

**Australian Government** 

Australian Pesticides and Veterinary Medicines Authority



# **APVMA risk assessment manual**

Human health MARCH 2019

#### © Australian Pesticides and Veterinary Medicines Authority 2019

ISSN 2652-0583 (electronic)

#### Ownership of intellectual property rights in this publication

Unless otherwise noted, copyright (and any other intellectual property rights, if any) in this publication is owned by the Australian Pesticides and Veterinary Medicines Authority (APVMA).

#### **Creative Commons licence**

With the exception of the Coat of Arms and other elements specifically identified, this publication is licensed under a Creative Commons Attribution 4.0 Australia Licence. This is a standard form agreement that allows you to copy, distribute, transmit and adapt this publication provided that you attribute the work.



A summary of the licence terms is available from <u>www.creativecommons.org/licenses/by/3.0/au/deed.en</u>. The full licence terms are available from <u>www.creativecommons.org/licenses/by/3.0/au/legalcode</u>.

The APVMA's preference is that you attribute this publication (and any approved material sourced from it) using the following wording:

Source: Licensed from the Australian Pesticides and Veterinary Medicines Authority (APVMA) under a Creative Commons Attribution 4.0 Australia Licence.

In referencing this document the Australian Pesticides and Veterinary Medicines Authority should be cited as the author, publisher and copyright owner.

Cover image: iStockphoto (www.istockphoto.com) iStockphoto images are not covered by this Creative Commons licence.

#### Use of the Coat of Arms

The terms under which the Coat of Arms can be used are set out on the Department of the Prime Minister and Cabinet website.

#### Disclaimer

The material in or linking from this report may contain the views or recommendations of third parties. Third party material does not necessarily reflect the views of the APVMA, or indicate a commitment to a particular course of action. There may be links in this document that will transfer you to external websites. The APVMA does not have responsibility for these websites, nor does linking to or from this document constitute any form of endorsement. The APVMA is not responsible for any errors, omissions or matters of interpretation in any third-party information contained within this document.

#### Comments and enquiries regarding copyright:

Assistant Director, Communications Australian Pesticides and Veterinary Medicines Authority PO Box 6182 KINGSTON ACT 2604 Australia

Telephone: +61 2 6210 4988

Email: communications@apvma.gov.au.

This publication is available from the APVMA website.

# **CONTENTS**

1	HUMAN HEALTH RISK ASSESSMENT	5
1.1	Assessing risks to human health	5
	Human health hazard assessment	5
	Human health exposure assessment	6
	Human health risk assessment	6
1.2	Managing risks to human health	6
2	REGULATORY FRAMEWORK	7
3	HAZARD ASSESSMENT	8
3.1	Information considered in the hazard assessment	8
3.2	Selection of a NOAEL/NOAEC for occupational or bystander risk assessment	9
3.3	Selection of a NOAEL for the dietary risk assessment	10
4	HEALTH STANDARDS	11
4.1	Acceptable Daily Intake (ADI)	11
4.2	Acute Reference Dose (ARfD)	12
4.3	Poisons Standard and Labelling	12
5	EXPOSURE ASSESSMENT	13
5.1	Exposure study data relevant to proposed product	13
5.2	Occupational exposure	13
	Exposure during use	13
5.3	Public Exposure	13
	Exposure during domestic use	13
	Bystander exposure	14
	Accidental exposure	14
5.4	Post-application exposure	14
	Public post-application exposure	14
	Occupational post-application exposure	14
6	RISK ASSESSMENT	16
6.1	Occupational risk assessment	16
	Acute risks	16
	Risk from repeat exposure	16
	Risk from re-entry/re-handling exposure	17
6.2	Public Risk Assessment	17
	Risks from residues in food	18
	Risks from accidental exposure	18
	Risks associated with domestic product use	18
	Bystander risks associated with product use	18

7	RISK MANAGEMENT	19
ABB	REVIATIONS	21

# LIST OF TABLES

Table 1:	Sample table of summary of relevant NOAELs from studies that have been used to establish an ADI	11
Table 2:	Sample MOE* values for workers from exposure to active constituent X in product Y	16
Table 3:	Sample PPE indicated from risks (MOEs) from exposure to active constituent X in product Y	17
Table 4:	Sample MOE* estimates for active constituent X for children playing on surfaces treated with product Y	18

# **1 HUMAN HEALTH RISK ASSESSMENT**

## **1.1** Assessing risks to human health

Protecting the health and safety of people from risks associated with agricultural and veterinary (agvet) chemicals involves both the assessment and the management of risks from the potential sources of exposure. Note that while reference is made to agvet chemicals in this document, the human health risk assessment will also consider biological agents for example whole microorganisms (including bacteria, fungi and viruses), immunobiological products and crude extracts of plants.

