



**National
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Authority**

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Veterinary Chemicals

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7-1 INTRODUCTION

Environment Australia is the environment program of the Commonwealth Department of the Environment. It undertakes environmental hazard assessments for new veterinary chemical products or variations to those products as defined in Module B of the *Vet Manual*. It performs these assessments on behalf of the Australian and New Zealand Environment and Conservation Council (ANZECC). This part of the manual discusses the assessment process and data requirements (section 7-2 and 7-3) and provides detailed notes and examples (section 7-4).

7-1.1 Reference materials

The details of documents referred to in these instructions (including codes and standards) is given in the References section. Bibliographic details and, where appropriate, ISBN and purchase information are given. Applicants should be aware that many of these documents are updated regularly (hence dates are not supplied in the text). It is therefore important to ensure that the latest editions of reference materials are obtained.

7-2 OVERVIEW OF THE ASSESSMENT PROCESS

Environment Australia establishes the hazard to the environment of a product from the assessment process by using the information the company provided. Information available from other sources, such as literature searches and United States Environmental Protection Agency (US EPA) reports, may also be used.

The environmental hazard of the chemical is determined, by a synthesis of data, for:

- the degree of environmental exposure, and
- the toxicity of the chemical to aquatic and terrestrial fauna and flora.

Such an assessment of hazard may highlight the need for further data or clarification. Environment Australia may therefore request additional information

(e.g. monitoring trials or elaboration of certain test methodologies or results).

Depending on the degree of environmental hazard, and to further minimise environmental risk, Environment Australia may also recommend:

- specific restraints (e.g. *Do not apply 6 months prior to shearing*); or
- label instructions and warnings (e.g. *Dangerous to fish and other aquatic organisms*).

7-3 OUTLINE OF DATA REQUIREMENTS AND APPLICATION LAYOUT

The data requirements for studies on environmental chemistry and fate and environmental toxicology of the application are given in Tables 7-1 and 7-2, respectively. Refinement of these requirements might be possible, and is discussed below. When available, dossiers prepared to European Union (EU) or United States (US) guidelines are acceptable, but may need to be re-ordered to meet the Australian format. Applicants may also need to re-work hazard calculations to meet any specific Australian conditions.

Applicants should present all relevant data under the appropriate section headings. These data should support the assessment of potential environmental exposure (see Explanatory Note 7-4.2) and assessment of environmental hazard (see Explanatory Note 7-4.3).

Alternatively, where the applicant considers that data are not required, their omission (or modification) should be justified by including a statement under the appropriate section heading (see Explanatory Note 7-4.1).

The environmental exposure and fate of a chemical depend on its movement, transport and likely destination compartment (defined as 'sink'). Environment Australia also considers the chemical in the 'cradle-to-grave' context, i.e. including the potential for release through manufacturing, formulation, and disposal of spent (tank-mixed) and unused product and containers, as well as the proposed use. To assess the environmental

risk of the chemical from such supply, use and disposal, the following data are requested:

- biological, physical and chemical properties of the active constituent;
- manufacturing and formulation details (including fate of off-specification batches);
- method of its application;
- use pattern; and
- details on disposal of unused and spent product, and empty containers.

Only data relevant to the likely environmental exposure of the chemical need to be submitted. The applicant should consider the likely exposure by:

- determining the relevant areas; and
- providing appropriate data or justifying any omissions and modifications.

Exposure may range from significant exposure (e.g. medicated drinking water to poultry) to very limited exposure (e.g. single dose hormonal treatment for individual mares). Metabolism data (see Part 4, Metabolism and Kinetics) should be provided, as excretion is often the main pathway for environmental exposure for many veterinary drugs.

The following examples (considering only use of the chemical) indicate how an application may be tailored to specific chemicals. Further discussion is in Explanatory Note 7-4.1, including what test guidelines are acceptable.

