Australian Government
Australian Pesticides and Veterinary Medicines Authority

AZINPHOS-METHYL
REVIEW FINDINGS REPORT

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

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FOREWORD

The Australian Pesticides and 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.

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

In undertaking reconsiderations (hereafter referred to as reviews), the APVMA works in close cooperation with advisory agencies including the Office of Chemical Safety and Environmental Health in the Department of Health and Ageing, the Department of Sustainability, Environment, Water, Population and Communities, 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 not use them for registration purposes unless they are also provided with the raw data from the relevant applicant.

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
- would not be likely to have an effect that is harmful to human beings
- would not be likely to 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.

This document, *Azinphos-methyl Review Findings Report: The reconsideration of the approvals of the active constituent azinphos-methyl, registration of products containing azinphos-methyl and their associated labels,* relates to all products containing azinphos-methyl.

The Review Findings, containing the APVMA's assessments (including the technical reports for all registrations and approvals relating to azinphos-methyl), is available from the 'Chemical Review Program' section of the APVMA website <http://www.apvma.gov.au/products/review/index.php>.

ACRONYMS AND ABBREVIATIONS

µg	microgram
ac	active constituent
ADI	Acceptable Daily Intake
ai	active ingredient
APGASA	Apple & Pear Growers Association of South Australia
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	Acute Reference Dose
bw	bodyweight
CDA	controlled droplet applicator
ChE	cholinesterase
cm	centimetre
Codex	FAO/WHO Codex Alimentarius Commission
d	day
DEEDI	Department of Employment, Economic Development and Innovation (Queensland)
DEF	*S, S, S*-tributylphosphorotrithioate
DSEWPaC	Department of Sustainability, Environment, Water, Population and Communities (Australian Government)
EC	emulsifiable concentrate
EC_{50}	concentration at which 50% of the test population are affected
EPA	Environment Protection Authority (Victoria)
EPN	*O*-ethyl *O*-4-nitrophenyl phenylphosphonothioate
FAISD	*Handbook of first aid instructions, safety directions and warning statements for agricultural and veterinary chemicals*
FAO	Food and Agriculture Organization
GAP	good agricultural practice
h	hour
ha	hectare
HAL	Horticulture Australia Ltd
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
iv	intravenous
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
LERAP	Local Environment Risk Assessment for Pesticides
LOQ	limit of quantitation

m	metre
MATC	maximum acceptable toxicant concentration
mg	milligram
mg/kg bw/day	mg/kg bodyweight/day
MIA	Murrumbidgee Irrigation Area
ml	millilitre
MOE	margin of exposure
MRL	maximum residue limit
NEDI	National Estimated Dietary Intake
NESTI	National Estimated Short-Term Intake
NOEC	No Observed Effect Concentration
NOEL	No Observable Effect Level
OCSEH	Office of Chemical Safety and Environmental Health
OECD	Organisation for Economic Co-operation and Development
OHS	occupational health and safety
OP	organophosphorus
PO	oral
PPE	personal protective equipment
ppm	parts per million
PRF	Preliminary Review Findings
SC	suspension concentrate
USA	United States of America
US EPA	United States Environmental Protection Agency
UV	ultraviolet
WHO	World Health Organization
WHP	withholding period
WP	wettable powder

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OVERVIEW

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has prepared a revised review findings report on the review of the active constituent azinphos-methyl and all products containing azinphos-methyl and their associated approved labels. This report superseded the review findings published in 2006.

Azinphos-methyl is an organophosphorus (OP) compound that is used as an insecticide, acaricide and molluscicide. At the start of this review, azinphos-methyl was registered in Australia for use on selected fruit and nut crops, including apples, apricots, blueberries, cherries, citrus, grapes, kiwifruit, lychees, macadamias, nectarines, peaches, pears, plums and quinces. Azinphos-methyl is non-systemic and, like all OP insecticides, exposure of biting and sucking insect pests to the compound (through contact, ingestion and/or inhalation) affects the nervous system by inhibiting the activity of acetylcholinesterase. Azinphos-methyl is currently registered in Cambodia and South Africa; use in Canada and the United States of America will be phased out by 2012, and use in New Zealand will be phased out by 2014.

In 1995 the APVMA began a review of the active constituent azinphos-methyl, product registrations containing azinphos-methyl and associated label approvals because of concerns relating to public health, occupational health and safety, residues and the environment. In 2006, the APVMA released the Preliminary Review Findings (PRF) report. The PRF proposed varying product labels and deleting some uses so that the continued use of azinphos-methyl would not pose an undue hazard to the safety of the public, occupational heath and safety, the environment and would not unduly prejudice Australian trade.

This document, entitled *Azinphos-methyl Review Findings Report, The reconsideration of the approvals of the active constituent azinphos-methyl, registration of products containing azinphos-methyl and their associated labels*, summarises the findings of the azinphos-methyl review. All public comments received since the release of the PRF documents (2006) were considered in the preparation of this report.

EXECUTIVE SUMMARY

Introduction

Azinphos-methyl is a broad-spectrum, non-systemic insecticide that has been registered for use in Australia for over 40 years. Like other organophosphorus (OP) insecticides, azinphos-methyl kills insects by interfering with the activity of an enzyme (acetylcholinesterase) in the nervous system.

In Australia, azinphos-methyl is mainly used in the horticultural industry for the control of codling moth and light brown apple moth on pome and stone fruit, citrus, macadamia nuts and grapes. Minor use of azinphos-methyl also occurs on crops such as lychees, kiwifruit and blueberries. As at July 2011, there was one azinphos-methyl active constituent approval and two registered azinphos-methyl products (Appendix A). All of the registered products are suspension concentrates and are only for use in commercial situations. Azinphos-methyl products are not registered for use in the home garden. Azinphos-methyl is currently registered in Cambodia and South Africa; use in Canada and the United States of America will be phased out by 2012., and use in New Zealand will be phased out by 2014.

The active constituent azinphos-methyl, product registrations containing azinphos-methyl and associated label approvals were placed under review in 1995 because of concerns about potential residues in food and trade, as well as worker and environmental exposure.

In 2006, the Australian Pesticides and Veterinary Medicines Authority (APVMA) released the Preliminary Review Findings (PRF) report. The PRF proposed varying product labels and deleting some uses so that the continued use of azinphos-methyl would not pose an undue hazard to the safety of the public, occupational health and safety, the environment and would not unduly prejudice Australian trade.

All public comments received since the release of the PRF document have been considered in the preparation of this report.

Review assessments

Active constituent azinphos-methyl

The chemistry evaluation found that the active constituent azinphos-methyl meets the required APVMA standard (Food and Agriculture Organization specification) for that active. The evaluation found that the method by which the active is manufactured, batch analysis results and analytical methods continue to acceptable.

Toxicological assessment

The toxicological assessment for the review of azinphos-methyl was undertaken by the Office of Chemical Safety and Environmental Health (OCSEH).

Azinphos-methyl is highly toxic to humans and animals. Poisoning can occur by oral ingestion, dermal absorption or inhaling the spray, although there is an effective antidote treatment for azinphos-methyl poisoning if medical assistance is prompt.

In mammals, azinphos-methyl is rapidly absorbed, metabolised and excreted, mainly in urine. Exposure to azinphos-methyl causes inhibition of cholinesterase activity and clinical signs consistent with other OP insecticides. Azinphos-methyl does not interact with genetic material. Long-term studies in animals give 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.

The findings of the toxicology evaluation were that existing product labels do not contain adequate instructions for the safe handling of existing products. It was recommended that the instructions be varied by including more safety directions and warning statements.

Public health standards

In considering dietary health standards, it was determined that the existing Acceptable Daily Intake (ADI) for azinphos-methyl of 0.001 mg/kg bw/day should be increased to 0.025 mg/kg bw/day, based on a 28-day repeat dose human study. In addition, prior to this review no Acute Reference Dose (ARfD) had been established for azinphos-methyl. An ARfD of 0.075 mg/kg bw/day was set by applying a 10-fold safety factor to a No Observable Effect Level (NOEL) of 0.75 mg/kg bw/day 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.

The National Drugs and Poisons Scheduling Committee (NDPSC) considered azinphos-methyl in 1971 and 1988 to establish azinphos-methyl as a Schedule 7 poison. The current assessment by the OCSEH confirmed that the current Schedule 7 entry for azinphos-methyl remains appropriate.

Occupational health and safety assessment

The occupational health and safety (OHS) assessment for the review of azinphos-methyl was undertaken by the OCSEH, which considered all the OHS data and information submitted for the review.

The APVMA considered the advice provided by the OCSEH and found that safety directions should be updated, and re-entry statements and precautionary statements should be included on product labels.

Residues assessment

The residue assessment for the review of azinphos-methyl was undertaken by the APVMA Pesticide Residues Section, which considered all the residue data and information submitted for the review.

The PRF published in 2006concluded that application of azinphos-methyl to apricots could not be supported as the acute dietary exposure calculations indicated an unacceptable risk to children. The PRF also identified that there were insufficient residue data for kiwifruit and that these uses could not be supported without additional residue data. However, after revision of the intake figures for whole stone fruit by the APVMA in 2007 (subsequent to the release of the PRF), the short-term exposure to azinphos-methyl from apricots was found to be below the Acute Reference Dose (ARfD) and it was concluded that the use of azinphos-methyl in **apricots could be supported**. In summary, the APVMA found that continued use of registered azinphos-methyl products on pome fruit (apples, pears, quinces), macadamias, stone fruit, citrus, blueberries, lychees and grapes would not be an undue hazard to the safety of people using anything containing its residues.

