularly under alkaline conditions.

4.4.1.2 Photolysis

Aquatic
Based on five studies using artificial light and sunlight, photo-degradation of azinphos-methyl in water is possible, with benzazimide and anthranilic acid the major metabolites. The half-lives were determined for two of these studies and ranged from <0.5-3 days. The half-life under environmental conditions was determined by modelling as 0.9-5.5 days for German spring and summer conditions.

It is concluded that photodegradation in water could be a significant route of degradation under Australian environmental conditions but the turbidity in Australian natural waters could decrease the rate of degradation.

Soil/Plants
Based on 2 soil photolysis studies using natural sunlight, the net half-life of photo-degradation of azinphos-methyl in air dried soils was calculated to be 232-241 days in sunlight. The main metabolites occurred at low concentrations and were not identified. On glass plates azinphos-methyl degradation was relatively slow, but on plant surfaces dissipation of azinphos-methyl appeared more rapid than from soils with 20-40% degradation after 8 h exposure to sunlight.

There were several additional studies that used artificial light. These showed that exposure to ultra violet (UV) light was effective in degrading azinphos-methyl, but the visible wavelengths were not effective. Half-lives for UV exposures were determined to be about 2-8 hours depending on conditions used, but as these studies used different lamps and conditions they cannot be readily related to natural conditions.

Photodegradation on plant surfaces may be a major route for environmental degradation in Australia, given the high light levels during summer, when most azinphos-methyl use occurs.

4.4.1.3 Metabolism in soils

A range of soil metabolism studies were performed using several soil types (two acceptable and seven supportive studies). It is concluded that microbial degradation of azinphos-methyl in soil systems is moderate under aerobic conditions (half-lives 21-49 days), and somewhat slower under anaerobic conditions (half-life 68 days). The considerably longer half-life (355 days) under sterile conditions indicates these rates are highly dependent on microbial activity. The main metabolites were similar throughout the degradation studies, largely a group of benzazimides and anthranilic acid, and eventually more complete mineralisation yielding CO_2. In Australia it is likely that hydrolysis and microbial degradation will occur in soils, especially under alkaline conditions, and it is expected this will occur at similar rates to those quoted above, depending on soil types/pH.

4.4.1.4 Aquatic metabolism

There were no studies provided on aquatic aerobic metabolism. However, the azinphos-methyl half-lives in the aquatic phase of the mesocosms were typically ~1-2 days.

4.4.1.5 Mobility in soil

Soil adsorption/desorption

The soil adsorption/desorption of azinphos-methyl was determined in two acceptable studies using 7 different soils. The K_{oc}s averaged 757 (range 407 to 1172, discarding one abnormal value of 3396) and show that azinphos-methyl is moderately absorbed to the six soils tested. The absorption appears strongly dependent on the organic matter content of the soil. The desorption studies indicated azinphos-methyl desorbs fairly readily and constantly from adsorption sites. These tests rank azinphos-methyl as having medium mobility in soils, which is supported by several other reports.

Leaching

Several soil column leaching studies using a range of different soils, both fresh and aged, showed there was little leaching of azinphos-methyl (<0.3%). Some metabolites were detected in the leachate, generally in low amounts (<5% of applied). In the one instance where there was no aging around 10% of applied radioactivity appeared in leachate, mainly degradation products. Soil R_f values were determined on TLC plates and indicated low mobility. Azinphos-methyl is unlikely to leach under field conditions.

Volatility

No studies on volatilisation of azinphos-methyl from soils presented, but this is not expected to be a significant route for the dissipation from soil, particularly where binding to soil organic matter occurs.

4.4.1.6 Field dissipation

Crop trials

US field trials on cotton, sugar and alfalfa, while not particularly relevant to the Australian use patterns, give a strong indication of azinphos-methyl's ability to enter waterways, particularly with run-off from heavy rainfall events. In two trials in cotton, one in Mississippi and the other Georgia, the field half-life of azinphos-methyl in soil was 5.7 and 6.4 days and on foliage 1.2 and 0.5 days respectively. There were rainfall events in the cotton trials that caused run-off to occur, with a maximum of 2.7% of the active applied detected in the run-off waters from one rainfall event.

The results indicate that in field use azinphos-methyl can be rated as readily degradable but it also demonstrates the propensity for potentially toxic run-off to occur, especially with rainfall soon after application. The likelihood of this occurring clearly increases when the OP are frequently applied, such as in these trials in cotton where repeat applications occurred every 3-7 days, and especially in summer rainfall zones. These results concur with the incidence reports from the US.

Two trials were conducted in California in fields of alfalfa, with the half-lives in soil of 5.3 and 10.9 days for single applications. In the plots receiving 2 applications there was no evidence of leaching despite high total application rates used (6.72 kg ai/ha).

An extensive agricultural run-off and water monitoring study was performed as a special study to assess/reduce the potential risk of fish kills. The overall site included extensive waterways adjacent to cane fields. The study was undertaken in 17 different waterways that had been reported as having azinphos-methyl related fish kills in the previous two years. Only one rainfall event (44 mm) in the entire trial triggered run-off from recently sprayed sugarcane fields. Sampling could not be conducted during this storm run-off event and in samples collected later azinphos-methyl levels were below detection limits. The lower seasonal rainfall (with less run-off) and label changes appear to have reduced fish kill incidents associated with this azinphos-methyl use in sugarcane in the one year trial (note: 1991 – 15 incidents, 1992 – 7, 1993 – 0).

A published study followed the dissipation of azinphos-methyl from leaves and soil in sugarcane field plots and in particular monitored azinphos-methyl in run-off. Azinphos-methyl was applied to maturing sugar cane three times (0.82 kg/ha each) later in the season over three consecutive years (1993-95). The conclusions of the trial were that the amounts of azinphos-methyl appearing in run-off are highly correlated to the residual azinphos-methyl levels on plants and the surface soil. There was a propensity for azinphos-methyl to wash-off plants with rainfall events soon after application. Even relatively small rain events dislodged a high percentage of the residual azinphos-methyl. The modelling of these data derived half-lives for azinphos-methyl of 2-8 days as leaf deposits and 6-66 days for soil.

Apple orchards trials designed to provide information on off-site movement of azinphos-methyl, largely for modelling purposes, showed little run-off due to seasonal and site conditions (low rainfall and heavy ground cover). There were four plots treated together with an untreated control, each set up such that all run-off from the plots was collected separately. Plots were mown prior to the first spray treatment and as required after that (nil in 1976 and twice more in 1977). The soils were sampled prior to and then periodically after each application.

For azinphos-methyl there was significant movement from the trees (target) to other segments (soil, grass, litter) during three seasons studied. However, there were few detections in run-off, largely due to the rare occurrence of run-off events at this site because of one dry season plus the heavy ground cover. Azinphos-methyl residues on the tree canopy apparently dissipate at a rate of 4.9% per day on average, and the modelling suggested that around 25% of the daily losses are redistributed within the orchard under dry conditions. Losses from the orchard's soil segment were estimated at 7.9% per day. Rainfall increased the loss of dislodgeable azinphos-methyl residues, especially "heavy" rain soon after application. These presumably might enter run-off where bare soil situations occur in orchards, for example in Australian macadamias.

Monitoring studies
Water monitoring studies conducted across the USA by the United States Geological Survey (USGS) show that in the 5133 samples taken some 164 (3.2%) contained detectable levels of azinphos-methyl, 4 of which were in groundwater. In the US EPA review of this report, it was considered that there was considerable under-reporting of the true level due to poor recoveries of azinphos-methyl in the analytical method used (13%). There were 16 detections in 60 groundwater samples in two counties in Virginia, USA, both with intensive agriculture and vulnerable aquifers.