Example 1: Poultry drug

Where it is proposed to add a product to poultry drinking water, the soil compartment is of most concern since it is likely that the chicken litter, containing the drug or its metabolites, will be used as manure or fertiliser. Therefore, soil metabolism and toxicity to terrestrial invertebrates need to be addressed in particular.

Example 2: Gonadotropin use in mares

Where a gonadotropin is proposed to regulate the estrous cycle in individual mares, minimal data will be required if it can be demonstrated that the chemical

Table 7-1: Data requirements for Part 7, Environmental Chemistry and Fate

Part 7-1 Environmental Chemistry and Fate	
7.1.1*	Table of contents
7.1.2*	Summary
7.1.3*	Assessment of extent of, and potential for, environmental exposure
	(a)* Amount of chemical to be used
	(b)* Manufacturing plant (active constituent)
	(c)* Formulating plant (product)
	(d)* Use and application
	(e)* Product disposal
	(f)* Accidental release
7.1.4*	Physicochemical degradation
	(a)* Hydrolysis
	(b) Photodegradation (aqueous, soil, degradation in air)
7.1.5*	Biodegradation
	(a)* Soils (aerobic, anaerobic)
	(b)* Water
7.1.6	Mobility
	(a) Volatility
	(b)* Adsorption/desorption
	(c) Leaching potential
7.1.7	Field dissipation
	(a) Soils
	(b) Water
	(c) Air
	(d) Plants
7.1.8	Accumulation/Metabolism
	(a) Bioaccumulation in fish/aquatic organisms
	(b) Accumulation potential in soils
	(c) Metabolism in target animals
	(d) Other (e.g. birds, earthworms)
7.1.9	Modelling studies
7.1.10	Applicant's proposed directions for storage and disposal

* Denotes base set studies—see Explanatory Note 7-4.1.

The emphasis should be on soil studies (e.g. soil photodegradation studies would generally be more relevant than air or water photodegradation studies) unless the fate is clearly likely to be to involve other environmental compartments (e.g. sheep lousicides and aquaculture chemicals would require the fate of the chemical in water to be considered as lousicides will reach water after scouring of wool and aquaculture chemicals will be added directly to water).

Table 7-2: Data requirements for Part 7, Environmental Toxicology

Part 7-2 Environmental Toxicology	
7.2.1*	Table of contents
7.2.2*	Summary
7.2.3	Birds, mammals and other vertebrates (wild)
	(a) Acute
	(b) Short-term
	(c) Special studies — chronic, reproduction, simulated or actual field-testing, etc.
7.2.4	Aquatic organisms (freshwater and marine)
	(a) Acute (fish, microcrustacean, algae)*
	(b) Short-term (sub-chronic)
	(c) Special studies—chronic, sediment, simulated or actual field-testing, etc.
7.2.5	Non-target invertebrates (terrestrial)
	(a) Predators
	(b) Parasites
	(c) Bees
	(d) Earthworms and soil invertebrates*
	(e) Soil micro-organisms*
	(f) Other
7.2.6	Non-target vegetation
	(a) Results from laboratory tests*
	(b) Observations from field trials/efficacy tests
7.2.7	Assessment of environmental hazard
7.2.8	Proposed environmental protection statement
* Denotes base set studies—see Explanatory Note 7-4.1.	
The emphasis should be on soil studies (e.g. soil micro-organism studies would generally be more relevant than aquatic organism studies) unless the fate is clearly likely to involve other environmental compartments (e.g. run-off carrying the chemical from land where manure is spread). If aquatic toxicity tests are not provided, then it should be clearly demonstrated that the chemical would not reach water.	

breaks down to its 'basic biochemical building blocks' (e.g. constituent amino acids) within the animal.

7-4 EXPLANATORY NOTES

Definitions of terms are given in the Glossary.

7-4.1 Data requirements

Environment Australia will review all new veterinary chemical products, even if environmental exposure may be expected to be low, and those resulting in a significant increase in environmental exposure. Anything resulting in widespread environmental exposure will potentially require the full data set, unless Environment Australia has previously assessed the chemical. If this is the case, then the data set would only be required to be updated and supplemented where needed.

