Australian Government

Australian Pesticides and Veterinary Medicines Authority

APVMA risk assessment manual

Environment

APRIL 2019

ISSN 2652-0583 (electronic)

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1 ENVIRONMENTAL RISK ASSESSMENT

The assessment of risk to the environment, like the assessment of risk to human health, is a three-step process. A Hazard Assessment determines how toxic a chemical is to non-target animals and plants an Exposure Assessment involves understanding what happens to a chemical once it enters the environment, and Risk Characterisation uses information from the first two steps combined to determine the overall level of risk.

This document intends to provide guidance on how to conduct a risk assessment for non-target species in the context of the review of pesticide and veterinary applications to the APVMA. The document is a working document, which will be updated to take on board scientific advances and expanded guidance as the necessity arises.

1.1 Step 1—Problem formulation

The objective of the problem formulation phase is to define the scope of the environmental assessment. The use pattern is critical in determining what potential groups of non-target species could be exposed that require assessment. For existing active constituents, the APVMA determines which previous decisions can be relied on in relation to a reference product, and what new risks require assessment. The formulation type, the method of application/administration, the mode of action of the active constituent, and its behaviour in the treated crop/animal are important considerations in determining the scope of the environmental assessment.

1.2 Step 2a—Environmental exposure assessment

Once a chemical enters the environment a lot of things can happen to it. It can be moved around by air or water or come to rest in soil. It can be broken down by sunlight, water or microorganisms. It can also be taken up by plants and animals, where it can either be metabolised (broken down by an organism) or bioaccumulate (stored in an organism's tissues). Scientists take all these factors into account when conducting studies to determine the behaviour, or fate, of a chemical in the environment.

A chemical's fate also depends upon how it is used. For example, a chemical delivered through a spray mechanism may behave differently from one added directly to soil or to one fed to an animal. When conducting environmental exposure assessment scientists consider factors such as the method of application, the target crops or animals, what time of the year it is usually applied and the geographic area in which it will be used.

The final product of an environmental exposure assessment is the calculation of a Predicted Environmental Concentration (PEC). A PEC is an estimated value of how much of a chemical (and its break-down components) is likely to be found in a particular part of the environment, such as water or soil or sediment, as a result of normal use. PECs are estimated using standard models that consider the application rate(s), chemical and environmental fate properties, including the dissipation/metabolism of the active constituent between applications/treatments. This value provides one part of the information needed to establish the overall level of risk, or **Risk Characterisation**.

1.3 Step 2b—Environmental hazard assessment

Some chemicals are more toxic than others. The purpose of the environmental hazard assessment is to determine the hazard to non-target plants and animals of a chemical, based on its toxicity.

Toxicity is generally established in controlled laboratory settings. Laboratory studies determine the effects of short and long-term exposure to particular chemicals on small numbers of selected animal and plant species, including birds, insects, earthworms and water-based plants and animals such as fish and aquatic invertebrates. Such tests typically use worst-case conditions, eg sensitive life stages and constant exposure. Appropriate end-points from mammalian toxicology data are used to support the wild mammal assessment.

Regulatory bodies around the world assess toxicity tests using the same general approach. Because of this harmonized approach for testing, registrants are often able to conduct one mutually acceptable study that satisfies global requirements.

When determining the toxicity of a particular chemical, scientists are interested in determining the lethal level of short-term exposure and also the longer-term impacts on growth, development and reproduction. Some more complex studies investigate the impact on the composition of a species, on an ecological community and on an entire ecosystem.

Ecotoxicity endpoints used in the risk assessments are adjusted to determine regulatory acceptable concentrations (RACs) to account for potential differences in species sensitivity as well as varying protection goals (ie protection at the community, population, or individual level). This value provides the other part of the information needed to establish the Risk Characterisation.

1.4 Step 3—Environmental risk characterisation

Risk characterisation is the final step in the risk assessment process. In this step, the results of the first two steps are combined to produce an estimate of the overall risk to the environment of a particular chemical.