The assessment of risk is conducted in three steps:

- 1. the hazard assessment determines how inherently dangerous a chemical is to human health using primarily toxicity studies on animals, and in vitro studies (tests on tissue or cell cultures)
- 2. the exposure assessment determines the way and the extent to which the chemical users, workers or the public may be exposed to an agvet chemical. Human exposure data are used where available, but if not, various exposure modelling techniques are used
- 3. the overall risk assessment is a function of exposure and hazard that permits appropriate risk management initiatives, including label directions, to be established.

## Human health hazard assessment

The term hazard refers to the intrinsic property of a chemical or biological agent to cause harm to humans. All chemical and biological agents have the capacity to cause harm in particular circumstances, however, this may never be realised under normal use. The nature of this harm varies from negligible to severe and can be immediate (acute) or long-term (chronic).

Hazards associated with chemicals are generally identified in standardised toxicity studies conducted in suitable laboratory animals and, in some cases, tests on tissue or cell cultures (otherwise known as in vitro assays). In silico computer models are used as a screening tool to predict potential hazards. Controlled studies in humans may sometimes be available, although this is generally uncommon for agvet chemicals. Wherever possible, the use of laboratory animals is minimised and in vitro studies are used instead to identify the hazards.

The toxicity studies required will depend on the nature of the chemical and the manner of its use. These studies generally follow international guidelines such as those published by the OECD and VICH. All studies are expected to comply with quality control benchmarks such as Good Laboratory Practice (GLP) (OECD, 1997 revision<sup>1</sup>).

<sup>&</sup>lt;sup>1</sup>OECD Principles of Good Laboratory Practice, Environment Directorate Organisation for Economic Co-operation and Development, Paris 1998

#### Human health exposure assessment

Assessing the potential exposure to agvet chemicals involves understanding the different ways that people can be exposed (exposure scenarios), assessing the likelihood of exposure and then measuring or modelling the extent of the exposure.

Human exposure can occur through several pathways:

- **ingestion** of small amounts of agvet chemicals can occur through the consumption of residues in food or water that has been treated or contaminated with chemicals, or after dermal contact followed by touching foods or the mouth, or putting treated material directly into the mouth as well as through accidental ingestion of the product such as by children
- inhaled air: Airborne particles of agvet chemicals can be breathed in by workers preparing or using these
  products (for example by spray drift). Farmers are commonly exposed by breathing chemical vapours and
  sprays. The public may be exposed by inhalation while using a home or garden product. The public can also
  be inadvertently exposed to spray drift or vapours from agricultural use of pesticides or from their use in public
  places
- skin or eye contact: Agvet chemicals can be absorbed through the skin or eyes of people preparing or using these products—either at work or in the home or garden. Workers may be exposed to agvet chemicals during their preparation and use, but they can also be exposed when entering treated areas or handling treated crops or animals.

Workers are generally exposed at higher levels than the public and may be required to use protective clothing and equipment to reduce exposure and the potential risk to human health. The APVMA considers the extent of exposure for adults and children in relation to products used in the workplace and the home.

#### Human health risk assessment

Risk assessment integrates the information from the hazard assessment and the exposure assessment to estimate the likely risks to human health associated with the various exposure scenarios.

## **1.2** Managing risks to human health

Human health risks are generally considered in two contexts: risks to public health (generally through the consumption of treated food, the use of agvet chemicals in a home and garden or people coming into contact with treated surfaces or animals) and risks to occupational health (workers exposed to chemicals while mixing, loading and applying agvet chemicals).

# 2 REGULATORY FRAMEWORK

The Agricultural and Veterinary Chemicals Code (Agvet Code), scheduled in the *Agricultural and Veterinary Chemicals Code Act 1994* (the Act), provides the basis for using risk analysis to regulate activities with agvet chemicals) in Australia.

The objective of the Code is for the evaluation, approval, and control of the supply, of active constituents for proposed or existing agricultural or veterinary chemical products; and the evaluation, registration, and control of the manufacture and supply, of agricultural chemical products and veterinary chemical products.