Environmental assessment

The environmental assessment for the review of azinphos-methyl was undertaken by the Department of Sustainability, Environment, Water, Population and Communities (DSEWPaC). DSEWPaC considered all the environmental data and information submitted for the review.

The APVMA considered the advice received from the DSEWPaC and found that the use of azinphos-methyl in citrus should be deleted from product labels, based on an unacceptable risk of spray drift to aquatic invertebrates. In addition, labels should to be varied to include restraint and protection statements to mitigate unintended effects that may be harmful to animals, plants or things, or to the environment.

Review findings

On the basis of the evaluation of the submitted data and information, the review findings for azinphos-methyl may be summarized as follows

(a) the active constituent approval can be affirmed (Appendix A, Table A1).

(b) voluntary label amendments (Appendix A, Table A2) can be approved by the APVMA to address the review findings as follows:

- Delete uses on kiwifruit and citrus.
- Add restraint statements to minimise the potential for spraydrift and/or runoff entering aquatic environments.
- Add a statement for the protection of wildlife, fish, crustaceans and the environment.
- Add a statement for the protection of bees.
- Amend the Withholding Period for blueberries.
- Amend re-entry periods.
- Amend Warning Statements and Safety Directions.

The concerns that were the basis for the review of azinphos-methyl have been addressed by the provision of amended label instructions. However, at the time of this report, azinphos-methyl has also been prioritised for spray drift review, which may affect the ongoing approval of azinphos-methyl and future registration of products containing azinphos-methyl.

Given the forthcoming removal of azinphos-methyl from use in many overseas countries (refer Section 5.5), the APVMA will examine overseas regulatory reports (in particular, the United States, Canada and more recently New Zealand) to determine if any of these reports contain information/studies that would cause the APVMA to doubt its satisfaction with the current regulatory status of this active. This work will need to be completed by September 2012 to ensure Australia has regard to the forthcoming change in regulatory status of azinphos-methyl in the United States, Canada and New Zealand. The result of this work will inform the APVMA's decision regarding the prioritisation of azinphos-methyl for the forthcoming spraydrift review.

1 INTRODUCTION

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is reviewing the approval of the active constituent azinphos-methyl, registered products containing azinphos-methyl and the associated label approvals for products containing azinphos-methyl. This document summarises the data evaluated and the findings of the review to date. This report superseded the PRF published in 2006.

1.1 Regulatory status of azinphos-methyl in Australia

Azinphos-methyl was first registered in Australia in the late 1960s and was commonly used as part of a broad-spectrum spraying strategy for the prevention and control of various insect pests of fruit, but has now generally been incorporated into integrated pest management (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).

Azinphos-methyl is a broad-spectrum, non-systemic organophosphorus insecticide (contact and stomach action). It affects the nervous system by inhibiting the activity of acetylcholinesterase, leading to the accumulation of acetylcholine at the neuron–neuron and neuron–muscle (neuromuscular) junctions or synapses.

As at July 2011, there was one active constituent approval for azinphos-methyl (Appendix A, Table A1), two registered products containing the active constituent azinphos-methyl and two registrants (Appendix A, Table A2). All product formulations of azinphos-methyl are suspension concentrates containing 200 g/L azinphos-methyl. One active constituent was cancelled and three azinphos-methyl products were stopped since the review began (Appendix A, Table A3). Information on the uses of azinphos-methyl products can be found in Chapter 2 of this document.

1.2 Reasons for azinphos-methyl review

A review of azinphos-methyl, all products containing azinphos-methyl, and their associated labels began in 1995 because of concerns over toxicological, occupational health and safety (OHS), environmental, residue and trade issues, in particular:

- the potential acute and chronic toxicity risk
- 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 of users during mixing and application of products.

1.3 Scope of the review

The extent of the review was scoped on the basis of the reasons for the nomination of azinphos-methyl, the information already available on this chemical and the approved uses of product containing azinphos-methyl in Australia.

The basis for a reconsideration of the registration and approvals for a chemical is whether the APVMA can be satisfied that the requirements prescribed by the Agvet Codes for continued registration and approval were being met. 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
- unduly prejudice trade or commerce between Australia and places outside Australia.

The APVMA conducted toxicological, OHS, residue and ecotoxicological assessments of azinphos-methyl.

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 public health, OHS, environmental and residue 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 approvals of the active constituent azinphos-methyl, registration of products containing azinphos-methyl and all associated 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 affirms 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 registrations and/or approvals.

2 APPROVED AZINPHOS-METHYL USE PATTERNS

2.1 Uses of azinphos-methyl products in Australia

Products containing azinphos-methyl are used on pome fruit and stone fruit, citrus, macadamia nuts and grapes; further minor use occurs on lychees, kiwifruit and blueberries (Table 1). The main use is for the control of codling moth and light brown apple moth, predominately in pome and stone fruit orchards. In Australia there are currently[1] two registered products containing azinphos-methyl; both are used in commercial situations.

The maximum use rates stated on the labels (tree butt and soil drench) correspond to 98 g ai/100 L, but most orchard rates correspond to 38–49 g ai/100 L.[2] Normal practice in orchards is to spray to run-off. Use in pome and stone fruit orchards accounts for about 80% of azinphos-methyl used; 10% is used on macadamias, with other registered crops accounting for the remaining 10%.[3]

1 As at the date of the preparation of this manuscript, that is, July 2011.

2 Actual use patterns reported by the Queensland Department of Primary Industries and Fisheries.

3 Estimated use of azinphos-methyl provided by industry.

Table 1: Approved uses of products containing azinphos-methyl

CROP	INSECT PEST SPECIES	RATE/100 L	APPLICATION METHODS	COMMENTS
Pome fruit (apples, pears, quinces)	Codling moth, light brown 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 woolly 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: 10 000 L/ha) Butt spray (using high-volume spray)	Apply as a full-cover spray at intervals of 2–3 weeks commencing with the emergence of the first codling moths in late October/early November.
	San Jose scale, oystershell scale	**200 SC**: 245 ml **350 SC**: 140 ml + summer oil 1.2 L		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**: 245 ml **350 SC**: 140 ml		Apply as a soil drench or all-over cover spray.
	Curculio beetle, Fuller's rose weevil	**200 SC**: 245–490 ml **350 SC**: 140–280 ml		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 3–4 weeks later.
Stone fruit (peaches, apricots, nectarines, plums)	Oriental fruit moth, light brown apple moth, bryobia mite, pear and cherry slug	**200 SC**: 245 ml **350 SC**: 140 ml	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 and 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**: 245 ml **350 SC**: 140 ml + winter oil 1.2 L		Apply at early budswell.
	Root borer	**200 SC**: 245 ml **350 SC**: 140 ml		Apply as a soil drench or all-over cover spray.

CROP	INSECT PEST SPECIES	RATE/100 L	APPLICATION METHODS	COMMENTS
Stone fruit (contd)	Curculio beetle, Fuller's rose weevil	**200 SC**: 245–490 ml **350 SC**: 140–280 ml		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 3–4 weeks later.
Blueberries	Light brown apple moth	**200 SC**: 245 ml	Applied using orchard airblast equipment applying approximately 300 L/ha spray mixture	Apply at 14-day intervals after flowering.
Cherries	Oriental fruit moth, light brown apple moth, bryobia mite	**200 SC**: 245 ml	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 and 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**: 245 ml		Apply as a full-cover spray when slugs appear in late November/early December. Repeat spray as necessary.
Citrus	Red scale, soft brown scale, black or olive scale, white wax scale, tortrix, aphids, yellow scale, light brown apple moth	**200 SC**: 245 ml **350 SC**: 140 ml + white or summer oil 1 L	Main methods of application are airblast, vertical booms and CDA.	Apply as a full-cover spray at intervals of 3–4 weeks in December and February.
Grapes	Grapevine scale	**200 SC**: 245 ml **350 SC**: 140 ml + 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**: 245 ml **350 SC**: 140 ml		Spray as required.
	Light brown apple moth	**200 SC**: 245 ml **350 SC**: 140 ml		Apply 3–4 weeks after flowering and later as required.

CROP	INSECT PEST SPECIES	RATE/100 L	APPLICATION METHODS	COMMENTS
Grapes (contd)	Fig longicorn, elephant weevil	**200 SC**: 245 ml		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, light brown 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 intervals while activity continues.
Lychees Macadamias	Macadamia nutborer, fruitspotting bug	**200 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 2–3 weekly schedule during the period when pests are normally active.

3 PUBLIC SUBMISSIONS

In response to the release of the Preliminary Review Findings (PRF) report in October 2006, the APVMA received six submissions from industry groups and state authorities about the proposed findings. The main areas of concern raised in these submissions were the recommendations to delete the application of azinphos-methyl to apricots, the need for a 100 metre (m) buffer zone and the proposed limitation to two sprays per season for all crops.