As azinphos-methyl does not have significant use in the Murrumbidgee Irrigation Area (MIA) and is not a cotton insecticide, it has not been tested for in major Australian water monitoring surveys in the MIA and northern NSW rivers programs.

4.4.1.7 Bioaccumulation

A bioaccumulation study with azinphos-methyl and channel catfish (*Ictalurus punctatus*) based on US EPA Guidelines indicated rapid uptake and depuration, with the steady state bioaccumulation factor determined to be 63. Based on this study, azinphos-methyl is not expected to bioaccumulate.

4.4.2 Environmental Effects

4.4.2.1 Avian toxicity

Results indicate that azinphos-methyl is very highly toxic to birds. The only species tested in the acute oral tests, conducted to US EPA requirements, was Bobwhite quail, with two tests giving LD_{50}sof 33 and 34 mg/kg bw using technical material and one test using formulated product (20% ai) with LD_{50} of 271 mg/kg bw (54 mg ai/kg bw). There were no 5 day dietary tests presented but the US EPA has reviewed such tests that meet their requirements and the LC_{50}s ranged between 488-1940 ppm for 4 species. The bobwhite quail was the most sensitive. Two 21 weeks single generation reproduction studies were presented for bobwhite quails and mallard ducks and the NOEL was 15.6 and 10.5 ppm respectively.

Field surveys within apple orchards detected wildlife casualties attributed to azinphos-methyl, however, it was not clear from the data what proportion of these casualties were birds. In one of these trials the results were confounded by rodenticide treatments, which clearly increased casualties, but apparently mostly in the small mammal category.

While literature reports on field studies in Canada using nesting birds in orchards showed there were effects on brain and plasma cholinesterase after 2 applications of azinphos-methyl

(2.1 kg ai/ha, 15 days apart), the level of these were not sufficient to cause mortality. The results for nestlings were the same, with brain and plasma cholinesterase affected and no mortality due to the chemical treatment. A follow-up study showed minimal effect on the behaviour of the nesting birds when sprayed and no difference in fledging time or mass of chicks at fledging. A similar result was obtained when quail were exposed to azinphos-methyl up to 3.1 kg ai/ha in plots of alfalfa.

4.4.2.2 Aquatic toxicity

Acute studies on a range of fish species, conducted to US EPA or Organisation for Economic Co-operation and Development (OECD) requirements, indicated that azinphos-methyl is highly toxic to fish. The LC_{50}s were between 1.86-3.2 µg/L for technical material and 21.5 to 40.1 µg/L for a number of formulations, which when converted to active material content correspond to between 5.4–8.8 µg ai/L. In the 4 chronic tests, conducted to US EPA or OECD requirements, the maximum acceptable toxicant concentration (MATC) ranged between 0.29 and 0.66 µg/L using technical material. The most sensitive species for both acute and chronic tests was Sheepshead minnow.

Azinphos-methyl shows very high acute toxicity to daphnia and mysid shrimp with 48 hour LC_{50}s of 1.1 µg/L and 0.12 µg/L respectively using technical material. The formulated product was less toxic to daphnia, with EC_{50}s of 2.2 to 2.9 µg ai/L. Literature results for two species of damselfly native to New Zealand using formulated product show that these are less sensitive, with LC_{50}s of 16 and 44 µg ai/L.

The test reports for molluscs, oysters and quahog, conducted to US EPA requirements using shell growth as the end point gave LC_{50}sof >3.1 and 7.5 mg ai/L respectively, which can be rated as moderately toxic.

In chronic tests conducted to standard protocols the MATC for daphnia and mysid shrimp were 0.25-0.4 µg/L and 0.0083-0.015 µg/L respectively using technical material. Tests using sediment/water systems showed there was little mitigation in toxicity, with EC_{50}s of 1.02 and 0.55 µg/L for daphnia and chironomids respectively.

A published study tested the toxicity of azinphos-methyl to Pacific tree-frog tadpoles using both technical grade azinphos-methyl (99.5% ai) and formulated product (Guthion 2S – 22% azinphos-methyl). The EC_{50}s were of 1.47 mg ai/L for formulated (expressed as active) and LC_{50} of 4.14 mg ai/L for the active constituent (AC). The larvae of the Northwestern salamander (*Ambystoma gracile*) and the spotted salamander (*Ambystoma maculatum*) were also tested using Guthion 2S. The 96 h LD_{50}s were 1.67 and 1.9 mg ai/L respectively. These results rate azinphos-methyl as moderately toxic to these amphibians.

The single aquatic plant toxicity test with azinphos-methyl used green algae gave an EC_{50} value (growth) of 3.6 mg/L showing this insecticide may exhibit moderate toxicity to these plant groups.

Mesocosms

The toxicity of azinphos-methyl to aquatic ecosystems was further examined in an intensive mesocosm study under US EPA's tier three testing regime, since azinphos-methyl had been linked to fish kills in the US. A series of mesocosms (control and 5 treatment rates in duplicate) received eight simulated run-off additions of Guthion 35 WP (29% azinphos-methyl) on a weekly regime. The nominal rates used were 0.056, 0.28, 1.3, 6.7 and 34 μg/L and the mean measured concentrations were within 70% of these target concentrations.

After dosing, azinphos-methyl concentrations in pond water declined rapidly to almost reach baseline levels prior to the subsequent dosing, except in the two higher doses. The dissipation half-life of azinphos-methyl in these mesocosms was between 0.51 and 7.75 days, calculated following each application.

Sampling of the aquatic fauna showed no treatment related effects for plants (algae and macrophytes) and there were few discernible treatment-related effects with the aquatic invertebrates, with the only significant differences being at the two highest rates. (This result is surprising given that the two highest treatment levels actually exceeded the LC_{50} for freshwater invertebrates and may indicate some mitigation of the toxicity was occurring.) By contrast survival of fish was clearly decreased at the two higher rates, which correlates with the laboratory results and the US EPA review, where a number of incidences and reports of fish deaths due to run-off were reported.

In a recent literature report, artificial enclosures in a pond were treated with single doses of azinphos-methyl, measured at 1.33, 1.72 and 20.4 μg/L, with the enclosures at nominal concentration of 0.2 μg/L that could not be measured. Principle component analysis and ordination plots were used to decipher effects in the natural populations within each enclosure. These plots showed that highest rate significantly affected the populations during the entire experiment and in the 4 μg/L enclosure from 2 to 22 DAT in one replicate and 8 to 36 DAT for the other replicate. Univariate analysis indicated that cladocerans were the most sensitive group, being affected at <1 μg/L and practically eliminated in treatments >2 μg/L. However, their numbers recovered within 42 days after treatment in all enclosures. Most copepods and rotifers appeared to be unaffected by the pesticide at all concentrations. Overall this trial shows the variable harmful effects and recovery rates of different aquatic invertebrates from a single azinphos-methyl treatment.

In another literature report adult bluegills were exposed to azinphos-methyl in littoral enclosures at nominal concentrations of 1.0 and 4.0 μg/L. The half-life of azinphos-methyl was determined as 2.3 and 2.4 days respectively and quantifiable residues remained for 8 days. There was no significant long-term effect on bluegill reproduction, embryo hatchability, larval survival growth or biomass 63 days after the single dosing. Aquatic invertebrates such as copepods (cf to previous studies) and cladocerans were significantly reduced after 7 days and recovered to levels equal or greater than controls after 35 days. The authors concluded that the lack of long term effects on reproductive success was due to the relatively short half-life of azinphos-methyl. A follow-up paper on the persistence and distribution of azinphos-methyl in similar mesocosms showed that half-life was between 1.2 and 2 days with 95% dissipation within 10 days. Residues were found in the sediment, macrophytes and fish. Only the residues in sediment were significant to the overall mass balance, the biota contained only trace levels of the applied active.