The decision on whether to approve an active constituent or register an agvet product is made by the Australian Pesticides and Veterinary Medicines Authority (the APVMA), an independent statutory office holder established by the Act.

The Act mandates that APVMA implement the Code in a manner that reflects 'established best-practice principles for the assessment and management of risk, based on science'. To do this, the APVMA's regulatory scientists must balance regulatory effort and regulatory burden with the potential risk that the use of agvet chemicals will present to the health and safety of human beings, animals and the environment.

The APVMA must be satisfied under s14 of the Agricultural and Veterinary Chemicals Code Act 1994 that:

- the proposed use of the product meets the safety criteria with respect to s5A(1)(a) and (b);
- the requirements of s5A(3)(a)(i), (v), (vi) & (vii); s5A(3)(b)(i), (ii), (iii) & (vi); and 5D(1)(a)-(e) are met.

## **3 HAZARD ASSESSMENT**

Assessment is made as to what adverse effects the active constituents and its formulated product have in vivo and in vitro, what is the toxicological mechanism of action (MOA) and how this is applicable to humans.

## **3.1** Information considered in the hazard assessment

Assessments consider the following areas:

- chemistry of the active constituent(s) and the formulated product—physicochemical features, impurity profile and formulation type
- toxicokinetics and metabolism—the absorption, distribution, metabolism and elimination (ADME) of the chemical in the mammalian body
- acute toxicity—oral, dermal, inhalation, skin irritation, eye irritation, skin sensitisation and respiratory tract irritation and sensitisation
- short-term/sub-chronic exposure—repeat dose exposure involving daily dosing for several weeks and up to but less than 12 months
- chronic/carcinogenicity—exposure running for 12 months or over the whole of life in an animal species
- reproductive toxicity—dosing of test animals to ascertain effects on fertility and pregnancy
- · developmental toxicity studies—studies in animals during foetal development to ascertain effects on the foetus
- genotoxicity—the effect of an agvet chemical on DNA and chromosomes, based on both in vitro (cells and tissue culture) and in vivo (in a living organism) studies
- neurotoxicity—investigate the effect on the growth, development and function of the nervous system, including the brain
- metabolites—the effects of by-products of the particular agvet chemical produced in the body
- mechanistic—investigations that help to determine how and why an agvet chemical has an effect in animals and its relevance to humans
- immunotoxicity—investigations that indicate whether an agvet chemical causes any effects in the immune system
- endocrine effects—active constituents are checked for endocrine disruption potential.

In reviewing the studies, the following approach is adopted:

- · identification and characterisation of the test substance, its isomers and their impurities
- whether the study meets GLP requirements and did it follow internationally recognised test guidelines for example OECD Test Guidelines
- how was the test substance administered, for example oral, dermal, inhalation, other
- what was the objective of the study and the depth of analysis that was undertaken

- sex and number of animals in each group given a placebo (control) or the test substance
- duration, route, dosage levels and frequency of administration of the test substance
- demonstration of impact through:
  - pharmacokinetics (absorption, distribution, metabolism, elimination)
  - observations and findings
  - consideration of the toxicological MOA
  - establishing toxicological endpoints, for example NOAEL/NOAEC or LOAEL/LOAEC.

In undertaking the hazard assessment, the APVMA consider whether there are adverse vs non-adverse effects. This is through understanding if an effect is based on an adaptive or pathological response, transient or reversible reaction, dose dependent response of an effect on an organ or system and secondary or general toxicity.

A key quantitative output from the studies is the identification of the highest dose/concentration tested that does not cause any significant observable adverse effects that are of a toxicological concern ie the No Observed Adverse Effect Level (NOAEL) or the No Observed Adverse Effect Concentration (NOAEC).

# **3.2** Selection of a NOAEL/NOAEC for occupational or bystander risk assessment

The toxicological studies are reviewed to assess the most suitable NOAEL/NOAEC that best represents the proposed use scenario(s) of the product. These use scenarios inform the selection of the NOAEL/NOAEC for occupational, public health or bystander assessments and the estimation of the Margin of Exposure (MOE). The MOE is calculated by dividing a NOAEL/NOAEC from an appropriate study on the active constituents with the estimated likely exposures from the proposed use scenarios.

The use scenarios consider:

- how will the product be applied?
- what is the maximum application rate?
- what is the potential route of exposure?
- what is the potential duration of use?
- is there a potential re-entry exposure pathway or other post application exposure?