Deletion of apricots

Submissions from Horticulture Australia Ltd (HAL) and the Queensland Department of Employment, Economic Development and Innovation (DEEDI) raised concerns over the proposed deletion of the use of azinphos-methyl on apricots, based on an unacceptably high short-term dietary intake estimate. The PRF for azinphos-methyl reported that the highest acute dietary intake was estimated at 104% of the Acute Reference Dose (ArfD) for apricots in 2–6 year old children. This indicated that the acute dietary exposure of azinphos-methyl was not acceptable following azinphos-methyl use on apricots.

However, a reconsideration of the 2006 PRF acute dietary intake estimate by the APVMA’s Pesticide Residues Section subsequently found that the 97.5% consumption figures used in the calculation for the 2–6 years age group for apricots, peaches, nectarines and plums were not statistically valid. Less than 39 consumers were reported for those commodities for that age group and therefore a higher level consumption figure (i.e., for the whole stone fruit group) should be used in the estimate. Although this a conservative approach, in cases where there are too few consumers for any commodity the intake for a higher level group entry or the intake for another related commodity is used. This is the procedure agreed with Food Standards Australia New Zealand (FSANZ).

Upon revision of the calculation for children (2–6 years) using the intake figures for the whole stone fruit group, the exposures as a percentage of the ARfD were:

Apricots 68%; nectarines 81%; peaches 90%; plums 57%.

Thus short-term exposures for all commodities for which there were adequate data were below the ARfD.

There are no changes to the National Estimated Dietary Intake (NEDI), as the consumption figure for the whole stonefruit group was used in the calculation.

On the basis of the revised assessment it was found that the previous recommendation to delete the use of azinphos-methyl in apricots, citrus and kiwifruit (as published in the PRF) was invalid. The review finding has been amended to **deletion of the use in citrus and kiwifruit only**.

Restraint statements: DO NOT apply more than two applications per season

This recommendation from the PRF was derived from the environmental risks identified by the APVMA from multiple applications of azinphos-methyl. Submissions from HAL, DEEDI and the Apple & Pear Growers Association of South Australia (APGASA) raised concerns that the basis for the recommendation is the extent to which program spraying might occur. In addition, many pome fruit growers would normally rely on more than two azinphos-methyl sprays for codling moth control throughout the season.

The primary users of azinphos-methyl in horticulture are pome fruit and stone fruit producers, industries in which IPM is extensively practised. The submission from HAL explained that the use of azinphos-methyl is regional and is applied on an as-needs basis (i.e., program spraying no longer occurs) due to the uptake of IPM. In stone fruit azinphos-methyl is primarily applied for Oriental fruit moth (*Grapholita molesta*) or light brown apple moth (*Epiphyas postvittana*). For both of these pests a number of alternative treatments exist, such as pheromone-based mating disruption and the conventional insecticides indoxacarb, spinosad, thiacloprid and fenthion. As a result, the submission from HAL questioned the need to restrict use to no more than two applications, particularly as it is acknowledged in the PRF that there have been no reports of bird fatalities attributed to azinphos-methyl use in Australia.

In addition, HAL estimated that the azinphos-methyl use pattern in Australia would extend to no more than four applications, with treatment intervals of greater than 28 days, due to rotations with other insecticides. On this basis, HAL suggested that a more appropriate recommendation would be to limit the total number of applications to four per season.

Finally, HAL considered that, as the intervals between azinphos-methyl applications are likely to be 21–28 days and the number of treatments would be no more than four, which would occur in only one region, the probable environmental impact would be minimal. As the degradation of azinphos-methyl residues is relatively rapid, HAL believed that any potential effects on aquatic invertebrates would be slight and transient.

In response to these public submissions, the aquatic risk assessment was revised by the Department of Sustainability, Environment, Water, Population and Communities (DSEWPaC) to a minimum spray interval of 28 days, allowing more time for aquatic ecosystems to recover between spray events if they were affected by azinphos-methyl. This would also limit the number of sprays that may be applied per year, but should still be consistent with the use patterns indicated as current practice.

Thus, while frequent repeat spraying presents the greatest risk to birds, the limited use of azinphos-methyl in IPM programs and rotation with other insecticide groups when spray programs are used would minimise the risk to birds. This will be ensured by the minimum spray interval of 28 days for the protection of aquatic organisms.

Restraint statements: DO NOT apply to deciduous trees between leaf fall and petal drop

Submissions from HAL, APGASA and DEEDI raised concerns about the proposed restriction to prevent application between leaf fall and petal drop in deciduous trees. This restraint was proposed to minimise potential bee exposure to azinphos-methyl.

However, as indicated in the PRF, the majority of azinphos-methyl use is post-flowering in tree and vine crops. As a result, HAL argued that a more suitable restraint would be to limit cover spray applications to post-flowering only. This would have the added benefit of ensuring there would be no foliar residues with which foraging bees could come into contact.

The submission from APGASA did not consider that this statement is supported by the environmental assessment and therefore did not support its inclusion on labels.

Under the revised APVMA–DSEWPaC policy, a warning about the hazard to bees was provided as follows, rather than specific protective measures. This is to replace the previous ‘Protection of Livestock’ statement in the PRF or on current product labels:

> PROTECTION OF LIVESTOCK:
>
> Azinphos-methyl is dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift. Residues toxic to bees may remain for several days after application.

Furthermore, advice indicates that in deciduous crops azinphos-methyl is unlikely to be used until after petal drop. DSEWPaC also wished to avoid spraying at this time to reduce the risk to aquatic organisms, as spray drift is greater in trees with sparse foliage, but this has been reconsidered as rates are likely to be lower at this stage. Therefore, the proposed restraint statement preventing application to deciduous trees between leaf fall and petal drop is no longer considered a necessary additional protective measure for either bees or aquatic organisms.

Protection of wildlife, fish, crustaceans and the environment: DO NOT apply within 100 m of a downwind aquatic and wetland area including agricultural ponds or surface streams and rivers

Submissions from HAL raised a number of criticisms of the way in which the 100 m downwind buffer was arrived at (i.e., aquatic invertebrate toxicity, rate and frequency of azinphos-methyl use) and the level of protection sought. APGASA also criticised this buffer statement and noted it would be totally impractical in the Adelaide Hills region, where 85% of South Australia’s apple and pear production occurs. HAL also considered the buffer distance impractical and unnecessary, given the location of the majority of Australian pome and stone fruit orchards surrounded by forested areas, and suggested a 20–30 m buffer would be more appropriate.

HAL was specifically concerned about the use of the pond assessment model, the relevance of an estuarine/marine invertebrate (mysid shrimp) in the fresh water aquatic risk assessment and the LC_{50} value used for mysid shrimp. The submission from HAL suggested that other risk management options such as employing vegetative buffer zones of unsprayed crop rows or tree windbreaks should be contemplated, particularly as the use of windbreaks has been shown to significantly reduce drift from orchards by 70-90% (Van de Zande et al., 1999; Walklate, 1999).[4]

In response to the submissions received from HAL and APGASA, DSEWPaC modelled the amount of drift from orchard/airblast equipment using the AgDRIFT® model (Version 2.0.07, Tier I Orchard/Airblast), and supplemented this with evaluation according to the ‘Ganzelmeier tables’, consistent with APVMA policy. DSEWPaC revised the aquatic risk assessment (Section 3.4.4.4) to address the various matters raised, and also to consider a No Observed Effect Concentration (NOEC) end point based on mesocosm data. However, this did not result in any change to the recommended 100 m spray drift buffer distance for pome and stone fruits. Specific criticisms and DSEWPaC’s response to each are as follows:

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4 Van de Zande et al., 1999. Drift measurements in the Netherlands as a basis for differentiation of risk mitigation measures.

Walklate, JP, 1999. Drift reduction by vegetation. In Workshop on Risk Assessment and Risk Mitigation Measures, Sept 1999. Federal Biological Research Centre for Agriculture and Forestry, Biology Division, Braunschweig, Germany.