There are a number of different methods available to determine the overall level of risk. The assessment usually begins at a ‘screening level’ that assumes the worst-case scenario of direct exposure to the maximum possible exposure concentration, dose or rate, in order to identify those substances and associated uses that do not pose a risk. The screening level assessment employs a deterministic approach, so-called because it determines a single numeric value known as a Risk Quotient, or RQ, which compares the PEC (derived in Step 1) to the regulatory acceptable value (derived in Step 2).

Some chemicals have the potential to be highly toxic and persistent in the environment for a very long time. Particular care is required when assessing persistent, bioaccumulative and toxic (PBT) chemicals, whose effects on the environment are often apparent only after a prolonged period of time. Australia has international obligations when assessing chemicals, including the Stockholm Convention on Persistent Organic Pollutants (POPs)[1]. The APVMA takes these obligations very seriously and assesses each Agvet chemical with respect to its persistence in the environment, the ability of the chemical to bioaccumulate and its toxicity to environmental organisms.

1 www.pops.int/Home/tabid/2121/Default.aspx

1.5 Refining the risk assessment

The APVMA can require additional studies to be conducted on a product. Additional studies are aimed at developing a more accurate understanding of the risks to the environment from a particular chemical product, which in turn allows regulators to establish more effective rules for its use. For example, a field study may be requested to determine whether or not a chemical behaves the same way ‘in nature’ as it does in a laboratory. Or an ecotoxicology test may be requested to ascertain if the impact of a chemical on one or two species in the laboratory is applicable to the impacts that might be seen on a whole ecosystem.

2 REGULATORY FRAMEWORK

The Agricultural and Veterinary Chemicals Code (Agvet Code), provides the basis for using risk analysis to regulate activities with agricultural and veterinary chemicals (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 chemical products or veterinary chemical products; and the evaluation, registration, and control of the manufacture and supply, of agricultural chemical products and veterinary chemical products.

The Act mandates that the APVMA implement the Code in a manner, amongst other things, that

- recognises that the health and safety of human beings, animals and the environment is the first priority of the regulatory system
- reflects established best-practice principles for the assessment and management of risk, based on science
- balances regulatory effort and any burden with the risk of the use of the products and constituents to the health and safety of human beings, animals and the environment.

In considering the environmental safety of the proposed use of a product, the APVMA must have regard to the toxicity of the active constituent and its residues, including metabolites and degradation products, in relation to relevant organisms and ecosystems. The APVMA must also be satisfied under s14 of the *Agricultural and Veterinary Chemicals Code Act 1994* that the proposed use of the product meets the environmental safety criteria with respect to s5A(1)(c), and the labelling criteria under s5D(1) (or s112(2)(d) for permits).

3 KEY FATE ENDPOINTS

The assessment should identify the key regulatory endpoints for use in the environmental exposure assessment.

For screening level assessments for products multiple times in one season, the predicted environmental concentration (PEC) is calculated assuming non-target species are exposed to the peak concentration immediately after the last application. Dissipation of the active constituent between applications is considered. The following equation is used to calculate the cumulative rate used in the exposure assessment.

Cumulative rate = Single rate $(1 - EXP(-N * ln2/DT_{50} * interval))/(1 - EXP(-ln2/DT_{50} * interval))$

in which:

Cumulative rate = accumulated application rate immediately after the last application (g ac/ha)

Single rate = single application rate (g ac/ha)

N = number of applications

DT_{50} = half-life in relevant environmental compartment

Interval = time between application (d)

For assessment of runoff risks to aquatic species, and risks to soil organisms and pre-emergent exposure to non-target terrestrial plants, a soil DT_{50} value is used in the calculation of the cumulative exposure rate. Typically the longest field DT_{50} is used for screening level assessments; however, the most appropriate value is determined using expert judgement based on the available data and the tier of assessment.

For the assessment of terrestrial vertebrates, bees & other non-target arthropods, the typically a default DT_{50} value of 10 days is applied for dissipation on foliage and/or food items. Dissipation data can be used to refine the assessment if it is shown that the dissipation of the active constituent is faster than assumed.

For assessment of aquatic species (screening level and spray drift assessments), a water phase or whole water/sediment system DT_{50} value is typically used. For assessment of sediment dwelling species (screening level and spray drift assessment), whole water/sediment system DT_{50} is typically used.