In an older literature report, four segmented ponds were given a range of treatments, including azinphos-methyl. Azinphos-methyl levels were monitored twice weekly and re-dosed to keep the concentration constantly near to 1 μg/L average, throughout the two seasons (May-August). The measured azinphos-methyl concentrations averaged 0.81 and 0.61 μg/L respectively and the half-lives were estimated as ~7 days in 1977 (average pH 8.1) and ~ 3 days in 1978 (average pH 9.3). At these levels significantly reduced numbers of cladocerans occurred but did not appear to affect other invertebrates. After treatment was ceased the numbers of *Daphnia* did not recover quickly while *Simocephalus vetulus* recovered somewhat. It was noted that effects of azinphos-methyl were slower to occur and recover than in the comparative parathion ponds.

A series of studies were reported investigating aspects of azinphos-methyl contamination in a South African river, arising from run-off and to a lesser extent, spray drift, from stone and pome fruit orchards in the catchment area. In a run-off simulation study, acute effects of particle-associated azinphos-methyl were determined in stream microcosms containing macroinvertebrate fauna from a South African river. Treatments with the two highest particle contamination levels (5000 and 200000 µg/kg at 1 g/L suspended solids for 1 h exposure) resulted in significantly reduced total numbers of individuals, and the highest treatment reduced the number of taxa. The measured azinphos-methyl concentrations in filtered water at these concentrations were 1.1 and 6.9 µg/L, respectively.

In a previous study with aqueous-phase application, toxicity to similar macroinvertebrate communities was observed at ≥ 5 µg/L. This suggests that toxicity in the second study may have partly been due to particle bound azinphos-methyl. Particularly affected taxa included mayfly and stonefly taxa. There was a large degree of consistency between the taxa affected in this study and those observed to be affected in monitoring studies of the river. An evaluation of the use of a wetland to intercept water containing azinphos-methyl residues from spray drift indicated it sorbed to plants or plant surfaces, leading to a peak concentration of 6.8 µg/kg dry weight.

4.4.2.3 Non-target invertebrates

The test results for bees show that azinphos-methyl is highly toxic to bees (oral/contact LD_{50} ~1 µg/bee). The US EPA report lists three further results for bee toxicity with one acute oral LD_{50} of 0.15 µg/bee and two acute contact LD_{50}s of 0.063 and 0.423 µg/bee that support this ranking. Also, there is a report that plant residues are highly toxic to bees for 4-13 days after application.

The 14 day LC_{50} for earthworms was 59 mg/kg soil using technical active and 158 (equivalent to 39 mg ai/kg soil) for Gusathion MS, which ranks azinphos-methyl as moderately toxic under the Dutch system. Field tests noted significant reductions in worm populations under pastures treated with Gusathion M (20% ai EC) at 6 kg ai/ha (exaggerated rate) and short term reductions when the highest label rate was used (1.5 kg ai/ha).

Tests using azinphos-methyl formulations applied to plants found that when it was slightly harmful (30-80% mortality) to predatory mites on the IOBC scale. Dried residues of azinphos-methyl on leaves were toxic to parasitic wasps, with an EC_{50} of 1.2 g ai/ha of leaf surface.

There was little effect noted on the soil respiration and nitrification activity of the soil micro-organisms at 1X or 10X the field rate of 0.45 kg ai/ha, but some inhibition of fungal growth was noted in one test. When azinphos-methyl was added to pot cultured soybeans in irrigation water at 2 mg/L, no effects were discernible on plant growth, nodulation or nitrogen fixation rates. In sewage sludge azinphos-methyl did not affect oxygen consumption nor microbial digestion.

4.4.2.4 Mammals

The toxicity of azinphos-methyl is very high to laboratory mammals with 14 days acute oral LD_{50}s ranging from 6.7 to 20 mg/kg. In orchard monitoring studies at maximum label rates and minimum re-treatment intervals it caused deaths ("casualties") and presumably other detrimental effects on mammals.

Gray tailed voles in grassed enclosures were treated with five applications of azinphos-methyl (Gusathion 2S) at 0, 0.88, 1.65, 2.63 and 4.48 kg ai/ha. Vole populations in the enclosures were statistically significantly reduced at 1.65 kg ai/ha and above for one sample only (~6 weeks after application). While survival rates were reduced compared to control in these higher treatments, this did not affect the size of the populations, which remained constant.

In another study, voles in grassed enclosures were treated with all habitat sprayed or half-sprayed (half the enclosure sprayed) at 1.5 kg ai/ha together with control (sprayed with water). There were no mortalities in any treatment and none of the monitored animals moved from their established home ranges after treatment. The authors also noted that behavioural responses are important in the exposures and these may be chemical, species and habitat specific. However, DEH notes that as the actual exposures were not sufficient to cause any adverse effects, changes in behaviour are unlikely unless there is a repellent effect from the chemical.

4.4.2.5 Phytotoxicity

Azinphos-methyl is not expected to show phytotoxicity in normal use patterns.

4.2.3 Prediction of Environmental Risk

4.2.3.1 Risk arising from use

The major uses are in pome fruit and stone fruit industries, with minor quantities used in macadamias, grapes and other minor crops. Use is declining with the introduction of IPM in most orchard systems, particularly for grapes and citrus, but azinphos-methyl remains a significant chemical for pome and stone fruit to establish IPM and to control break-outs of pest problems in IPM. The rates stated on the labels correspond to 36-49 g ai/100 L, with the volume applied varying considerably between crops and planting density (low, medium or high density), between growth stages (immature v mature trees) and application target (foliage versus soil drenching).

Traditionally application to orchards is by orchard air blasters using high volume equipment. However, many orchardists are now using low volume sprayers, and in some cases ultra low volume equipment, although this is not very common due to its higher equipment costs. The directions on the label for such equipment specify that growers should apply the same amount of azinphos-methyl to the target crop using a low volume rate as by the high volume rate. Thus, the rate of active ingredient (ai) applied to trees should remain constant whatever the method of spraying.

4.2.3.2 Risk evaluation.

Terrestrial organisms

Mammals

Terrestrial animals may be at risk from azinphos-methyl when applications of the chemical are made directly over them or from contact with sprayed surfaces, such as from orchard tree leaves or inter-row cover crops. It is expected that over-spray by tractor powered equipment is unlikely and most mammals are not expected to be directly over-sprayed.

It is difficult to assess the risk to terrestrial organisms, such as possums, that enter sprayed areas and are exposed to residues (dermal or dietary). Two field trials in US apple orchards did note "casualties", although there were confounding factors including the effect of other chemicals used and in one case, rodenticides.

Tests using gray-tailed voles (LD_{50} of 32 mg/kg bw and LC_{50} of 406 ppm) showed that when oversprayed at the maximum Australian rate of 1.5 kg ai/ha, there were no mortalities. When sprayed at higher rates, up to 4.48 kg ai/ha, there were effects on the populations but of limited duration (9 weeks). While these voles are not the most sensitive mammals tested, the result does indicate that a significant risk to small mammals is unlikely.

It is concluded that while there are unlikely to be significant effects on mammal populations from orchard spraying, some individuals, especially those living and feeding in orchards, could be affected.

Birds

Birds feeding on sprayed fruit could be exposed to residues of azinphos-methyl. There are a number of bird species that are pests in orchards, grapevines etc.