- Protection of ‘agricultural ponds’ would extend to farm water storages and dams, which is not warranted: DSEWPaC notes that the proposed drift warning statement referred to by HAL in fact refers to ‘aquacultural’ ponds (i.e., ponds used to produce fish or crustaceans). Aquacultural (as opposed to ‘agricultural’) ponds clearly do need to be protected, although for economic reasons rather than environmental. DSEWPaC’s purpose in this statement is to protect aquatic organisms in natural streams, ponds and wetlands, not necessarily to protect on-farm storages or irrigation channels.
- The use of shallow, fixed ponds in modelling spray drift: This is standard practice by DSEWPaC as a generally applicable, worst case situation. Mitigation for greater water depth (30 cm rather than 15 cm) was considered. Consideration of stream contamination does not result in a greatly different concentration as the effect of drift onto a stream is to produce a pulse of contaminated water moving downstream, rather than continuing dilution in the entire stream, and it cannot be assumed that orchards do not occur in the vicinity of fixed ponds.
- The use and relevance of mysid shrimp (an estuarine/marine organism) and value of 0.12 µg ac/L value used by DSEWPaC in its assessment, noting that the US Environmental Protection Agency (US EPA) preliminary risk assessment used a higher LC_{50} level of 0.21 µg ac/L: DSEWPaC acknowledged that mysid shrimp is an estuarine/marine species, but considered mysid shrimp to be a surrogate for sensitive freshwater invertebrates such as the Australian freshwater species *Paretya*. There are three values available for mysid shrimp (0.12, 0.22 and 0.23 µg ac/L), and also a result available from the US EPA assessment report for azinphos-methyl for the freshwater amphipod *Gammarus fasciatus* (0.16 and 0.25 µg ac/L), which shows similar sensitivity to mysid shrimp. DSEWPaC revised the aquatic risk assessment to use a value of 0.16 µg ac/L (as also used by the US EPA) to represent these most sensitive aquatic species.
- The formulated product was shown to be appreciably less toxic to daphnids than the technical material: DSEWPaC followed its standard practice in using the most sensitive end points available for the active constituent and noted that the EC_{50} value for the formulation expressed as active constituent was similar to that from the active constituent study itself (1.1–2.9 µg ac/L).
- The rate of 1.5 kg ac/ha used as the basis for calculating pome and stone fruit risks was a little higher than the 0.98–1.225 kg ac/ha in more common use, and suggested the possibility of capping the rate per hectare to that actually being used. The lower typical rate was noted as a further mitigating factor in the risk assessment, but did not significantly affect the buffer recommendation.
- Measures such as vegetated buffers of unsprayed crop rows or tree windbreaks should be contemplated, and a more flexible approach considered, such as the Local Environment Risk Assessment for Pesticides (LERAP) classification system used in the United Kingdom: DSEWPaC is aware of the LERAP approach of adjusting buffer widths according to the presence or absence of a windbreak, type of sprayer used and rate to be applied, but this would need to be adopted by the Australian regulatory system after they have been adjusted for Australian conditions and equipment. In the absence of such a well-described and managed process, interception by natural vegetation or planted windbreaks cannot be relied upon as generally protective measures because of the wide variability in individual situations (including the location and nature of vegetation).

In addition, a wider no-spray zone was recommended for macadamias by DSEWPaC as follows:

> For crops other than macadamias, DO NOT apply within 100 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers. For macadamias, DO NOT apply within 200 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers.

DSEWPaC revised the assessment of the risk from spray drift with use on macadamias in recognition that interception of drift by windbreaks or streamside vegetation cannot be relied upon as generally applicable protective measures, as there are too many variables and uncertainties involved. Allowance had been made in the 2006 PRF for azinphos-methyl for capture of 75% of drift by such vegetation, and this made a 100 m buffer acceptable. Removal of this means of mitigation has led to an increase in the required buffer to 200 m, due to the higher application rate and greater drift potential expected for macadamias as a dense orchard tree.

Economic significance of the light brown apple moth

A submission from the APGASA raised concerns over the light brown apple moth as an increasing pest in South Australia's apple-growing regions. APGASA also reported that the incidence of the light brown apple moth was also increasing in other growing regions in Australia, suggesting that of the reasons may be that, as growers move to more IPM as a means of controlling pests like codling moth, some of the 'secondary' pests become more predominant; the light brown apple moth appears to be one of those 'secondary' pests. APGASA reported that, according to Australia's trading partners, the light brown apple moth was a pest of increasing concern and argued that any loss and/or reduction in the use of azinphos-methyl would be most detrimental to production and potential trade.

Re-entry periods

A submission by DEEDI expressed concerns over potentially confusing re-entry periods proposed in the PRF for azinphos-methyl. The re-entry period on labels was considered confusing because it sought to include both the risks associated with re-entering a crop and risks from occupationally handling treated produce. A separate re-entry and re-handling period statement was suggested by DEEDI in order to alleviate this confusion.

The OCSEH considered the concerns expressed by the DEEDI submission; however, these issues were debated previously. As a result, the re-entry periods outlined in the PRF for azinphos-methyl were considered to be appropriate by the OCSEH and the APVMA.

International action

A submission received from the Environment Protection Authority (EPA) Victoria expressed concerns over the APVMA's intention to mitigate environmental risk associated with azinphos-methyl by adding restraint and protection statements to the label. The EPA Victoria submission expressed concerns that review outcomes in the United States of America (USA) and Canada have resulted in azinphos-methyl being phased out, in part because of environmental concerns. Controlling risk through label statements was considered in those reviews and found to be inadequate. In addition, the EPA Victoria called for environmental monitoring studies to be conducted to determine the effectiveness of label controls.

DSEWPaC assessed the available environmental fate and ecotoxicity data based on the uses of azinphos-methyl in Australia, and proposed various measures to reduce the risk to the environment. This has resulted in the recommended label advice being similar to or more demanding than those on previously approved on US product labels.

In addition, EPA Victoria indicated that a joint study conducted by Goulburn–Murray Water and the Victorian government detected azinphos-methyl in water samples collected from irrigation channels at a number of sites. While the level of contamination of irrigation channels was not necessarily a concern, EPA Victoria commented that the results demonstrated that significant contamination of the environment may be occurring.

DSEWPaC has since obtained the report referred to by EPA Victoria and concluded that the contamination most likely resulted from spray drift to channels close to sprayed orchards but did not indicate contamination of waters where the protection of aquatic organisms is needed. Concentrations detected were at trace levels, with the exception of one spot sample in an irrigation channel.

DSEWPaC agrees that azinphos-methyl is an appropriate chemical for inclusion when monitoring programs are conducted in areas such as the Goulburn–Murray Valley, where it is used extensively. However, if the environment recommendations from DSEWPaC are followed, contamination of the environment would not be likely to pose an unacceptable risk.

3.1 Regulatory responses to submissions

In response to the public submissions received, the following regulatory outcomes were recommended:

- On the basis of the revised assessment by the APVMA Chemistry and Residue Program, it was concluded that the previous recommendation to delete the use of azinphos-methyl in apricots, citrus and kiwifruit, as published in the PRF, should be amended to **deletion of the use on citrus and kiwifruit only**.
- The recommendation from DSEWPaC's aquatic risk assessment was revised from a maximum of 2 sprays per year to a **minimum spray interval of 28 days**. This was to allow more time for aquatic ecosystems to recover between spray events if they are affected by azinphos-methyl and to minimise the risk to birds. Further, this restriction is considered to be consistent with current practice.
- On the basis of a revised assessment by DSEWPaC, the restraint 'DO NOT apply to deciduous tress between leaf fall and petal drop' was replaced with the following recommended restraint to minimise potential bee exposure to azinphos-methyl:

  PROTECTION OF LIVESTOCK:

  Azinphos-methyl is dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift. Residues toxic to bees may remain for several days after application.

- On the basis of a revised assessment by DSEWPaC, the buffer warning statement under 'Protection of wildlife, fish, crustaceans and environment' was amended to indicate a greater buffer distance for macadamias as follows:

> For crops other than macadamias, DO NOT apply within 100 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers. For macadamias, DO NOT apply within 200 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers.

DSEWPaC revised the assessment of the risk from spray drift arising from use on macadamias in recognition that interception of drift by windbreaks or streamside vegetation cannot be relied upon as generally applicable protective measures, on the grounds that there are too many variables and uncertainties involved. Allowance had been made in the 2006 PRF for azinphos-methyl for capture of 75% of drift by such vegetation, and this made a 100 m buffer acceptable. Removal of this means of mitigation has led to an increase in the required buffer to 200 m, due to the higher application rate and greater drift potential expected for macadamias as a dense orchard tree.

- On the basis of a revised assessment by OCSEH, concerns over potentially confusing re-entry periods proposed in the PRF for azinphos-methyl were considered; however, these issues have been debated previously. As a result, there was **no change to the re-entry** periods outlined in the PRF for azinphos-methyl; they were considered to be appropriate by the OCSEH and the APVMA.

4 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 on the following page.

Henry's Law constant

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

Summary of physico-chemical data

Azinphos-methyl is moderately soluble in water and highly soluble in organic solvents. It has a moderate partition coefficient and moderate binding to sediment or soil is expected. It is slightly volatile but has low volatility from water.

4.1 Composition of azinphos-methyl active constituent

FAO Specification

The Food and Agriculture Organization (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.

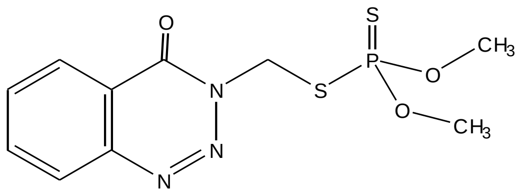
Azinphos-methyl content:		not less than 870 g/kg
Impurities:	Water	2 g/kg maximum
	Acetone insoluble	5 g/kg maximum

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 approved source of technical azinphos-methyl from Makhteshim Agan (Australia) Pty Ltd meets the Australian requirements.