In general, the lowest NOAEL/NOAEC in the most appropriate species is used for the risk assessment, although the use scenarios of the agvet chemical play an important role when selecting the most appropriate NOAEL/NOAEC. For instance, if exposure is intermittent (for example seasonal use) a short-term study NOAEL may be used.

## 3.3 Selection of a NOAEL for the dietary risk assessment

The APVMA determines a NOAEL in order to establish the Health Based Guidance Values (HBGVs), in particular an Acceptable Daily Intake (ADI) and Acute Reference Dose (ARfD). Information may be summarised to include relevant NOAELs from various toxicity studies with the active constituent. This information will include the study duration, species and route, doses used, NOAEL, LOAEL and toxic end points. The assessment will ascertain which of these studies are considered the most appropriate for establishing HBGVs.

# 4 HEALTH STANDARDS

As part of its assessment, the APVMA may require particular health standards to be established for agvet chemicals. Health Based Guidance Values (HBGV) are generally established when the use of an agvet chemical is likely to result in residues being found in the diet. Where appropriate, an ADI and/or and ARfD may be established. In addition, agvet chemicals are considered for inclusion in the Poisons Standard and may result in the chemical being included in one of a number of Schedules in the Poisons Standard.

## 4.1 Acceptable Daily Intake (ADI)

The ADI for humans is the level of intake of a chemical that can be ingested daily over an entire lifetime without appreciable risk to health. It is calculated through assessing the overall NOAEL for the most sensitive toxicological endpoint from a suitable study (typically a chronic animal study) against an appropriate uncertainty (safety) factor. The magnitude of the uncertainty factor is selected to account for uncertainties in extrapolation of animal data to humans (interspecies variation), variation in human population (intraspecies variation), and the completeness of the toxicological database.

Studies from the toxicological database for the active constituents are evaluated. These studies may include shortmedium term, reproduction studies, developmental studies, chronic studies and carcinogenicity studies.

The ADI can be established by using the appropriate NOAEL (expressed as mg/kg bw/d) and applying an uncertainty factor (nominally 100 consisting of a 10 fold uncertainty factor for inter-species variation and a second 10 fold factor for intraspecies variation) (Table 1).

Chemical	ADI (mg/kg bw/d)	NOAEL (mg/kg bw/d)	Year	Description
Epoxiconazole	0.01	1	16 April 2002	1 year dietary dog study; based on the absence of any treatment related effects at the highest tested dose of 1.1 mg/kg bw/d. 78 week dietary mouse study; a NOAEL of 0.81 mg/kg bw/d was based on reduced bodyweight gain and increased liver weight at the higher dose (36 mg/kg bw/d)
Streptomycin (and dihydrostreptom ycin)	0.05	5 (JECFA '97)*	28 June 2001	2 year dietary rat study; a NOAEL of 5mg/kg/bw/d was based on decreased body weight gains at the next higher dose of 10 mg/kg bw/d dihydrostreptomycin

Table 1:	Sample table of summary of	f relevant NOAELs from studies that have been used to establish an ADI
----------	----------------------------	--

\*Reference is made here to a toxicological endpoint that was established by the FAO/WHO Joint Expert Committee on Food Additives (JECFA) that was adopted by the APVMA.

## 4.2 Acute Reference Dose (ARfD)

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

The approach in setting the ARfD is based on:

- evaluating the total data set on the test substance and establishing whether there are any demonstrable toxicological effects from a single dose on a test animal or human
- selecting appropriate end-points for establishing an ARfD—toxicological end points most relevant for a single (day) exposure, select the most relevant study based on the endpoints (in the absence of a single dose study use of a repeated-dose toxicity study), identify the NOAELs for the end points.

Endpoints relevant to the ARfD includes:

- acute toxicity studies including behavioural effects
- developmental effects
- effects on organ function including clinical chemistry and haematology
- neurotoxicity
- immunotoxicity.

If an ARfD needs to be established, it will be based on the lowest appropriate NOAEL with an uncertainty factor, nominally 100 consisting of a ten–fold uncertainty factor for intraspecies and another ten–fold factor for interspecies variability.

## 4.3 Poisons Standard and labelling

Requirements from the Poisons Standard (also known as the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) are assessed on a case by case basis. Reference is made to <u>Scheduling of medicines & poisons</u>.