Incidents of azinphos-methyl poisoning of birds in Australia have not been noted in literature or press reports. However, in the US there have been reports of azinphos-methyl implicated in bird deaths associated with field/orchard uses of azinphos-methyl. In field studies (apple orchards) where azinphos-methyl was used with 7 days between applications and at maximum use rates, there were a number of avian casualties, 54 in one study with 3 applications but only 2 in the second study with 4 applications. While these studies indicate a potential risk, it must be noted that use of a rodenticide confounded the results in the former. In the two field studies from Ontario, Canada, where birds were oversprayed at higher rates than that used in Australia, there were no mortalities and detectable effects were limited to moderate inhibition of cholinesterase and minor behavioural changes.

For fruit sprayed at 1.5 kg ai/ha, the maximum rate expected for pome and stone fruit trees, the concentration of azinphos-methyl on the fruit is calculated as 19.5 mg/kg wet weight (99 mg ai/kg dry weight). There were no acute dietary results presented by registrants but using the acute oral test value (bobwhite LD_{50} = 33 mg/kg,) the LD_{50} was estimated at approximately 107 ppm in the diet. Assuming that approximately 50% of the dietary intake is treated, risk was calculated as minimal. Using the LC_{50} of 488 ppm from the US EPA review, the risk is again minimal.

Effects on birds are possible from birds eating insects that are dead or dying from contact with azinphos-methyl. Using the EPA food chain nomogram, the concentration of residues on large insects from applications at 1.5 kg ai/ha is 19.5 mg ai/kg. This is the same as above and the risk was calculated as minimal.

While the analysis showed that risk from dietary intake was minimal, it must be noted that food items are not the only route of exposure. In the field studies conducted in orchards with treatments every 7-10 days, ie program spraying, and at the maximum rate, there were effects on birds in and around the orchards. On the other hand, the studies conducted in orchards with infrequent applications showed minimal effects on birds, even birds with nests in the treated orchards treated at higher rates. These studies indicate that effects on birds cannot be ruled out and with multiple applications, the effects could be more significant.

The duration of any possible effects on birds is expected to be of relatively short duration. The half-life of degradation on apple leaves in the orchard field studies was approximately 7 days and there was significant degradation of azinphos-methyl on leaves (and presumably fruit), with 20-40% degradation after 8 hours of sunlight. Under Australian conditions with stronger and more intense sunlight, significant degradation of azinphos-methyl is anticipated, thus reducing the period when residues are toxic to birds.

In conclusion, while calculations indicate there could be a slight risk from a single treatment to birds frequenting and feeding in azinphos-methyl treated orchards, the risk is greater with repeated spraying, and there have been reports from overseas of adverse effects in a variety of situations, especially with multiple applications. Applications are expected to be greatly limited under IPM programs, but to ensure a risk to birds does not result from repeated/program use, use should be restricted on the label to no more than two applications per productions season.

Bees

Bees are at risk if spraying occurs when they are present in the crop and most labels include a precaution - "dangerous to bees, do not spray flowering plants while bees are foraging". Bees are very important to the yield potential of orchard crops and most orchardists are well aware of the harmful effects of OP sprays (and other chemicals) on bees. In addition, azinphos-methyl is used after fruit set, ie 2-3 weeks after flowering, and as such exposure to bees is unlikely. Nevertheless, if bees were oversprayed at the lowest application rate expected in orchards calculations show that 100% kill rates would occur. To limit the exposure of bees to the pesticide, the crop should not be sprayed when there are bees present. As foliar residues may remain highly toxic to bees 4-13 days after application, trees or vines should not be sprayed while they are flowering.

Spray drift could also expected to be extremely toxic to bees. Spray drift studies show that worst case (early bud swell), the risk to bees was acceptable at 30 metres away. For application in full leaf, the more likely usage, the risk was calculated as low at 30 metres away. It should be noted that the conditions from which these results were derived are those considered ideal to minimise spray drift – under more adverse conditions the spray drift could increase substantially and likewise the risk.

Soil invertebrates

Earthworms and other soil dwelling invertebrates could be exposed to the pesticide, and at an application rate of 1.5 kg ai/ha, the top 5 cm of soil would contain azinphos-methyl residues at 0.04 mg/kg of soil (assumes no crop cover, density of soil 1300 kg/m^3). This is significantly below the LD_{50} for worms and the NOEC but in the reproduction test, effects on earthworms were noted for an emulsifiable concentrate (EC) 200 formulation (20% ai) applied at 1 kg/ha, with a NOEC < 1 kg/ha. Some adverse effects on worm populations were noted in German field trials, but these were apparent at extremely high application rates (6 kg/ha direct to pasture).

Other soil arthropods may be significantly affected but as there are no toxicity data available for these organisms, the risk cannot be determined.

The toxicity data available for soil micro-organisms indicate the risk is likely to be low as soil-N metabolism was not affected. Some growth inhibition (4-18%) was noted for soil fungi at 2 and 10 ppm on paper discs but it is unclear as to how this relates to soil concentrations.

Aquatic organisms

Direct over spray
Direct application of azinphos-methyl to a body of water 15 cm deep at a rate of 1.5 kg ai/ha is calculated to give a concentration in the water of 1.0 mg/L. This concentration is likely to cause mortalities in the majority of fish species, daphnia and other aquatic insects/invertebrates, based on the tests reviewed. Application by orchard air blasters is unlikely to result in direct over-spray of waterbodies and therefore spray drift is considered as more realistic for Australian use patterns.

Spray drift
1st level assessment - 10% Spray drift onto pond.
Using the US EPA worst case assumption that 10% spray drift reaches water, this would result in a concentration of 100 µg/L for a shallow pond 15 cm deep (rate 1.5 kg/ha). This is above the LC_{50} for all fish tested and well above the EC_{50} for daphnia and mysid shrimp and indicates a risk to invertebrates. This concentration is also likely to be a significant risk to freshwater crayfish, with the US EPA review listing an EC_{50} for a crayfish species as 56 µg/L but there are no endpoints for Australian freshwater macro-crustacea.

Aerial application
Aerial application is not regarded as the normal practice for applying pesticides to orchards.

Ground based spraying

Orchard Air-Blast Spray Drift.
The Spray Drift Task Force, set up to undertake trials to measure the spray drift, including that from orchard spraying in several orchard crops: grapes, apples (foliated and dormant), oranges, grapefruits, almonds and pecans. Due to the limited number of applications made to any given crop, the results for crop/situation giving similar levels of drift were pooled into three groups: normal (grapes wrap-around sprayer, pome fruit and grapes with air blast), dense (citrus [airblast and mister] and nut trees and sparse (small trees and dormant trees).

Calculations using the AgDRIFT results, clearly showed that with ‘normal’ orchard spraying (pome and stone fruit trees with full foliage at up to 1.5 kg ai/ha) there is a limited risk to fish and daphnia in a 15 or 30 cm deep pond at 50 metres. However, using the salt water mysid shrimp, a surrogate for sensitive invertebrates, the risk in 15 or 30 cm deep water extends to beyond 100 metres. However, for other orchard trees such as macadamias and dormant spraying (or bud swell/green-tip) there is a high risk to all aquatic organisms at 100 metres from the orchards and beyond. Degradation of azinphos-methyl is expected to commence once spray drift reaches water, potentially reducing concentrations by of the order of 50% by

48 h after application. However, due to the acute nature of toxicity from azinphos-methyl, diminishing concentration due to degradation or adsorption to organic matter or other surfaces has not been considered as a mitigating factor.

The risk was also estimated using German studies that specifically trialled orchard airblast sprayers according to strict protocols and standard conditions to test spray drift in grapes, fruit crops and hops, at both early and later growth stages, under GAP. The multiple trials on fruit trees appear useful in comparison with equivalent Australian crops. Apart from Australian weather conditions, where air temperatures are likely higher and humidity lower, the results should be useful in estimating drift in orchard situations under typical usage.