When a runoff assessment is required, it is also necessary to consider adsorption parameters to soil and sediment. For a screening level assessment, the predicted K_d value for the soil of 1 per cent organic carbon is used (and 5 per cent organic carbon when predicting adsorption to sediment) using a regression analysis of the available data. Higher tier assessments would consider more realistic K_d values based on the region or that appropriate for the crop/site being assessed.

Table 1: Key regulatory endpoints for exposure assessment

Compartment	Value	Source
Foliage/food items	DT_{50}Xd	eg default
Soil	DT_{50}Xd	eg longest field half-life from eight sites
	K_dX mL/g	eg predicted for 1% OC based on regression
Water	DT_{50}Xd	eg longest water phase value from two water/sediment systems
Sediment	DT_{50}Xd	eg geomean whole system value from two water/sediment systems
	K_p X mL/g	eg predicted for 5% OC based on regression
Air	eg Not relevant. Not volatile.	

4 COMBINED RESIDUES

For new combinations of active constituents, whether as a mandatory tank mix or in formulation, short-term risks of direct exposure to combined residues to non-target species immediately after application are assessed.

Wild mammals and birds could be exposed to combined residues if over-sprayed food sources are consumed immediately after application. Aquatic species and non-target terrestrial plants could be exposed after application as a result of spray drift. Bees could be exposed to combined residues when visiting over-sprayed plants in bloom during treatment, or immediately after application. Similarly, other beneficial (predatory and parasitic) arthropods could be exposed to combined residues on treated plants during or immediately after treatment. Soil organisms (macro- and micro-organisms) could be directly exposed to combined residues in over-sprayed soil within the treatment area.

Endpoints are obtained from formulation toxicity data provided. In the absence of formulation toxicity data, combination toxicity is estimated assuming additive toxicity for organisms. The method for predicting the toxicity value for combined residues follows a pragmatic approach using the concentration addition model detailed by Altenburger et al. (2013). It is assumed that the toxicity of the mixture is attributed to the active constituents. Where one active constituent is calculated to contribute to >90 per cent of the toxicity of combined residues, then risks of combined residues are considered to be no greater than the individual active constituents.

Predicted formulation toxicity values can also be calculated to compare with the toxicity studies provided as to provide validation of the predicted values. EFSA (2013) provides rationale for checking the plausibility of the measured formulation toxicity against the calculated mixture toxicity. This is defined as the model deviation ratio (MDR) where the ratio of the calculated value is divided by that of the measured value. In interpreting the MDR, if the value falls between 0.2 and 5, CA is assumed to hold for the mixture. Where the MDR is >5, the toxicity of the mixture is considered more than additive, and where the MDR is <0.2, the toxicity of the mixture is considered to be less than additive.

Table 2: Toxicity of combined residues to non-target species

	Active 1	Active 2	Combined residues [2] [3] [4]
Fraction in combination	0.XX	0.XX	1.00
Acute toxicity to mammals	LD_{50} XX mg ac/kg bw Test item *Test species* Reference	LD_{50} XX mg ac/kg bw Test item *Test species* Reference	Measured: LD_{50} XX mg acs/kg bw Test item *Test species* Reference Predicted: LD_{50} XX mg acs/kg bw Relative toxicity contributions: X% + X% MDR X
Acute toxicity to birds	LD_{50} XX mg ac/kg bw Test item *Test species* Reference	LD_{50} XX mg ac/kg bw Test item *Test species* Reference	Measured: LD_{50} XX mg acs/kg bw Test item *Test species* Reference Predicted: LD_{50} XX mg acs/kg bw Relative toxicity contributions: X% + X% MDR X

[2]Predicted values calculated assuming additive toxicity of active constituents in a the specified ration ($_{P1}$:$_{P2}$) using most sensitive endpoints reported for that organism group where:

$$ECx_{CA} = \left(\frac{1}{\sum_{i-1}^{n} \frac{P_i}{ECx_i}} \right)$$

Where:
ECx_{CA} is the predicted additive toxic effect of the active constituent in combination
Pi = is the fraction of individual active constituent in the product