The APVMA is required to approve the label particulars for the product container. The Agricultural and Veterinary Chemicals Code (Agvet Code) prescribe the approval process and content requirements for labels for containers for agricultural and veterinary products. The suitability of the label is assessed based on health risks and appropriate mitigation. The APVMA must also ensure that the label complies with Poisons Standard.

# **5 EXPOSURE ASSESSMENT**

## 5.1 Exposure study data relevant to proposed product

The APVMA will assess submitted exposure studies (which may include chemical specific worker monitoring studies or air dispersion modelling studies) which are relevant to the active constituent or product.

## 5.2 Occupational exposure

Workers may be exposed to the product when opening containers, mixing/loading or preparing the product for use, during application or administration, cleaning up spills, maintaining equipment and entering treated areas as well as handling treated animals. In all cases, it is necessary to consider whether protective clothing or equipment is necessary to reduce the likely extent of exposure.

The main routes of exposure to agvet products include dermal, ocular and inhalational.

## Exposure during use

In the absence of chemical specific worker exposure data, the APVMA may rely on surrogate models of human exposure to estimate the exposure of workers to agvet chemicals.

The APVMA uses these surrogate models together with the product's use scenarios to ascertain worker exposure during use. The parameters that are considered in estimating worker exposure include:

- concentration of active constituent (ac) in the product formulation, maximum application rate of the product (kg/ha or dose/animal), work rate (ha/day or animals/day) and quantity of each active constituent handled each day (kg ac/day)
- dermal absorption factor
- inhalation absorption factor
- bodyweight (in Australia considered to be 70kg for an adult).

The total exposure is calculated based on the level of dermal and inhalational exposure by application method for example aerial or back pack sprayer, and whether basic Personal Protective Equipment (PPE) for example single layer of clothing and gloves, in addition to engineering controls for example closed cab on a tractor powered air blast sprayer, can reduce exposure to acceptable levels. Additional PPE and more stringent engineering controls (for example closed mixing and loading) can also be modelled.

## 5.3 Public exposure

## Exposure during domestic use

The APVMA determines the potential for public exposure during use based on the label and likely use scenarios of the product. As with occupational exposure, the APVMA may use surrogate models of human exposure to

estimate exposure to domestic users, using the same parameters mentioned above for occupational exposure. Importantly, there is a limit to the PPE that is permitted for use in domestic settings (home, garden and home veterinary). Additional control of use in domestic settings may include specific directions for use, packaging design, container size and label warnings.

## **Bystander exposure**

Application of the product via some methods may lead on occasion to unintended bystander exposure, such as via chemical spray drift. This may be in the form of a single random exposure or repeat exposures of residents who reside adjacent to areas being treated with the product. Spray drift impacts are calculated as part of the APVMA risk assessment where relevant. In certain situations, buffer zones are established for bystanders for example use of soil fumigants.

The APVMA also assesses exposure to product residues in food may also occur through a specific residues assessment.

## **Accidental exposure**

The APVMA determines accidental exposure based on the label instructions and likely use scenario of the product. Consideration is given to likely risks from accidental exposure such as splash exposure or needle stick injuries, and for products used in the home, ingestion of the product by children and the potential outcome of that exposure.

## 5.4 Post-application exposure

### Public post-application exposure

There are a number of ways the public may be exposed to an agvet product following use. These can broadly be categorised as follows:

- re-entry into treated areas for example homes treated with insecticides, domestic lawns, parks, golf-courses or bowling greens treated with herbicides
- handling of treated animals, for example petting of dogs/cats treated with insecticidal spot-on products
- ingestion of product residues in food, for example vegetables treated with pesticides, meat from animals treated with veterinary products.

The APVMA assesses the exposure of the Australian population to residues of agricultural and veterinary chemicals in food crops and target animals. The APVMA also considers potential exposure through contact with products, treated materials and treated animals.

### **Occupational post-application exposure**

There are a number of ways workers may be exposed to an agvet product following use. These can broadly be categorised as follows:

- re-entry into treated fields or crops to perform post application activities such as irrigation or harvesting
- exposure to product residues in or on treated animals by veterinarians, pet groomers
- exposure to residues or airborne levels of pesticides in treated areas such as animal houses, warehouses, homes.