Pome and stone fruit

The estimated spray drift for pome and stone fruit were calculated using the German results. Spray drift at 30-50 metres from these orchard resulted in significant acute risk to fish, daphnia and mysids in a 15 or 30 cm deep pond based on an azinphos-methyl application rate of 1.5 kg ai/ha. Where orchards are directly juxtaposed with natural watercourses, ie trees within 20-50 metres of water, these aquatic toxicities are likely to cause concern.

For inland irrigation areas the risk to aquatic animals was regarded as relatively low as orchard areas are usually some distance from rivers. In contrast, adequate separation of pome and stone fruit orchards (and spraying) from water courses is less likely to occur in older and cooler orchards. Ground-based sprayers no doubt frequently traverse within 10-50 m of the smaller watercourses that lead into the larger creeks and rivers.

In the major mesocosm study there were no detectable effects on aquatic invertebrates at a mean concentration of 0.95 μg/L (comparable to the 48 h EC50 of 1.1 μg/L used for daphnids in the above assessments), despite multiple applications. In contrast, the 3 other literature studies showed that at around 1.0 μg/L there were significant effects on cladocerans. In another study univariate analysis of littoral enclosures showed that cladocerans were affected at <1.0 μg/L. As the cladocerans and other organisms affected recovered after 5 weeks in all the studies to the levels in the controls, any sensitive invertebrates that are affected from spray drift are expected to recover. However, to minimise the risk from spray drift, a downwind buffer of 100 m is recommended. Program spraying could present an additional risk to aquatic organisms, as they may be unable to recover between spray events. However, this risk can be mitigated by limiting applications to no more than twice per production season.

Macadamias

The above analysis mainly focused on pome and stone fruits, the major use of azinphos-methyl. While azinphos-methyl is used in macadamias and represents approximately 10% of the entire active sold, it is not considered the principle insecticide for control of pests, with its use in macadamia orchard being more occasional. The AgDRIFT model included nut trees in the grouping “dense”, but Ganzelmeier does not have data specifically for nut trees.

Using AgDRIFT for dense trees at 2 kg ai/ha (4000 L/ha of spray at 49 g ai/100 L, large tree) calculations indicated a high risk to most aquatic organisms in a 15 or 30 cm deep pond beyond 200 m. However, in the regions where macadamias are grown, the streamside vegetation is expected to be luxuriant and should act as a buffer reducing the risk. Assuming that this vegetation captured between 70-80%, based on literature results for the situation in orchards, then the risk would be significantly reduced and at 100 metres the risk for fish and daphnia is marginal, though still very high for mysid. However, by limiting the application rates to no more than twice per production season, this risk can be satisfactorily mitigated.

Citrus
For citrus use, with very high applications volumes (6-8000 L/ha, 3-4 kg ai/ha) and scale as the principle targeted pest, the risk to aquatic invertebrates from spray drift is high, using AgDRIFT for dense foliage (the German studies did not include citrus). While it is recognised that AgDRIFT is worst case and that the use is infrequent, the use in citrus represents a high risk for aquatic invertebrates. As an impracticably high buffer would be required, and due to the greater risk from run-off at these application rates, it is recommended that use on citrus should be deleted from the label.

Other orchard crops
The other orchard crops on the labels are quinces and lychees. Quinces are a pome fruit and these have been extensively examined above. Lychees are a tropical fruit with the trees being dense and up to 10 metres in height. As this is somewhat similar to the macadamia nut trees above and grown in similar areas, a similar risk is likely.

Non-orchard crops
The other minor crops where azinphos-methyl is registered are grapes, kiwifruit and blueberries. Given that kiwifruit are vine crops, they will be considered with grapes. Assuming a volume of 1200 L/ha as a maximum for grapes and using the Ganzelmeier tables for grapes, calculations indicate that to protect aquatic organisms in a 15 or 30 cm deep pond, a buffer of at least 50 m is required. Hence the proposed 100 m buffer for other crops will be protective for use on grapes and other vine crops, and also for blueberries.

Other Spray Equipment
Orchardists are increasingly using spray equipment other than the high volume conventional sprayers, with low volume methods being the main alternative to the traditional sprayers. The LV equipment that is increasingly being employed has smaller droplet sizes. The spray drift from low volume applications to citrus orchards has previously been studied and modelled and the low volume spraying gives less drift than from high volume spraying close to the spray site but higher drift further away.

Risk to algae
Azinphos-methyl is rated as moderately toxic to algae (E_bC_{50} of 3.5 mg/L). As direct application to water is not expected and assuming 10% spray drift the concentration in shallow water is 100 µg/L, approximately an order of magnitude below the algae EC_{50}, effects on algae are unlikely.

Risk to amphibians
Azinphos-methyl is rated as moderately toxic to tree frogs and two species of salamanders with LC_{50}s of 1.47 and 1.9 mg/L. Using the same argument as above for algae, the risk from 10% spray drift is minimal.

Multiple applications
Information provided to the review indicates that current usage is limited, with application on pome and stone fruit being the principle uses but mainly as a clean-up spray to start IPM or when IPM system breaks down. In addition, the current pattern is of intermittent use in response to insect pressure rather than program spraying, although with high insect pressure multiple applications are more likely (under these conditions it is expected that alternative sprays would also be used to avoid insect resistance). The other major users of azinphos-methyl are macadamia growers, but again the use is relatively low. Other minor crops could

use azinphos-methyl as a mainline chemical. In contrast information provided to the review indicated that program spraying occurs in Queensland for pome fruit and very frequent applications (4-8 per season) in NSW for both pome and stone fruit.

Calculation showed that assuming a half-life in water of 2 days (from mesocosm studies) and 10 days between spray applications, then the carryover is approximately 3.1%, ie >95% dissipation has occurred. The mesocosm study clearly shows that even with just 7 days between each application, the concentration in the water column only increased slightly, if at all. There is unlikely to be a significant increase in concentration from multiple applications, even under worst-case conditions with a high level of multiple applications.

However, the main problem is repeated effects on organisms and 10 days between sprays may not allow affected populations to recover, especially if this is repeated for up to 14 times a season, as could occur with program spraying. With affected organisms needing 5 weeks to fully recover following a single application, program spraying using azinphos methyl represents a high risk and should be actively discouraged. Hence it is recommended that use be restricted to no more than two applications per production season.

Run-off

Calculations based on a simplistic model for run-off showed that was a very high hazard to aquatic organisms from run-off. While this analysis showed that there is potential for run-off to be problematical, most orchardists manage the inter-row area and limit erosion by such strategies as maintaining grass between rows, inter-row mulching and contour plantings. These factors reduce the risk of run-off occurring. In addition, the current use pattern in many situations reduces the frequency of use and therefore minimises the probability of run-off occurring.

While the above model analysis suggests that azinphos-methyl could cause significant contamination due to run-off from treated areas, there is no evidence for this in Australia. However, run-off has been a major cause of aquatic incidents with azinphos-methyl overseas. The US EPA indicates that azinphos-methyl has accounted for more aquatic incidents in their ecological incident database than any other pesticide, and there have been some major fish kills. These incidents were mainly associated with use on sugarcane and cotton crops, in areas where intense and frequent rainfall favoured run-off into nearby water. These uses were therefore prohibited or restricted in the USA. There have also been aquatic incidents associated with the use of azinphos-methyl in US orchard crops, but such incidents have been less common than for cotton and sugarcane, despite greater use on orchards. Reasons suggested for this included climatic differences affecting run-off likelihood, use of aerial application in field crops (hence greater spray drift risks), the presence beneath orchards of at least a partial sod to intercept run-off, and greater proximity to water with sugarcane and some cotton production areas.