The use pattern together with its scale of use, type of formulation and mode of application, however, could modify the data requirements and is now discussed.

(a) Factors determining data requirements

Figure 7-1 gives an idea of the potential complexity in being prescriptive in setting data requirements, given all the possible permutations of the four categories listed. Each column is arranged in approximate decreasing order of potential environmental exposure, from high at the top, to low at the bottom. This may be used as a rough scale of the extent of environmental data likely to be required. While applicants may consider the 'base sets' described in Tables 7-1 and 7-2 as those requirements which are likely to be needed given any use, the applicant should argue the case for omitting data.

Given the constraints above, Table 7-3 gives an indication of the data requirements needed to be addressed for

Figure 7-1: Matrix of some factors determining environmental data requirements (indicative)

Group	X	Scale of Use	X	Type of formulation	X	Mode of application
intensive animal production e.g. pigs, poultry		intensive/extensive production		internal parasite agents		dip
cattle and sheep e.g. dairy, beef, wool		multiple application		lousicide/insecticide		pour-on
aquaculture e.g. Atlantic salmon, prawns, shell-fish	X	herd application	X	coccidiostat	X	drench
horses		part-herd application		antibiotic		injection
companion animals e.g. dogs, cats		single application		anti-inflammatory		tablet
other e.g. breeding stock				hormone		topical cream

each of the six 'groups' given in Figure 7-1. This is not an exhaustive tabulation but should act as an example and a guide in the applicant's decision-making process (that is, it is not definitive). For example, injections or pour-ons with highly toxic anthelmintic active constituents for controlling internal parasites may pose a high hazard to dung beetles, and substantial data in this area (i.e. fate in dung and soil and effects on terrestrial non-target invertebrates) would need to be provided. Similarly, coccidiostats to control coccidiosis in poultry would need data on the effects on terrestrial non-target invertebrates likely to be exposed through the spreading of chicken manure to land. Potential variations are further discussed in 7-4.1(b).

(b) Variations in data requirements

Environment Australia will review all new veterinary chemical products, even though environmental exposure may be expected to be low. In these instances, however, data requirements may be varied:

- Environmental assessments for *similar* products will not generally be performed;
- Environmental assessments for *vaccines* will not generally be performed;
- Any extension in claims of use for a veterinary chemical product already in widespread use is not likely to warrant

assessment. This would be meaningless unless all current uses were also assessed (e.g. through the Existing Chemicals Review Program). An exception would be if the extension in claim clearly led to a significant increase in environmental exposure, or Environment Australia had already performed a comprehensive assessment;

- For those compounds which are naturally occurring substances used at natural concentrations as well as those extensively metabolised to 'basic biochemical building blocks', a brief environmental exposure assessment will be undertaken, for which metabolism data (as provided in Part 4, Metabolism and Kinetics) will be needed but no environmental effects data may be necessary;
- For some groups (those marked * in Table 7-3), environmental assessment will be undertaken but, except for metabolism information, environmental data may not be required if the volumes for use in these categories is low. The actual limit will depend on the application (e.g. 25 kg if the proposed use is for fleas where a relatively toxic insecticide will be used; or 100 kg where the active constituent is expected to be less toxic to non-target organisms, such as an anti-inflammatory agent). It will also depend on the actual