4.2 Chemistry identity

Table 2: Chemical identity

Common name	Azinphos-methyl
Developmental codes	Bayer 17 147; R1582; E1582
Chemical name	*S*-(3,4-dihydro-4-oxobenzo[*d*]-[1,2,3]-triazin-3-ylmethyl) *O*,*O*-dimethyl phosphorodithioate (IUPAC) *O*,*O*-dimethyl *S*-[(4-oxo-1,2,3-benzotriazin-3(4*H*)-yl)methyl] phosphorodithioate
CAS number	86-50-0
Molecular formula	$C_{10}H_{12}N_3O_3PS_2$
Molecular weight	317.33 g/mol
Chemical structure	

4.3 Physical and chemical properties

Table 3: Physical and chemical properties of the active constituent

Physical state	Yellowish crystals
Colour	Colourless
Odour	AC described as mercaptan-like
Melting point	72.4 °C
Density/specific gravity	1.518 g/cm^3 (21 °C)
Solubility in water	33 mg/L (20 °C)
Solubility in other solvents (20 °C)	In dichloroethane, acetone, acetonitrile, ethyl acetate, dimethyl sulfoxide >250 g/L In n-hetptane 1.2 g/L In xylene 170 g/L
Octanol/water partition coefficient	Log P_{ow} = 2.96
Vapour pressure	1.8 x 10^{-4} Pa @ 20 °C 5 x 10^{-4} mPa @ 20 °C (Tomlin, 1997) 1 x 10^{-3} mPa @ 25 °C (Tomlin, 1997)
Stability	Rapidly hydrolysed in alkaline and acidic media; DT50 (22 °C), 87 d (pH 4), 50 d (pH 7), 4 d (pH 9). Photodegrades on soil surfaces and readily photodegrades in water. Decomposes above 200 °C.
Impurities	Phosphorodithioic acid O,O,S-trimethyl ester 1,2,3-benzotriazin-4-(3H)-one Phosphorodithioic acid O,S-dimethyl S[(4-oxo-1,2,3-benzotriazin-3(4H)yl)methyl]ester 3,3’-bis[4-oxo-1,2,3-benzotriazin-3(4H)-yl]([methylene] 1,2,3-benzotriazin-4-(3H)-one,3-3’-dithiobis (methylene) bis 1,2,3-benzotriazin-4-(3H)-one,3-3’-(thiomethyl)bis Water Chloride (as sodium chloride)
Henry’s constant	1.73 x 10^{-3} atm m^3/mol (calculated) 5.70 x 10^{-6} Pa m^3/mol (Tomlin, 1997) 3.66 x 10^{-9} m^3/mol (US EPA, 1999)

5 SUMMARY OF DATA ASSESSMENTS

The following provides a summary of the data assessments for azinphos-methyl (refer to Volumes 2 and 3, published 2006, and the OHS supplementary report, published 2011).

5.1 Toxicology

Introduction

The toxicological assessment for the review of azinphos-methyl was undertaken by the OCSEH. The OCSEH considered all the toxicological data and information submitted for the review. The toxicological findings are summarised overleaf. These are unchanged from the 2006 PRF for azinphos-methyl.

Public health aspects

Azinphos-methyl is an organophosphorus (OP) pesticide. Like other OP pesticides, 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 OP pesticides 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 OP pesticides. 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.

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; 1 h 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/day)	0.25 (28-d human study)
Lowest relevant dermal NOEL (mg/kg bw/day)	2.0 (3-wk rabbit study)
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/day)	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/day)	1.2 (rats)

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

Summary

	NOEL (MG/KG BW/DAY)	STUDY	SAFETY FACTOR
Previous ADI (0.001 mg/kg bw/day) [Plasma ChE inhibition]	0.125	2-y feeding dog	100
New ADI (0.025 mg/kg bw/day) [Plasma ChE inhibition]	0.25	28-d repeat-dose human	10
ARfD	0.075 mg/kg bw/day		

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, that 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.

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 human volunteer study, the dermal absorption of a single dose of azinphos-methyl in was approximately 22–29%. 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.

Acute studies

Azinphos-methyl was highly acutely toxic and its profile of clinical signs was consistent with other OP pesticides. 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 and 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 over 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 the 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).

Short-term and intermediate 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/day), 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/day, 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/day. 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/day. At 3.44 mg/kg bw/day, 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 tested (lowest dose of 0.5 mg/kg bw/day). The general condition of the animals was impaired at 1.25 mg/kg bw/day and above, with cholinergic signs seen at and above 2.5 mg/kg bw/day. Doses of 1.25 mg/kg bw/day and above caused weight loss, and at 10 mg/kg bw/day dogs frequently refused to eat. At 10 mg/kg bw/day, one dog (female) died after 9 weeks.

Long-term studies

As with other OP pesticides, the typical toxicological effects of azinphos-methyl seen in 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/day 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.

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. An increased incidence of supernumerary ribs and some retarded ossification were seen in a single rat study at an apparently non-maternally toxic dose (3.6 mg/kg bw/day) 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/day 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.

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.

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.

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/day. 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 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.

Bystander exposure

Issues relating to bystander exposure, especially for households adjacent to orchards, were not specifically considered in the PRF for azinphos-methyl in 2006. Prior to the finalisation of the review of azinphos-methyl and the release of the final review findings, the APVMA Board made the decision to request an assessment of bystander exposure to azinphos-methyl. However, at the time of this report the APVMA and the OCSEH are developing spray drift guidelines, which also consider bystander exposure. The outcomes from this assessment will be released with the finalisation of the spraydrift review. To expedite the current regulatory outcomes of the azinphos-methyl review, the review findings has been released ahead of consideration of bystander exposure.

Conclusion

Based on an assessment of the toxicology, it is considered that there are unlikely to be harmful effects to human beings from the continued registration of products containing azinphos-methyl if used in accordance with label instructions.

5.2 Occupational health and safety

Azinphos-methyl products are applied by mechanised sprayers (airblast, 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.

An initial OHS assessment of azinphos-methyl by OCSEH in January 2005 concluded that the use of currently registered azinphos-methyl products may pose an unacceptable risk to worker safety during mixing, loading and application. In addition, post-application exposure data showed that despite wearing gloves, hand harvesters of fruit had unacceptable levels of plasma and red blood cell cholinesterase (ChE) inhibition. As a result, additional studies were provided to the APVMA by industry and were assessed by OCSEH in November 2005.

Biomonitoring and dislodgeable foliar residue 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 OCSEH, 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 the 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 was 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 MOEs for each Australian use scenario (eight in all). As a human toxicity end point was used, MOEs 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.

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 conventional PPE of cotton overalls and gloves. However, for mixers and loaders, suitable MOEs were attained when waterproof clothing and footwear were 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), provided acceptable MOEs. No other modes of application, such as a hand-held apparatus, were 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 nut, citrus, pome fruit and stone fruit crops were assessed as acceptable. Re-entry intervals were set at one day for these crops. However, a relatively prolonged re-entry interval of 14 days has been recommended for kiwifruit 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 patterns, foliar residues or worker exposure became available.

After the release of the PRF for azinphos-methyl, a submission was received from DEEDI which expressed concerns over potentially confusing re-entry periods proposed in the PRF for azinphos-methyl (refer Chapter 3). The OCSEH considered the concerns expressed by the DEEDI submission however the re-entry periods outlined in the PRF for azinphos-methyl were considered to be appropriate by the OCSEH and the APVMA.

5.3 Residues and trade

The residues aspects of the use of azinphos-methyl on crops were reviewed by the APVMA Residues Program which examined metabolism, analytical methods and residues data. This 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 in support of the establishment of maximum residue limits (MRLs) was also included. Recent data reviewed by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) were incorporated into the assessment where relevant.

Residues evaluation

Metabolism

Metabolism data for plants, and 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 from 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.

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 4.

Table 4: 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 the 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.

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.

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 5.

Table 5: Residues of azinphos-methyl in fruit commodities at the withholding period

COMMODITY	APPLICATION RATE (KG AI/100L)	WHP (DAYS)	RETREATMENT INTERVAL (DAYS)	AZINPHOS-METHYL RESIDUES (MG/KG)	
				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	?
Blueberries	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 peaches and blueberries. For peaches, a maximum residue of 2.6 mg/kg occurred in fruit in one trial and an increase of the MRL to 5 mg/kg will be required. For blueberries, an increase in the MRL from 1 mg/kg to 5 mg/kg will be required, due to the uncertainty of the available data.

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.

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 pulp/dry	3 mg/kg

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.

Dietary risk assessment

The following health standards (Table 6) were recommended by the OCSEH.

Table 6: Health standards for azinphos-methyl

COMPOUND	DIETARY STANDARD MG/KG BW		NO OBSERVABLE EFFECT LEVEL (NOEL), MG/KG BW	SAFETY FACTOR	REFERENCE (OSCEH/ JMPR DATE)
Azinphos-methyl	ADI[5]	0.025	0.25	10	28.02.05
	ARfD[6]	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.

Chronic dietary exposure assessment

The chronic dietary exposure to azinphos-methyl was 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 was made in accordance with international guidelines[7] 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 was concluded that the chronic dietary exposure of azinphos-methyl is acceptable.

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[8], 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 7.

The PRF for azinphos-methyl concluded that the highest acute dietary intake was estimated at 104% of the ARfD for apricots in 2–6 year old children. This demonstrated that the acute dietary exposure of azinphos-methyl was not acceptable for apricots. All other acute exposures were considered to be acceptable. However, following a submission from HAL requesting reconsideration of this estimate, the APVMA's Pesticide Residues Section found the short-term dietary estimates used in the 2006 PRF were not statistically significant. Upon revision of the calculation for children (2–6 years) using the intake figures for the whole stonefruit group, the short-term exposures for all commodities (including apricots) were found to be below the ARfD and therefore acceptable. Changes to the NESTI estimates are bolded in Table 7.