If there are no chemical specific exposure study data available, the APVMA will use surrogate models of postapplication exposure to estimate the likely exposure following different re-entry activities in treated areas or crops. Similarly, with the re-handling of treated animals, other surrogate models of post-application exposure may be used to estimate exposure. All these models require similar input variables and include:

- transfer coefficient
- dislodgeable residues
- dissipation rate
- exposure duration
- body weight
- NOAEL.

Re-entry or re-handling intervals (REIs or RHIs) are determined and will be based on various activities that may occur following treatment for example pruning and harvesting for crops and petting treated animals.

# 6 RISK ASSESSMENT

Risk assessment is achieved through consideration of the hazard profile of the agvet product in conjunction with the systemic exposure expected through the use or subsequent potential exposure to the product according to the label instructions.

The acute hazard of the product may require specific precautionary statements and contribute to the minimum management approaches and/or PPE requirements in the product's safety directions. The risk is characterised from its oral, dermal and inhalational toxicity and combined acute and repeated dose. The risk assessment will determine the management requirements for the product.

## 6.1 Occupational risk assessment

### Acute risks

The acute hazard of the product may require specific precautionary statements and contribute to the engineering and/or PPE requirements in the product's safety directions.

### **Risk from repeat exposure**

An appropriate NOAEL for the active constituent will be selected to support the risk assessment of the product's occupational use. The MOE is calculated by dividing the NOAEL from an appropriate study on the active constituent(s) with the estimated likely exposures. In general, an MOE of 100 or above (based on laboratory animal data) is considered to be an acceptable risk (Table 2).

Estimates	Gloves	Mixer/loader dermal	Applicator dermal	Mixer/loader inhalation	Applicator inhalation	Total MOE*
	Ν	32	51	2611	40	13
Estimate 1: Open mixing and loading &	Y	4010	144	2611	40	30
high pressure hand wand application	PPE'A'	28004	3354	6615	1005	676
	PPE'B'	4010	163	2611	397	108
Estimate 2: Open	Ν	33	0	2691	10	0
mixing and loading & backpack application	Y	4133	0	2691	10	0
	PPE'A'	11391	2	2691	98	2

Table 2:	Sample MOE*	values for workers	s from exposure to	o active constituent X in	product Y

\*Based on a NOAEL of 3mg/kg bw/d. Estimates are for workers wearing long pants and long sleeved shirt (single layer of clothing), MOE values were based on person of 70 kg bw, 3.4% dermal absorption factor during mixing/loading and application, and a 100% default inhalational absorption factor. Total MOE = 1/(1/ML MOE dermal) + (1/ML MOE inhalation) + (1/Applicator MOE dermal) + (1/Applicator MOE inhalation).

PPE'A' consists of wearing cotton overalls over normal clothing, washable hat and chemical resistant gloves during mixing and loading and application and a respirator during application.

PPE'B' consists of wearing normal clothing with chemical-resistant gloves during mixing and loading and application, plus a washable hat and respirator during application.

In its risk assessment, the APVMA will consider whether the margins of exposure (MOEs) to the active constituents are acceptable (ie  $\geq$ 100) when appropriate levels of PPE are included in the relevant use scenarios (Table 3).

Table 3:	Sample PPE indicated from	risks (MOEs) from exposure to	active constituent X in product Y

PHED estimate	Use scenario	Personal protective equipment		
		M/L	Application	
Estimate 1	Open mixing and loading & high pressure hand wand application	Single layer clothing plus hat and gloves	Single layer of clothing plus hat, gloves and a respirator.	
Estimate 2	Open mixing and loading & backpack application	Single layer clothing plus hat and gloves	Use NOT supported, as unable to increase MOE above 2 for dermal exposure with maximum PPE.	

The APVMA will require the labelling to contain PPE and other management approaches based on the acceptable MOE.

### Risk from re-entry/re-handling exposure

The risks associated with workers re-entering treated areas or crops is dependent on the MOE to the active constituent based on the number of days (examined from day zero) after treatment. A re-entry interval (REI) may be required. The MOE values for different activities (for example pruning and harvesting) are generally acceptable if they are equal to or greater than 100.

Similarly, the risks associated with workers re-handling treated animals (for example sheep treated with a lousicide) or treated articles (for example timber treated with a fungicide) is also dependent on the MOE to the active constituent based on the number of days (examined from day zero) after treatment. A re-handling interval (RHI) may be required. The MOE values for different activities are generally acceptable if they are equal to or greater than 100.

## 6.2 Public risk assessment

The potential for public exposure is based largely on the likely use of the product. If the product is not intended for domestic use, then in general the risk to the public is considered to be low.