Azinphos-methyl is not registered for use in cotton or sugarcane production in Australia. With other uses, there is a need for users to ensure that azinphos-methyl is not used if rain is expected, in order to reduce the risk of contamination of surface run-off. Hence a label statement restricting use if heavy rainfall is expected within 48 hours has been proposed. Restriction of use to once or twice per production season and not using azinphos-methyl at the high rates required for citrus will also minimise the risk from run-off.

Desirable terrestrial vegetation

Azinphos-methyl is known to be non-phytotoxic though russetting may occur on some on some fruits. There were no phytoxicity studies presented. Effects on non-target plants are expected to be minimal.

4.5 INTERNATIONAL REGULATORY STATUS

4.5.1 Joint FAO/WHO Meeting of Pesticide Residues (JMPR)

Azinphos-methyl has been reviewed by the Joint FAO/WHO Meeting of Pesticide Residues (JMPR) in 1965, 1968, 1973 and 1991. In 1965, the JMPR established an ADI for azinphos-methyl of 0.0025 mg/kg bw/d based on plasma ChE inhibition in a 17-week rat study. In 1968, the ADI was reaffirmed despite there being long-term studies (2 yr) in rats and dogs with lower NOELs (ie at 0.125 mg/kg bw/d).

The most recent review, in 1991, incorporating the change in JMPR policy to use inhibition of brain ChE (or RBC ChE inhibition as a surrogate) as the toxicologically-relevant endpoint, identified reduced ChE activity in the brain of parental animals together with reduced fertility in females and diminished pup viability at 15 ppm (1.3 mg/kg bw/d) in a 2-generation rat reproduction study. These results were confirmed in a subsequent 1-generation study with the NOEL being 5 ppm (0.43 mg/kg bw/d) (Holzum 1990). Hence, using a 100-fold safety factor, a new ADI was established at 0.005 mg/kg bw/d.

4.5.2 United States Environmental Protection Agency (USEPA) activity

The USEPA has reviewed azinphos-methyl as part of their review and re-registration process for all organophosphate insecticides. In their interim Re-registration Eligibility Decision, 30 uses are to be cancelled (little used or low benefits and alternative chemicals available). The crop groups were split into three groups with Group 1 having 23 uses that have already been cancelled. Group 2 consists of 7 uses are to be cancelled and phase out by September 2006, these include uses on caneberries, cotton, cranberries, peaches/nectarines, potatoes, and Southern pine seed orchards and with Group 3 comprised of the only 10 remaining uses which have time-limited registrations that are currently in the process of being re-evaluated.

4.5.3 Canadian Pest Management Regulatory Agency

The Canadian Pest Management Regulatory Agency (PMRA) has completed the re-assessment of azinphos-methyl and determined that due to unacceptable worker exposure all uses of azinphos-methyl are to be phased out. The decision and time frames to phase out uses in Canada are similar to the decisions reached for this chemical in the United States.

4.5.4 United Kingdom Department of Environment, Food and Rural Affairs

Azinphos-methyl is not registered in the United Kingdom.

4.5.5 European Union

The European Union is currently reviewing azinphos-methyl as part of its re-evaluation program under Council Directive (91/414/EEC). Azinphos-methyl is at stage 1 of the process with assessments ongoing.

5. SUMMARY OF PUBLIC SUBMISSIONS & CONCLUSIONS

Two submissions from the public were received for the review azinphos-methyl. The first submission, from the Childers and District Fruit and Vegetable Growers Association, stated that azinphos-methyl was the preferred chemical for control of Macadamia Nut Borer in Lychees, and voiced concern that the viability of individual farmers and associated employment opportunities within the district could depend upon the continued registration of azinphos-methyl. The second submission, from the Victorian Farmers Federation (Grains Group), indicated that azinphos-methyl use in the grain industry was limited, and no concerns regarding its continued registration status were raised.

6. PROPOSED REGULATORY OUTCOMES

On the basis of the evaluation of the submitted data and information, the following recommendations are made with regard to the continued approval of the active constituent azinphos-methyl, registration of azinphos-methyl products and label approvals in Australia.

6.1 AFFIRM APPROVALS OF THE ACTIVE CONSTITUENT

The APVMA is satisfied that, provided the conditions to which an approval is currently subject are complied with, the continued use of, or any other dealings with, the active constituent azinphos-methyl would not be likely to have an effect that is harmful to human beings. The APVMA recommends that active constituent approval listed in Table 9 be affirmed.

Table 9: Active constituent approval to be affirmed

Approval number	Approval holder
44081	Bayer CropScience Pty Ltd
44188	Makhteshim-Agan (Australia) Pty Limited

6.2 VARIATIONS TO PRODUCT REGISTRATIONS AND LABEL APPROVALS

6.2.1 Changes to containers

Based on the occupational health and safety assessment it is recommended that wide neck containers be used for packing the SC products, to minimise dermal exposure when pouring the concentrate.

6.2.2 Deletion of use patterns

The following uses are recommended to be deleted from approved labels based on residues and environmental concerns:

- Use on apricots
- Use on kiwi fruit
- Use on citrus

6.2.3 Withholding Periods (WHP)

Details of recommended withholding periods are listed below.

Blueberries

Available data indicated that the MRL for blueberries should be altered to 5 mg/kg, with a WHP of 7 days, reduced from the present WHP of 14 days.

Insert: **DO NOT** harvest for 7 days after application

Pome fruit

Retain: **DO NOT** harvest for 14 days after application

Stone fruit (except apricots)

Retain: **DO NOT** harvest for 14 days after application

Grape

Retain: **DO NOT** harvest for 14 days after application

Macadamia

Retain: **DO NOT** harvest for 7 days after application

Lychees

Retain: **DO NOT** harvest for 1 day after application

6.2.4 Restraint Statements

The environmental assessment has found that there are potential risk to the environment from the use of azinphos-methyl, to mitigate this risk the following restraint statements are recommended:

DO NOT apply aerially

DO NOT apply under meteorological conditions or from spray equipment that could be expected to cause spray drift onto natural streams, rivers or waterways.

DO NOT apply if heavy rain or storms are forecast with greater than 50% probability within 48 hours of application.

DO NOT apply more than two applications per production season.

DO NOT apply to deciduous trees between leaf fall and petal drop.

6.2.5 Re-entry periods

As a result of the occupational health and safety assessment, the following re-entry period statements are recommended to be added to labels.

Blueberry, macadamia, citrus, lychees, pome (apples, pears, quinces) and stone-fruit (peaches, nectarines, plums, cherries)

DO NOT allow entry into treated areas for 1 day after treatment. When prior entry is required wear rubber gloves and cotton overalls buttoned to the neck and wrist. Clothing and gloves must be washed after each day's use.

Grapes (except grape girdling and cane turning)

DO NOT allow entry into treated areas for 14 days after treatment. When prior entry is required wear rubber gloves and cotton overalls buttoned to the neck and wrist. Clothing and gloves must be washed after each day's use.

Grape girdling and cane turning

DO NOT allow entry into treated areas for 44 days after treatment. When prior entry is required wear rubber gloves and cotton overalls buttoned to the neck and wrist. Clothing and gloves must be washed after each day's use.

6.2.6 Protection of wildlife, fish, crustaceans and environment

The environmental assessment has found that there are potential risk to wildlife, fish, crustaceans and environment from the use of azinphos-methyl, to mitigate this risk the following statements are recommended:

Dangerous to fish and other aquatic organisms.

DO NOT allow spray drift on to aquatic area including natural streams, rivers or waterways.

DO NOT contaminate streams, rivers or waterways with the chemical or used containers.

DO NOT apply within 100 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers.