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5 http://www.tga.gov.au/docs/pdf/adi.pdf

6 http://www.tga.gov.au/docs/pdf/arfd.pdf

7 Food and Agriculture Organization of the United Nations, 2002. Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. Rome: FAO.

8 World Health Organization & Food and Agriculture Organization of the United Nations, 2008. Dietary exposure assessment of chemicals in food: report of a joint FAO/WHO consultation. Annapolis, Maryland, USA, 2–6 May 2005. Geneva: WHO.

Table 7: 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	12.6	MM 0095	Meat [mammalian]	0.5	0.9
FC004	Oranges, raw (including peel)	9.8	31.6	ML 0106	Milks	2.0	5.1
FC 0203	Grapefruit (raw)	9.5	0.0	FP 0226	Apples, raw, unpeeled	14.8	45.2
FC 0204	Lemons, raw (including peel)	2.5	0.0	FP 0230	Pears, raw, unpeeled	16.1	60.7
FC 0206	Mandarins, raw	10.1	36.0	FS 0240	Apricots, raw	25.2	**67.6**
MO 0105	Edible offal (mammalian)	0.2	0.1	FS 0245	Nectarines, raw, unpeeled	34.0	**80.7**
FB 0269	Grapes	7.9	18.5	FS 0247	Peaches, raw, unpeeled	36.7	**90.4**
FI 0341	Kiwifruit	14.9	10.7	FS 0248	Plums, raw	21.3	**56.7**
FI 0343	Litchis	3.9	12.6	FS 0244	Cherries, raw	7.0	24.6
TN 0669	Macadamia nuts	0.0	0.0				

Residue-related aspects of trade

Blueberries, kiwifruit, lychees (*Litchi*) and macadamia nuts are not major export commodities[9] 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 and stakeholders should become aware of any potential trade risks to their industry.

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.

Destination and value of exports

The three largest export markets for individual commodities by value for the season 2002–2003 are shown in Table 8 (*The Australian Horticultural Statistics Handbook 2004*).

9 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>.

Table 8: Export markets for individual commodities by value for the season 2002-2003

COMMODITY	DESTINATIONS	VALUE, $ MILLION
Apples	United Kingdom, 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, United Arab Emirates	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

Comparison of Australian MRLs with 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 established for azinphos-methyl are in Table 9.

Table 9: Comparison of overseas MRLs and tolerances that have been established

COMMODITY	TOLERANCE, MG/KG			
	AUSTRALIA	TAIWAN	CODEX	EU
Apples	2	2	2	0.5
Pears	2	2	2	0.5
Apricots	2	2	1	0.5
Cherries	2	2	2	0.5
Nectarines	2	2	2	0.5
Peaches	2	2	2	0.5
Plums	2	2	2	0.5
Oranges	2	2	1	1
Lemons	2	2	1	1
Grapes	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. This ensures 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 occurring in animal feeds (6.4 ppm) are well below this, so that there should be compliance with the MRLs for animal tissues.

Potential risk to trade

Export of treated produce containing measurable residues of azinphos-methyl may pose a risk to Australian trade in situations where:

1. no residue tolerance (import tolerance) is established in the importing country, or
2. where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

Australian MRLs are similar to 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 generated by the National Residues Survey[10], there have been no reported violations of the MRL.

Conclusions

The APVMA has assessed that there is no undue hazard to the health of consumers, **except** potentially from treated kiwifruit, for which insufficient data were available to support ongoing use. Prior to the release of these review findings, the PRF stated that apricots, citrus and kiwifruit could not be supported. However, a revision of the acute dietary exposure of azinphos-methyl was completed by the APVMA in 2007 using the intake figures for the whole stone fruit group. It was found that the short-term exposures for all commodities (including apricots) were found to be below the ARfD and therefore acceptable. 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.

In conclusion, it has been assessed that there is unlikely to be any 'undue' risk to Australia's trade from the uses of azinphos-methyl supported by this review.

10 Current to June 2004.

5.4 Environment

Environmental fate and degradation

Hydrolysis

Azinphos-methyl was 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 at pH 4; ~23–25 days at pH 7; ~2–2.5 days at 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.

Photolysis

AQUATIC

Based on five studies using artificial light and sunlight, photodegradation 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 to 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 AND PLANTS

Based on two soil photolysis studies using natural sunlight, the net half-life of photodegradation 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 ultraviolet (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.

Metabolism in soils

A range of soil metabolism studies were performed using several soil types (two acceptable and seven supportive studies). It was 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 and pH.

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.

Mobility in soil

SOIL ADSORPTION AND DESORPTION

The soil adsorption and desorption of azinphos-methyl was determined in two acceptable studies using seven 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 ageing, around 10% of applied radioactivity appeared in leachate, mainly degradation products. Soil R_f values were determined on thin layer chromatography 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.

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 in 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 is 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 USA.

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 two 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 and 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 sugarcane 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 show that, in the 5133 samples taken, some 164 (3.2%) contained detectable levels of azinphos-methyl, four 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 New South Wales rivers programs.

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.

Environmental effects

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}s of 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 and 1940 ppm for four species. The bobwhite quail was the most sensitive. Two 21-week single-generation reproduction studies were presented for bobwhite quails and mallard ducks, and the NOELs were 15.6 and 10.5 ppm respectively.

Field surveys in 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 among small mammals.

While literature reports on field studies in Canada using nesting birds in orchards showed there were effects on brain and plasma cholinesterase after two applications of azinphos-methyl (2.1 kg ai/ha, 15 days apart), the levels 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.

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 and 3.2 μg/L for technical material and between 21.5 and 40.1 μg/L for a number of formulations, which, when converted to active material content, corresponded to between 5.4 and 8.8 μg ai/L. In the four 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}s of >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 or 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} was 1.47 mg ai/L for formulated (expressed as active), and the LC_{50} was 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, and gave an EC_{50} value (growth) of 3.6 mg/L, showing that 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 the US EPA's tier three testing regime, since azinphos-methyl had been linked to fish kills in the USA. A series of mesocosms (control and five 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). There were few discernible treatment-related effects for 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 that 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. Principal 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 (compared with 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 containing 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 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 200 000 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.

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 it was slightly harmful (30–80% mortality) to predatory mites on the International Organization for Biological Control (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 1 times or 10 times 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 or microbial digestion.

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 with 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 specific to the chemicals, species and habitats. However, the South Australian Department of Environment and Natural Resources 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.

Phytotoxicity

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

Prediction of environmental risk

Risk arising from use

The major uses are in the 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. 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 versus mature trees) and application target (foliage versus soil drenching).

Traditionally, application to orchards is by orchard airblasters 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.

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 there were no mortalities when oversprayed at the maximum Australian rate of 1.5 kg ai/ha. 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, and on grapevines and other vines.

Incidents of azinphos-methyl poisoning of birds in Australia have not been noted in literature or press reports. However, in the USA there have been reports of azinphos-methyl implicated in bird deaths associated with field and 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 three applications but only 2 in the second study with four 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 through the birds eating insects that are dead or dying from contact with azinphos-methyl. Using the US 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 (i.e., 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 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.

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 or program use, use should be restricted on the label to no more than one application every 28 days.

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 (i.e., 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. To make users and beekeepers aware of these risks, a suitable 'Protection of Livestock' statement has been suggested by DSEWPaC.

Spray drift could also expected to be extremely toxic to bees. Spray drift studies show that, in the worst case (early bud swell), the risk to bees was acceptable at 30 m away. For application in full leaf, the more likely usage, the risk was calculated as low at 30 m 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, and therefore the risk, could increase substantially.

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 (assuming there is no crop cover and the density of soil is 1300 kg/m^3). This is significantly below the LD_{50} for worms and the NOEC. However, 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 the risk cannot be determined as there are no toxicity data available for these organisms.

The toxicity data available for soil micro-organisms indicate that 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 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 most fish species, daphnia and other aquatic insects/invertebrates, based on the tests reviewed. Application by orchard airblasters is unlikely to result in direct over-spray of waterbodies and therefore spray drift is considered to be 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. The US EPA review listed an EC_{50} for a crayfish species as 56 µg/L but there are no end points 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 airblast spray drift

The Spray Drift Task Force undertook trials to measure spray drift, including that from orchard spraying in several orchard crops: grapes, apples (foliated and dormant), oranges, grapefruit, 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 airblast), 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 m. However, using the salt water mysid shrimp, a surrogate for sensitive invertebrates, the risk in 15 or 30 cm deep water extends beyond 100 m. 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 m from the orchards and beyond. Degradation of azinphos-methyl is expected to begin 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 to be higher and the 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 m from these orchards 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 (i.e., trees within 20–50 m 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 fruit and stone fruit orchards (and spraying) from watercourses 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 EC_{50} of 1.1 μg/L used for daphnids in the above assessments), despite multiple applications. In contrast, the three 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 affected by 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 one application per 28 days.