### **Risks from residues in food**

Assessment will be made as to whether there is the potential for any risk associated with food produce through undertaking a residues risk assessment (refer to the Residues and Trade Risk Assessment Manual).

## **Risks from accidental exposure**

The type of use determines whether there is likely to be a risk from accidental exposure. This may include assessing the potential for self-injection injuries, and exposure to the active constituent through splashes, accidental ingestion or contact. For products likely to be used in the home, risks to children from accidental ingestion of the product are evaluated.

### Risks associated with domestic product use

The type of use determines whether there is likely to be risks related to the product's domestic use. If the product is for home garden (HG) or home veterinary (HV) use, the risk assessment is undertaken in much the same way as the occupational risk assessment (see Section 6.1).

Additional non-intended impacts such as post-application exposure through contact with treated surfaces or pets are also considered. Risks to children playing on treated turf (lawns, parks) merit special consideration and are evaluated using a specific turf exposure-risk calculator. The MOE values for children coming into contact with treated turf are generally acceptable if they are equal to or greater than 100 (Table 4).

# Table 4: Sample MOE\* estimates for active constituent X for children playing on surfaces treated with product Y

	MOE					
	1–2 year	1–2 year olds		2-3 year	2–3 year olds	
	Total	Dermal	Oral	Total	Dermal	Oral
Estimated MOE	1485	2602	3460	2605	3173	14530

\*Based on a dermal NOAEL of 100 mg/kg bw/d and an oral NOAEL of 1.5 mg/kg bw/d. Assumed a 1–2 year old child is 11 kg and a 2–3 year old child is 15 kg.

## Bystander risks associated with product use

The risk assessment may consider whether bystanders (including both workers and the general public) may be exposed incidentally to a product for example spray drift or atmospheric vapours. Routes for exposure are likely to be dermal, inhalation and ocular. Parameters for assessing bystander exposure and risks may need to be further determined by the APVMA.

# 7 RISK MANAGEMENT

Risk management is achieved through consideration of the hazard profile of a product in conjunction with the overall risks from the use of a product according to the label instructions.

Possible risk management recommendations made by APVMA include:

- establishing or amending HBGVs, for example ADI and ARfD
- a recommendation for the Scheduling of an active constituent or excipient in the Poisons Standard
- guidance and restrictions on use for example restriction of particular application method; the use of closed mixing and loading systems, or a limit to the maximum quantity of product to be used per day
- guidance on engineering controls for example use of close-cab tractors; incorporation of child-resistant packaging
- safety directions including the use of personal protective equipment
- first aid instructions
- warning statements for example 'not to be handled during pregnancy'
- re-entry or re-handling intervals or statements.



# Appendix

# ABBREVIATIONS

Abbreviation	Full phrase
ADI	Acceptable daily intake
ADME	Absorption, distribution, metabolism and elimination
ADWG	Australian Drinking Water Guidelines
AERP	Adverse Experience Reporting Program
ALARA	As low as reasonably achievable
APVMA	Australian Pesticides and Veterinary Medicines Authority
DAWR	Department of Agriculture and Water Resources
DEE	Department of the Environment and Energy
EPA	Environment Protection Agency
FAISD	First aid instructions and safety directions
FAO	Food and Agriculture Organisation
FSANZ	Food Standards Australia New Zealand
GHS	Globally Harmonised System of Classification and Labelling of Chemicals
GLP	Good laboratory practices
GMP	Good manufacturing practices
HBGV	Health Based Guidance Values
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	Lowest-observed-adverse-effect level
MLS	Manufacturers Licensing Scheme
МОА	Modes of Action
MOE	Margin of exposure
MRL	Maximum residue limit
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
NRS	National Residue Survey

Abbreviation	Full phrase
OCS	Office of Chemical Safety
OECD	Organisation for Economic Co-operation and Development
OGTR	Office of the Gene Technology Regulator
РВТ	Persistent, bioaccumulative and toxic
PEC	Predicted environmental concentration
PHED	US EPA Pesticide Handler Exposure Database
POP	Persistent organic pollutants
PPE	Personal Protective Equipment
REI	Re-entry interval
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
USEPA	USA Environmental Protection Authority
VICH	International Cooperation on Harmonization of Technical Requirements of Veterinary Medicinal Products
WHO	World Health Organization
WHP	Withholding period