DO NOT apply in orchards or vineyards when the wind speed is less than 3 or more than 20 kilometers per hour as measured 15 meters outside of the orchard/vineyard on the upwind side.

DO NOT direct the spray above trees or vines during airblast applications.

TURN OFF outward pointing nozzles at row ends and outer rows during airblast applications.

Azinphos-methyl must not be allowed to contaminate waterways. Some of the labels do not contain adequate instructions with respect to rinsing and disposal of used containers, it is recommended that the following statement be added to all labels:

Triple rinse or pressure rinse empty containers before disposal or recycling. Add rinsings to the spray tank. Do not dispose of undiluted chemical on site. If recycling is not possible, break, crush or puncture and bury empty containers in a local authority landfill. If not available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose, clear of waterways, vegetation and roots. Empty containers and product should not be burnt.

For refillable containers the following should be added:

Empty contents fully into application equipment. Close all valves and return to point of supply for refill or storage.

6.2.7 Protection of Livestock

The environmental assessment has found that there are potential risk to bees from the use of azinphos-methyl, to mitigate this risk the following statement is recommended:

> Dangerous to bees. **DO NOT** spray any plants in flower, including ground covers and adjacent foliage. Spray drift is also highly toxic to bees.

6.2.8 Summaries of recommendations for continued uses

A summary of the recommended changes to use patterns as a result of proposed recommendations detailed in Sections 6.2.1 – 6.2.7 (above) is provided in Tables 10.

Table 10: Summary of proposed changes to use patterns

Crop	Pests	Proposed Recommendations
Apples	Codling moth, lightbrown apple moth, spring beetle, apple leaf hopper, bryobia mite, pear and cherry slug, woolly aphid, San Jose scale, oystershell scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use
Apricots	Oriental fruit moth, lightbrown apple moth, bryobia mite, pear and cherry slug, San Jose scale, root borer, curculio beetle, Fuller's rose weevil	**Delete from labels** Use exceeds the ARfD
Blueberries	Lightbrown apple moth	Retains Use
Cherries	Oriental fruit moth, lightbrown apple, moth, bryobia mite, pear and cherry slug	Retains Use
Citrus	Red scale, soft brown scale, black or olive scale, white wax scale, tortrix, aphids, yellow scale, lightbrown apple moth	**Delete from labels** High environmental exposure
Grapes	Grapevine scale, grapevine hawk moth, grapevine moth, fig longicorn, elephant weevil, lightbrown apple moth	Retains Use
Kiwi fruit	Scale insects, lightbrown apple moth	**Delete from labels** Insufficient data to set an MRL
Lychees	Macadamia nutborer, fruitspotting bug	Retains Use
Macadamias	Macadamia nutborer, fruitspotting bug	Retains Use
Nectarines	Oriental fruit moth, lightbrown apple moth, bryobia mite, pear and cherry slug, San Jose scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use
Peaches	Oriental fruit moth, lightbrown apple moth, bryobia mite, pear and cherry slug, San Jose scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use
Pears	Codling moth, lightbrown apple moth, spring beetle, apple leaf hopper, bryobia mite, pear and cherry slug, woolly aphid, San Jose scale, oystershell scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use
Plums	Oriental fruit moth, lightbrown apple moth, bryobia mite, pear and cherry slug, San Jose scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use
Quinces	Codling moth, lightbrown apple moth, spring beetle, apple leaf hopper, bryobia mite, pear and cherry slug, woolly aphid, San Jose scale, oystershell scale, root borer, curculio beetle, Fuller's rose weevil	Retains Use

6.3 AFFIRM REGISTRATION AND LABEL APPROVALS

Section 6.2 (above) identifies various changes to labels as an outcome of the review. These variations to label instructions would satisfy the requirements for continued registration of products identified in Table 11 and the APVMA recommends that these product registrations be affirmed.

Table 11: Azinphos-methyl products included in the review

Product number	Product name	Registrant	Label approval number
39216	Campbell Benthion 350 Flowable Insecticide	Colin Campbell (Chemicals) Pty Ltd	39216/1197
39427	Cotnion 350 Fl Insecticide	Makhteshim-Agan (Australia) Pty Limited	39427/0802
45727	Gusathion 200 SC Insecticide	Bayer Cropscience Pty Ltd	45727/0903

6.4 PROPOSED REGISTRATION AFFIRMATION AS AN OUTCOME OF REVIEW FINDINGS

One product Campbell Benthion 200 Flowable Insecticide (53215) was registered after the commencement of the review, however is subject to the outcomes of the review (NRA Gazette No.7, 2 July 2002, p. 27).

The proposed regulatory findings discussed in Section 6.2 (above) directly affect Campbell Benthion 200 Flowable Insecticide. If the variations to the label for Campbell Benthion 200 Flowable Insecticide (53215/0800) as listed in Section 6.2 are made this would satisfy the requirements for continued registration of product and the APVMA recommends that this product registration would be affirmed.

6.5 NON-CURRENT APPROVED LABELS

The non-current approved labels for currently registered products do not contain adequate instructions and are to be cancelled (see Table 12).

Table 12: Label approvals to be cancelled as not containing adequate instructions

Product number	Label approval number
45727	45727/01 45727/02 45727/1199 45727/0300

6.6 WITHDRAWN AZINPHOS-METHYL PRODUCTS

Four azinphos-methyl products (Table 13) have been voluntarily withdrawn since the commencement of the review (once cancellation of registration is formally effected, reconsideration is no longer required).

Table 13: Azinphos-methyl products included in the review that have been withdrawn prior to the completion of the review

Product number	Product name	Registrant	Label approval number
32860	Gusathion 350 Insecticide Spray	Bayer CropScience Pty Ltd	32860/01 32860/1199
45156	Campbell Benthion 500 WP Insecticide Spray	Campbell Chemicals Pty Ltd	45156/01
45230	Contnion methyl Azinphos Methyl Wettable Powder Insecticide	Makhteshim-Agan (Australia) Pty Limited	45230/02 45230/0200
48199	Farmoz Azinphos 500 Insecticide Spray	Farmoz Pty Limited	48199/01

7. CONSIDERATION OF STANDARDS

7.1 PUBLIC HEALTH STANDARDS

Arising from the OCS assessment of data submitted to the review of azinphos-methyl and the consideration of the expanded toxicological database, the following advice is provided by the OCS.

7.1.1 Acceptable Daily Intake (ADI)

The existing Australian ADI for azinphos-methyl is 0.001 mg/kg bw/d. Based on the results of a 28-day repeat-dose study conducted in humans a new ADI for azinphos-methyl of 0.025 mg/kg bw/d has been established. The new ADI of 0.025 mg/kg bw/d was established by applying a 10-fold safety factor to the NOEL of 0.25 mg/kg bw/d based on the absence of inhibition of plasma or red blood cell cholinesterase activities (or any other treatment-related effects) in males at this dose.

7.1.2 Acute Reference Dose (ARfD)

Arising from the assessment of the data submitted to the review, the OCS set an ARfD of 0.075 mg/kg bw/d is established by applying a 10-fold safety factor to the NOEL of 0.75 mg/kg bw/d based on the absence of plasma or red blood cell cholinesterase inhibition or any other treatment-related effects in females during a single-dose human study.

7.1.3 Water Quality Guidelines

It is recommended that the National Health and Medical Research Council (NHMRC) revise the current Health Value for azinphos-methyl in drinking water from 0.003 mg/L to 0.09 mg/L, this is based on the recommended a new ADI of 0.025 mg/kg bw/d.

7.1.4 Poisons Scheduling

The existing Schedule 7 entry for azinphos-methyl remains appropriate.