EC_{xi} is the effect concentration of the individual active constituent

[3] $$\%_{relative_{ecotoxicity_{contribution}}} = \frac{\frac{p_i}{EC_{x_i}}}{\sum_{i=1}^{n} \frac{p_i}{EC_{x_i}}} \times 100$$

[4] MDR = model deviation ratio (unitless) = measured EC_{50} / predicted EC_{50}, toxicity of combined residues is considered more than additive if MDR <0.2, additive if MDR 0.2-5, and less than additive if MDR >5

	Active 1	Active 2	Combined residues [2] [3] [4]
Fraction in combination	0.XX	0.XX	1.00
Acute toxicity to fish	LC_{50} XX mg ac/L Test item *Test species* Reference	LC_{50} XX mg ac/L Test item *Test species* Reference	Measured: LC_{50} XX mg acs/L Test item *Test species* Reference Predicted: LC_{50} XX mg acs/L Relative toxicity contributions: X% + X% MDR X
Acute toxicity to aquatic invertebrates	EC_{50} XX mg ac/L Test item *Test species* Reference	EC_{50} XX mg ac/L Test item *Test species* Reference	Measured: EC_{50} XX mg acs/L Test item *Test species* Reference Predicted: EC_{50} XX mg acs/L Relative toxicity contributions: X% + X% MDR X
Toxicity to algae	E_rC_{50} XX mg ac/L Test item *Test species* Reference	E_rC_{50} XX mg ac/L Test item *Test species* Reference	Measured: E_rC_{50} XX mg acs/L Test item *Test species* Reference Predicted: E_rC_{50} XX mg acs/L Relative toxicity contributions: X% + X% MDR X

	Active 1	Active 2	Combined residues [2] [3] [4]
Fraction in combination	0.XX	0.XX	1.00
Toxicity to aquatic plants	EC_{50} XX mg ac/L Test item *Test species* Reference	EC_{50} XX mg ac/L Test item *Test species* Reference	Measured: EC_{50} XX mg acs/L Test item *Test species* Reference Predicted: EC_{50} XX mg acs/L Relative toxicity contributions: X% + X% MDR X
Oral toxicity to bees	LD_{50} XX µg ac/bee Test item Test species Reference	LD_{50} XX µg ac/bee Test item Test species Reference	Measured: LD_{50} XX µg acs/bee Test item *Test species* Reference Predicted: LD_{50} XX µg acs/bee Relative toxicity contributions: X% + X% MDR X
Contact toxicity to bees	LD_{50} XX µg ac/bee Test item *Test species* Reference	LD_{50} XX µg ac/bee Test item *Test species* Reference	Measured: LD_{50} XX µg acs/bee Test item *Test species* Reference Predicted: LD_{50} XX µg acs/bee Relative toxicity contributions: X% + X% MDR X

	Active 1	Active 2	Combined residues [2] [3] [4]
Fraction in combination	0.XX	0.XX	1.00
Toxicity to predatory arthropods	LR_{50} XX g ac/ha Test item *Test species* Reference	LR_{50} XX g ac/ha Test item *Test species* Reference	Measured: LR_{50} XX g acs/ha Test item *Test species* Reference Predicted: LR_{50} XX g acs/ha Relative toxicity contributions: X% + X% MDR X
Toxicity to parasitic arthropods	LR_{50} XX g ac/ha Test item *Test species* Reference	LR_{50} XX g ac/ha Test item *Test species* Reference	Measured: LR_{50} XX g acs/ha Test item Test duration + medium *Test species* Reference Predicted: LR_{50} XX g acs/ha Relative toxicity contributions: X% + X% MDR X
Acute toxicity to soil macro-organisms	LC_{50} XX mg ac/kg dry soil Test item *Test species* Reference	LC_{50} XX mg ac/kg dry soil Test item *Test species* Reference	Measured: LC_{50} XX mg acs/kg dry soil Test item Test duration + medium *Test species* Reference Predicted: LC_{50} XX mg acs/kg dry soil Relative toxicity contributions: X% + X% MDR X