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 about 10% of the entire active sold, it is not considered the principal 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. DSEWPaC conducted an assessment of azinphos-methyl in 2005 and the PRF subsequently reported that in the regions where macadamias are grown, the streamside vegetation is expected to be luxuriant and should act as a buffer reducing the risk. It was then assumed that this vegetation could capture between 70 and 80%, based on literature results for the situation in orchards, and the risk would be significantly reduced. At 100 m the risk for fish and daphnia is marginal, though still very high for mysid.

Following the release of the proposed 100 m buffer for macadamias in the PRF for azinphos-methyl in 2006, several public submissions were received. As a result, DSEWPaC revised the assessment of the risk from spray drift with use on macadamias in recognition that interception of drift by windbreaks or streamside vegetation cannot be relied upon as generally applicable protective measures, as there are too many variables and uncertainties involved. Removal of this means of mitigation has led to an increase in the required buffer to 200 m, due to the higher application rate and greater drift potential expected for macadamias as a dense orchard tree.

Citrus

For citrus use, with very high application volumes (6000–8000 L/ha, 3–4 kg ai/ha) and scale as the principal 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 presents the worst case and that the use is infrequent, the use of azinphos-methyl 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 its 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, borne on dense trees up to 10 m in height. As they are somewhat similar to macadamia trees, 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. As 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 conventional high-volume sprayers, with low-volume methods being the main alternative to the traditional sprayers. The low-volume 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, if 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 indicated that current usage is limited, with application on pome and stone fruit being the principal uses but mainly as a clean-up spray to start IPM or when the 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 New South Wales 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, the carryover is approximately 3.1% (i.e., >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 its use be restricted to no more than one application per 28 days.

RUN-OFF

Calculations based on a simplistic model for run-off showed that there was a very high hazard to aquatic organisms from run-off. While this analysis showed that there is potential for run-off to be problematic, 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 was no evidence for this in Australia. However, run-off has been a major cause of aquatic incidents with azinphos-methyl overseas. The US EPA indicated 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 the likelihood of run-off, the use of aerial application in field crops (hence a greater risk of spray drift), the presence beneath orchards of at least a partial sod to intercept run-off and the greater proximity to water of 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.

5.5 Overseas regulatory status

According to the Pesticide Action Network (PAN) North America Pesticides Database, azinphos-methyl is registered for use in the following countries:

Australia, South Africa, New Zealand, Cambodia, Canada and the United States of America (USA).

Azinphos-methyl is not registered in the EU or the UK and its use will be phased out by 2012 in Canada and the USA, and in New Zealand by 2014 (see below). However, the application rate of products in the EU, USA and Canada is up to three times the rate approved for use in Australia. Azinphos-methyl was removed as a plant protection product in the EU largely because of the unacceptable risk to aquatic life. Additional data requirements are yet to be fulfilled by registrants in the EU[11]. Additional information in relation to some of these registrations is given below.

Joint FAO/WHO Meeting of Pesticides Residues (JMPR)

Azinphos-methyl was reviewed by the Joint FAO/WHO Meeting of Pesticide Residues (JMPR) in 1965, 1968, 1973, 1991 and 2004. In 1965, the JMPR established an ADI for azinphos-methyl of 0.0025 mg/kg bw/day based on plasma ChE inhibition in a 17-week rat study. In 1968, the ADI was reaffirmed despite there being long-term studies (2 years) in rats and dogs with lower NOELs (i.e., at 0.125 mg/kg bw/day).

In 1991, incorporating the change in JMPR policy to use inhibition of brain ChE (or red blood cell ChE inhibition as a surrogate) as the toxicologically relevant end point, 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/day) 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/day) (Holzum 1990). Hence, using a 100-fold safety factor, a new ADI was established at 0.005 mg/kg bw/day.

United States Environmental Protection Agency (USEPA)

At the time of commencement of this review, azinphos-methyl was registered in the USA for application to blueberries, blackberries, boysenberries, loganberries, raspberries, cranberries, almonds, pistachio nuts, walnuts, apples, pears, cherries, nectarines, peaches, brussel sprouts, potatos and cotton. The USEPA reviewed azinphos-methyl as part of their review and re-registration process for all organophosphate insecticides. In its assessment, the USEPA considered that azinphos-methyl posed potential risks of concern to farm workers, pesticide applicators, and aquatic ecosystems, while also providing important pest control benefits to growers of apples and other crops. In 2006, the USEPA issued its final decision on azinphos-methyl to prohibit the use of azinphos-methyl on brussel sprouts and nursery stock by 2008. As of 30 October 2009, the use of azinphos-methyl on almonds, pistachios and walnuts was prohibited, and as of 30 September 2012, the use of azinphos-methyl will be prohibited on the last remaining uses, namely alkali bee beds, apples, blueberries, cherries, parsley and pears. All other uses of azinphos-methyl in the USA have been voluntarily cancelled by the manufacturer.

Canadian Pest Management Regulatory Agency (PMRA)

At the time of this review, azinphos-methyl was registered for application to the a similar range of crops as the USA, including apples, crab apples, apricots, blackberries, cherries, cranberries, grapes, pears, peaches, plums, prunes and raspberries. The Canadian Pest Management Regulatory Agency (PMRA) completed the re-assessment of azinphos-methyl in 2007 and determined that due to unacceptable worker exposure, all uses of azinphos-methyl were to be phased out by 2012.

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[11] As at the date of the preparation of this manuscript viz. July 2011.

United Kingdom Department of Environment, Food and Rural Affairs

Azinphos-methyl is not registered in the United Kingdom.

European Union

Approvals for azinphos-methyl were revoked in the European Union on 31 December 2006. The main area of concern was the risk to aquatic life based on the existing information. Operator exposure and residue concerns also formed the basis of the suspension of azinphos-methyl from the EU market. However, registrants had not provided suitable environmental, toxicological or OHS studies to allay the concerns associated with azinphos-methyl use in the EU. As a result, additional studies are required for registration of azinphos-methyl to be re-considered in the EU.

New Zealand (NZ)

At the time of this review, there was one azinphos-methyl product registered in New Zealand for application to summer fruit (including kiwifruit, pipfruit, grapes and strawberry runners) and potatoes (azinphos-methyl is not registered for application to any other vegetable crop, apart from potatoes). In 2007, MRLs for azinphos-methyl were established for fruits except kiwifruit (2 mg/kg), and for kiwifruit (4 mg/kg). The New Zealand Food Safety Authority proposed a MRL of 0.05 mg/kg for azinphos-methyl in potatoes as a replacement for the 2 mg/kg MRL for azinphos-methyl in vegetables, due to the loss of the vegetable use pattern from azinphos product labels in 2002.

In 2009, the Environmental Risk Management Authority New Zealand completed an assessment of azinphos-methyl and recommended that approvals for azinphos-methyl and its formulations be phased out by 2010 for potatoes, and 2014 for strawberry runner plants and summer fruit, based on human health and environmental concerns. The assessment of azinphos-methyl used by the Environmental Risk Management Authority New Zealand considered the risks, costs and benefits associated with azinphos-methyl. In the absence of exposure information, assessment models were used by the Environmental Risk Management Authority New Zealand to determine the levels of risk to the environment and human health. The New Zealand Agency concluded that the level of adverse effects (risks and costs) to the environment, human health, society and economy outweigh any positive effects (benefits) associated with the availability of azinphos-methyl in New Zealand for all cases except for use on potatoes, summerfruit and strawberry runner plants. A five year phase out period for azinphos-methyl was provided to allow time for alternative insecticides to be registered.

In contrast, when an active is placed under review in Australia, the APVMA conducts a risk assessment of the active constituent and products containing the active constituent. Regulatory outcomes for any continued uses in Australia are on the basis of identified risks that can be managed. The findings are not influenced by any non-scientific costs or benefits.

Further consideration of overseas findings to be undertaken

Given the forthcoming removal of azinphos-methyl from use in many overseas countries, the APVMA will examine overseas regulatory reports (in particular, the United States, Canada and more recently New Zealand) in conjunction with its advisory Agencies to determine if any of these reports contain information/studies that could cause the APVMA to doubt its satisfaction with the current regulatory status of this active. This will require further advice from the Department of Health and the Department of Sustainability, Environment, Water, Population and Communities. This work will need to be completed by September 2012 to ensure Australia has regard to the forthcoming changes in regulatory status of azinphos-methyl in the United States and Canada. The result of this work will inform the APVMAs decision regarding the prioritisation of azinphos-methyl for the forthcoming spraydrift review.

6 REVIEW FINDINGS

On the basis of the evaluation of the submitted data and information, the review findings for azinphos-methyl may be summarized as follows:

1. The continued approval of azinphos-methyl active constituent is supported.
2. voluntary label amendments have been approved.

The concerns that were the basis for the review of azinphos-methyl have been addressed by the provision of amended label instructions. However, at the time of this report, azinphos-methyl has also been prioritised for spray drift review, which may affect the ongoing approval of azinphos-methyl and future registration of products containing azinphos-methyl.

6.1 Variations to label instructions

All products registered at the beginning of the review (Table A3) are no longer registered. As a result, no further action is required for these products. For products registered after the commencement of the review (Table A2), amended labels have voluntarily been submitted to the APVMA.

Voluntarily amended labels have been varied in the following manner.

Deletion of use patterns

- kiwifruit: based on lack of residue data
- citrus: based on lack of environmental data.