7.1.5 First Aid Instructions

No changes are recommended to the current First Aid Instructions for azinphos-methyl.

The following standard statements for azinphos-methyl (Table 14) are currently specified in the *Handbook of First Aid Instructions, Safety Directions, Warning Statements and General Safety Precautions for Agricultural and Veterinary Chemicals* (FAISD) (31 March 2006), http://www.health.gov.au/ocs/docs/pdf/faisd.pdf.

Table 14: Current First Aid Instructions for azinphos-methyl.

Code	*First Aid Instruction*
m	If swallowed, splashed on skin or in eyes, or inhaled, contact a Poisons Information Centre (Phone Australia 131 126) or a doctor at once. Remove any contaminated clothing and wash skin thoroughly. If swallowed, activated charcoal may be advised. Give atropine if instructed.

7.1.6 Safety Directions

The following safety directions for azinphos-methyl are currently specified in the, FAISD 31 March 2006, http://www.tga.gov.au/docs/pdf/faisd.pdf

The current safety directions (including PPE) for wettable powder (WP) or SC products containing less than 350 g/kg azinphos-methyl are as follows:

Azinphos-methyl WP 350 g/kg or less, SC 350 g/L or less	
Very dangerous, particularly the concentrate	100, 101
Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed	120, 121, 130, 131, 132, 133
May irritate the eyes and skin	161, 162, 164
Repeated exposure may cause allergic disorders	180
Repeated minor exposure may have a cumulative poisoning effect	190
Avoid contact with eyes and skin and clothing	210, 211, 212
Do not inhale dust (WP), vapour (SC) or spray mist	220, 221, 222, 223
When opening the container, preparing spray and using the prepared spray: wear cotton overalls buttoned to the neck and wrist and a washable hat, and elbow-length PVC gloves and full facepiece respirator [NB: comment, not for label: this category includes air-purifying respirator] with combined dust and gas cartridge	279, 280, 281, 282, 290, 292, 294, 301, 303
If clothing becomes contaminated with product or wet with spray remove clothing immediately	330, 331, 332
If product on skin, immediately wash area with soap and water	340, 342
After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water	350
After each day's use, wash gloves and respirator (and if rubber wash with detergent and warm water), and contaminated clothing	360, 361, 364, 366
Obtain an emergency supply of atropine tablets 0.6 mg	373

The recommended revised safety directions are summarised below. Only SC formulations are registered in Australia. As all azinphos-methyl products are in Schedule 7 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), the SD statement "very dangerous" duplicates the signal heading already contained on the product label and so can be deleted.

A previous quantitative OHS risk assessment has indicated that mixer/loaders handling SC products need to wear waterproof clothing over one layer of their own clothing, impervious footwear and elbow length PVC gloves. Eye protection should also be worn, given that the OCS toxicology review of azinphos-methyl concluded that SC products are expected to be slight to moderate eye irritants.

Based on the findings of the currently reviewed operator exposure studies, it is recommended that if workers are protected by a closed cab fully equipped with appropriate filters during application, their exposure will be acceptable if they wear overalls buttoned to the neck and wrist and normal enclosed footwear. However, applicators should also have access to gloves and waterproof clothing (similar to that for mixing/loading) to protect themselves if maintenance during application is required (eg. to clear a blocked spray nozzle). This should be located outside the cab but protected from contamination (ie. in a waterproof container).

Suitable wash equipment also needs to be available to wash the hands to minimise any subsequent contamination of the tractor cab.

Workers applying the product who are not protected with an enclosed cab should wear PPE comprise overalls, protective waterproof clothing including a hood or waterproof hat, elbow-length PVC gloves, respirator and water resistant footwear.

Therefore, the FAISD Handbook should be modified by amending the current entry for SC products containing 350 g/kg azinphos-methyl or less, as follows:

Azinphos-methyl SC 350 g/L or less	
Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed	120, 121, 130, 131, 132, 133
Will irritate the eyes and skin	161, 162, 164
May irritate the nose and throat	160, 163
Repeated exposure may cause allergic disorders	180
Repeated minor exposure may have a cumulative poisoning effect	190
Avoid contact with eyes and skin and clothing	210, 211, 212
Do not inhale vapour or spray mist	220, 222, 223
When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), protective waterproof clothing, elbow-length PVC gloves, water resistant footwear and face shield or goggles	279, 280, 281, 290, 292b, 291, 294, 298b, 299
When using the prepared spray (open cab), wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), protective waterproof clothing including a hood or waterproof hat**,** elbow-length PVC gloves, water resistant footwear and half facepiece respirator with combined dust and gas cartridge	279, 282 [open cab], 290, 291c*, 292b, 294, 298b, 300, 303
When using the prepared spray (closed cab fitted with charcoal filters), wear cotton overalls buttoned to the neck and wrists (or equivalent clothing).	279, 282 [closed cab fitted with charcoal filters], 290, 292b
If clothing becomes contaminated with product or wet with spray remove clothing immediately	330, 331, 332
If product on skin, immediately wash area with soap and water	340, 342
If product in eyes, wash it out immediately with water	340, 343
After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water	350
After each day’s use, wash gloves and respirator (and if rubber wash with detergent and warm water), face shield or goggles and contaminated clothing	360, 361, 364, 365, 366
Obtain an emergency supply of atropine tablets 0.6 mg	373

* Proposed new FAISD Handbook standard statement

The entries referring to WP formulations are to be deleted as they are no longer appropriate.

7.2 MRL STANDARDS

Arising from the assessment of data submitted to the review of azinphos-methyl, the following changes to the *MRL Standard* are to be made.

Table 1

Compound	Food			MRL (mg/kg)
Azinphos-methyl				
DELETE:	FB	0020	Blueberries	1
	FI	0341	Kiwifruit	2
	FB	0272	Raspberries, Red, Black	1
	FS	0012	Stone fruit	2
	SO	0088	Oilseed	*0.05
ADD:				
	FB	0020	Blueberries	5
	FS	0012	Stone fruit (except apricots)	2

Table 1

Compound	Food			MRL (mg/kg)
Azinphos-methyl				
RETAIN:	FC	0001	Citrus fruits	2
	MO	0105	Edible offal (mammalian)	*0.05
	FB	0269	Grapes	2
	FI	0343	Litchi	2
	TN	0669	Macadamia nuts	*0.01
	MM	0095	Meat [mammalian]	*0.05
	ML	0106	Milks	*0.05
	FP	0009	Pome fruits	2

Table 4

Compound	Animal feed commodity			MRL (mg/kg)
Azinphos-methyl				
ADD:	AB	0226	Apple pomace, dry	8
	AB	0269	Grape pomace, dry	3
			Citrus peel/rind	3

Appendix 1

Table A: Active Constituents included in the review

Approval Number	Active Name	Registrant
44081	Azinphos-methyl	Bayer CropScience Pty Ltd
44188	Azinphos-methyl	Makhteshim-Agan (Australia) Pty Ltd

Table B: Products included in the review

Product Number	Product Name	Registrant	Label approval numbers
39216	Campbell Benthion 350 Flowable Insecticide	Colin Campbell (Chemicals) Pty Ltd	39216/1197
39427	Cotnion 350 FL Insecticide	Makhteshim-Agan (Australia) Pty Ltd	39427/0802
45727	Gusathion 200 SC Insecticide	Bayer CropScience Pty Ltd	45727/02 45727/01 45727/1199 45727/0300 45727/0903

Table C: Products registered after the commencement of the review that are subject to the outcomes of the review

Product Number	Product Name	Registrant	Label approval number
53215	Campbell Benthion 200 Flowable Insecticide	Colin Campbell (Chemicals) Pty Ltd	53215/0800

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