	Active 1	Active 2	Combined residues [2] [3] [4]
Fraction in combination	0.XX	0.XX	1.00
Toxicity to soil micro-organisms	NOEC XX mg ac/kg dry soil (indicate % effect at LOEC or <25% effect at limit dose) Test item Soil process Reference	NOEC XX mg ac/kg dry soil (indicate % effect at LOEC or <25% effect at limit dose) Test item Soil process Reference	Measured: NOEC XX mg acs/kg dry soil (indicate % effect at LOEC or <25% effect at limit dose) Test item Soil process Reference Predicted: NOEC XX mg acs/kg dry soil Relative toxicity contributions: X% + X% MDRX
Effects of seedling emergence	ER_{50} XXg ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference	ER_{50} XXg ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference	Measured: ER_{50} XXg ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference Predicted: ER_{50} XX mg acs/kg bw Relative toxicity contributions: X% + X% MDR X
Effects on vegetative vigour	ER_{50} XX g ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference	ER_{50} XX g ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference	Measured: ER_{50} XXg ac/ha Test item Tier of testing *Test species* (or #species tested if >value) Reference Predicted: ER_{50} XX mg acs/kg bw Relative toxicity contributions: X% + X% MDR X

5 OVERALL CONCLUSIONS

Overall conclusion statements for each of the potential environmental impacts are presented, with appropriate restraints and protection measures that enable a conclusion of acceptable risk (or otherwise) to non-target species. This includes:

- fate and transport considerations
- effects and associated risks to:
    - terrestrial vertebrates (including birds and mammals)
    - aquatic species (including fish, invertebrates, algae and aquatic plants)
    - bees
    - other beneficial (predatory and parasitic) arthropods
    - soil organisms (macro- and micro-organisms)
    - non-target terrestrial plants.

6 LABELLING RECOMMENDATIONS

Recommendations for labelling will be based on the outcomes of the risk assessments, reference product labels and current labelling standards. The environmental assessment does not consider storage conditions of the product; however, appropriate disposal statements will be recommended as per the Ag and Vet labelling codes.

7 REFERENCES

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ABBREVIATIONS

AC	Active constituent
ACS	Active constituents
APVMA	Australian Pesticides and Veterinary Medicines Authority
BW	Body weight
DDD	Daily dietary dose
DDSD	Daily dry soil dose
DGD	Daily granule dose
DT_{50}	Period required for 50 per cent dissipation
DT_{90}	Period required for 90 per cent dissipation
EC_{50}	Effective concentration, median
E_rC_{50}	Effective concentration, median, growth rate
E_yC_{50}	Effective concentration, median, yield
EFSA	European Food Safety Authority
EPHC	Environment Protection and Heritage Council
EPPO	European and Mediterranean Plant Protection Organization
ER_{25}	Effective rate, 25th per centile
ER_{50}	Effective rate, median
EUBEES	European Union Biocides Environmental Exposure Scenario working group
FIR	Food Intake Rates
HR5	Hazardous rate to 5% of the species
IPM	Integrated Pest Management
K_d	Adsorption constant
K_{oc}	Organic carbon absorption coefficient
K_{ow}	Octanol-water partition coefficient
LC_{50}	Lethal concentration, median
LD_{50}	Lethal dose, median

LOEC	Lowest observed effect concentration
LR_{50}	Lethal rate, median
MDR	Model deviation ratio
MRL	Maximum residue limit
NAR	Nominal (loading) application rate
NOAEL	No-observed-adverse-effect level
NOEC	No-observed-effect concentration
NOEL	No-observed-adverse level
OECD	Organisation for Economic Co-operation and Development
PAA	Pre-application Assistance
PBT	Persistent, bioaccumulative and toxic
PD	Composition of diet obtained from treated area
PEC	Predicted environmental concentration
pKa	Negative logarithm (to the base 10) of the dissociation constant
POP	Persistent organic pollutants
PT	Proportion of diet obtained from treated area
RAC	Regulatory acceptable concentration
RAD	Regulatory acceptable dose
RAL	Regulatory acceptable level
RAR	Regulatory acceptable rate
RQ	Risk quotient
USEPA	USA Environmental Protection Authority
VICH	International Cooperation on Harmonization of Technical Requirements of Veterinary Medicinal Products