Additional label statements

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 corresponding WHP of 7 days, reduced from the present WHP of 14 days.

Insert:

WITHOLDING PERIODS: Blueberries: DO NOT harvest for 7 days after application.

No changes were made to the following withholding periods:

Pome fruit: DO NOT harvest for 14 days after application.

Stone fruit: DO NOT harvest for 14 days after application.

Grape: DO NOT harvest for 14 days after application.

Macadamia: DO NOT harvest for 7 days after application.

Lychees: DO NOT harvest for 1 day after application.

Restraint statements

The environmental assessment found that there are potential risks to the environment from the use of azinphos-methyl. To mitigate these risks, the following restraint statements have been included:

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 at a spray interval closer than 28 days.

Re-entry periods

As a result of the OHS assessment, the following re-entry period statements have been added to labels:

Blueberry, macadamia, lychees, pome fruit (apples, pears, quinces) and stone fruit (apricots, 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.

Protection of wildlife, fish, crustaceans and environment

The environmental assessment found that there are potential risks to wildlife, fish, crustaceans and the environment from the use of azinphos-methyl. To mitigate these risks, the following statements have been added to labels:

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.

For crops other than macadamias: DO NOT apply within 100 meters of downwind aquatic and wetland areas including aquacultural ponds or surface streams and rivers.

For macadamias: DO NOT apply within 200 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 or 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.

Rinsing and disposal of containers

The following statements have been added to labels:

Triple rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

For refillable containers the following has been added:

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

Protection of livestock

The environmental assessment found that there are potential risks to bees from the use of azinphos-methyl. To mitigate these risks, the following statement has been added to labels:

Azinphos-methyl is dangerous to bees and will kill bees foraging in the crop to be treated or in hives which are over-sprayed or reached by spray drift. Residues toxic to bees may remain for several days after application.

7 AMENDMENTS TO STANDARDS

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

7.1 Public health standards

Impurity limits

No change.

Acceptable Daily Intake (ADI)

The existing Australian ADI for azinphos-methyl at the commencement of the review was 0.001 mg/kg bw/day. 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/day was established. The new ADI of 0.025 mg/kg bw/day was established by applying a 10-fold safety factor to the NOEL of 0.25 mg/kg bw/day based on the absence of inhibition of plasma or red blood cell cholinesterase activities (or any other treatment-related effects) in male volunteers at this oral dose.

Acute Reference Dose (ARfD)

Arising from the assessment of the data submitted to the review, the OSCEH set an ARfD of 0.075 mg/kg bw/day by applying a 10-fold safety factor to the NOEL of 0.75 mg/kg bw/day 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.

Health value for Australian drinking water

It was 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, based on the recommended new ADI of 0.025 mg/kg bw/day.

Poisons schedule

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

First-aid instructions

Existing first aid instructions for azinphos-methyl as they appear in the First Aid Instruction and Safety Directions Handbook (*FAISD handbook*[12]) are as follows and remain appropriate:

CODE	FIRST AID INSTRUCTION
m	If swallowed, splashed on skin or in eyes, or inhaled, contact a doctor or Poisons Information Centre (Phone, eg Australia 131 126; New Zealand 0800 764 766) or a doctor at once. Remove any contaminated clothing and wash skin thoroughly. If swallowed, activated charcoal may be advised. Give atropine if instructed.

Existing safety directions and personal protective equipment (PPE)

The existing safety directions for Australian products containing azinphos-methyl, as recommended in the *FAISD handbook*, are shown below.

CODE	SAFETY DIRECTIONS
AZINPHOS-METHYL WP OVER 350 G/L	
100, 101	Very dangerous, particularly the concentrate
120, 121, 130, 131, 132, 133	Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed
190	Repeated minor exposure may have a cumulative poisoning effect
210, 211, 212	Avoid contact with eyes and skin and clothing
220, 221, 223	Do not inhale dust or spray mist
279, 280, 281, 282, 290, 291, 292, 294, 298, 301, 303	When opening the container, preparing spray and using the prepared spray: wear protective waterproof clothing and cotton overalls buttoned to the neck and wrist and a washable hat, and elbow-length PVC gloves and impervious footwear and full facepiece respirator [NB: comment, not for label: this category includes air-purifying respirator] with combined dust and gas cartridge
330, 331, 332	If clothing becomes contaminated with product or wet with spray remove clothing immediately
340, 342	If product on skin, immediately wash area with soap and water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360, 361, 364, 366	After each day's use, wash gloves and respirator (and if rubber wash with detergent and warm water), and contaminated clothing

12 *FAISD handbook: handbook of first aid instructions, safety directions and warning statements for agricultural and veterinary chemicals*, Therapeutic Goods Administration, 2009.

CODE	SAFETY DIRECTIONS
AZINPHOS-METHYL WP 350 G/KG OR LESS	
100, 101	Very dangerous, particularly the concentrate
120, 121, 130, 131, 132, 133	Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed
161, 162, 164	Will irritate the eyes and skin
180	Repeated exposure may cause allergic disorders
190	Repeated minor exposure may have a cumulative poisoning effect
210, 211, 212	Avoid contact with eyes and skin and clothing
220, 221, 223	Do not inhale dust or spray mist
279, 280, 281, 282, 290, 292, 294, 301, 303	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
330, 331, 332	If clothing becomes contaminated with product or wet with spray remove clothing immediately
340, 342	If product on skin, immediately wash area with soap and water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360, 361, 364, 366	After each day’s use, wash gloves and respirator (and if rubber wash with detergent and warm water), and contaminated clothing
AZINPHOS-METHYL SC 350 G/L OR LESS	
100, 101	Very dangerous, particularly the concentrate
120, 121, 130, 131, 132, 133	Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed
161, 162, 164	Will irritate the eyes and skin
180	Repeated exposure may cause allergic disorders
190	Repeated minor exposure may have a cumulative poisoning effect
210, 211, 212	Avoid contact with eyes and skin and clothing
220, 222, 223	Do not inhale vapour or spray mist
279, 280, 281, 282, 290, 292, 294, 301, 303	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
330, 331, 332	If clothing becomes contaminated with product or wet with spray remove clothing immediately
340, 342	If product on skin, immediately wash area with soap and water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360, 361, 364, 366	After each day’s use, wash gloves and respirator (and if rubber wash with detergent and warm water), and contaminated clothing

Amendments to existing safety directions and personal protective equipment (PPE)

Based on a consideration of the toxicity of each constituent in registered azinphos-methyl products, the following amended hazard-based safety directions and PPE are appropriate. Safety directions for suspension concentrate (SC) formulations are provided as they are the only azinphos-methyl formulations registered in Australia (as of December 2010).

CODE	SAFETY DIRECTIONS
AZINPHOS-METHYL SC 350 G/L OR LESS	
120, 121, 130, 131, 132, 133	Product and spray are poisonous if absorbed by skin contact or inhaled or swallowed
161, 162, 164	Will irritate the eyes and skin
160, 163	May irritate the nose and throat
180	Repeated exposure may cause allergic disorders
190	Repeated minor exposure may have a cumulative poisoning effect
210, 211, 212	Avoid contact with eyes and skin and clothing
220, 222, 223	Do not inhale vapour or spray mist
279, 280, 281, 290, 292b, 291, 294, 298b, 299	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, 282 [open cab], 290, **291c***, 292b, 294, 298b, 300, 303	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 [closed cab fitted with charcoal filters], 290, 292b	When using the prepared spray (closed cab fitted with charcoal filters), wear cotton overalls buttoned to the neck and wrists (or equivalent clothing).
330, 331, 332	If clothing becomes contaminated with product or wet with spray remove clothing immediately
340, 342	If product on skin, immediately wash area with soap and water
340, 343	If product in eyes, wash it out immediately with water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360, 361, 364, 365, 366	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

* Proposed new FAISD Handbook standard statement.

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	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 pulp/dry	3

8 APPENDIX A ACTIVE CONSTITUENT AND REGISTERED PRODUCTS INCLUDED IN THE REVIEW

Table A1: Active constituents included in the review

APPROVAL NUMBER	ACTIVE CONSTITUENT NAME	APPROVAL HOLDER
44188	Azinphos-methyl	Farmoz Pty Limited

Table A2: Products registered after the commencement of the review that are subject to the outcomes of the review

PRODUCT NUMBER	PRODUCT NAME	REGISTRANT	LABEL APPROVAL NUMBERS TO BE VARIED	NEW LABEL APPROVAL NUMBERS
53215#	Campbell Benthion 200 Flowable Insecticide	Colin Campbell (Chemicals) Pty Ltd	53215/0800	53215/0511
62221#	Farmoz Gusathion 200 SC Insecticide	Farmoz Pty Limited	62221/0609	62221/0511

Table A3: Products and active constituents no longer on the register

PRODUCT NUMBER	PRODUCT NAME	REGISTRANT	LABEL APPROVAL NUMBER
PRODUCTS			
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
ACTIVE CONSTITUENTS			
APPROVAL NUMBER	ACTIVE CONSTITUENT NAME	APPROVAL HOLDER	LABEL APPROVAL NUMBER
44081	Azinphos-methyl	Bayer CropScience Pty Ltd	–