Table 7-3: Data requirements for groups given in Figure 7-1

Group	Factors to consider	Minimal data requirements to be addressed#
intensive animal production	Use and mode of application lead to wide environmental exposure (e.g. multiple shed application at one site of coccidiostats as prophylactics in broiler production from which manure is then used in agriculture).	all parts in Tables 7-1 and 7-2
	Use and mode of application lead to localised environmental exposure (e.g. effluent from pig production is irrigated on adjacent fields for disposal).	all parts in Tables 7-1 and 7-2
	Use and mode of application lead to low environmental exposure (e.g. single animal/single injection).	base set in Tables 7-1 and 7-2, although a case could be argued to further restrict data set (e.g. tests under 7-1.4(a), 7-1.5, 7-2.4(a), 7-2.5 and 7-2.6(a) may not be needed depending on the expected fate of the chemical)
cattle, sheep	Use and mode of application lead to wide environmental exposure (e.g. herd application of an anthelmintic chemical).	all parts in Tables 7-1 and 7-2
	Use and mode of application lead to localised environmental exposure (e.g. effluent from intensive beef production is irrigated on adjacent fields for disposal).	all parts in Tables 7-1 and 7-2
	Use and mode of application lead to low environmental exposure (e.g. single animal/single injection).	base set in Tables 7-1 and 7-2, although a case could be argued to further restrict data set (e.g. tests under 7-1.4(a), 7-1.5, 7-2.4(a), 7-2.5 and 7-2.6(a) may not be needed depending on the expected fate of the chemical)
aquaculture	Single or multiple application with a range of possible environmental exposures — from land-based tanks and ponds to ocean pens.	base set in Tables 7-1 and 7-2, although a case could be argued to further restrict data set (e.g. 7-1.5(a), 7-2.5(d) may not be needed)
horses*	Single or multiple application with generally limited environmental exposure. The treatment of whole stables may be an exception.	base set in Tables 7-1 and 7-2, although a case could be argued to further restrict data set if use was very limited (e.g. tests under 7-1.4(a), 7-1.5, 7-2.4(a), 7-2.5 and 7-2.6(a) may not be needed depending on the expected fate of the chemical)
companion animals*	Single or multiple application but tending to be on a restricted scale (i.e. single animals). However, in cases of widespread use, broad environmental exposure (e.g. whole kennels) could result.	all parts in Tables 7-1 and 7-2, although a case could be argued to further restrict data set (e.g. 7-1.4(a), 7-1.5, 7-2.4(a) and 7-2.6(a) may not be needed)
other* e.g. breeding stock	Single or multiple application to small animals with generally limited environmental exposure.	base set in Tables 7-1 and 7-2, although a case could be argued to further restrict data set (e.g. 7-1.4(a), 7-1.5, 7-2.4(a), 7-2.5 and 7-2.6(a) may not be needed)

The data for each submission is decided on a case-by-case basis — the listing of requirements gives only an indication of the likely minimal level of data requirements to be provided.

* If the volumes for use in these categories is low (see text for details), Environment Australia will assess the product using only the metabolism data provided in Part 4, Metabolism and Kinetics: see text for further details.

dose, length of treatment, and the extent of the metabolism in the target animal. In these cases the applicant should contact the Manager, Risk Assessment and Policy Section, Environment Australia by phone on (02) 6274 1643 or by fax (02) 6274 1610;

- If any volumes of active constituent increase significantly after extension in claims for use, Environment Australia may then determine that the product be assessed. In this instance, the dot point above gives some guidance. It remains though, a judgement by Environment Australia given the circumstances and history of the particular active constituent, and the applicant should contact the Manager of the Risk Assessment and Policy Section (details above) if in any doubt;
- The applicant, in addressing the data requirements, may argue that the data requirement is not needed or needs only minimal data, because of use pattern or indications from other data. For example, if the chemical's soil biodegradation is very rapid, then comprehensive soil adsorption/desorption studies would not be required, or if acute toxicity studies indicate it is practically non-toxic, then short-term and chronic studies may not be needed, unless it is persistent). The reasoning for omitting data must be clearly stated.

For example, an applicant wants to register *Wonderwormer*, a new endoparasiticide of a class of chemicals not previously registered. Data indicates that up to 75% is not metabolised and will be excreted with the faeces, with it being strongly absorbed to the faeces. Environmental exposure to *Wonderwormer* will mainly occur in soil which receives residues of the drug in cattle dung, with significant aquatic contamination not expected because of the strong affinity of the drug for organic matter. As *Wonderwormer* will be available as a pour-on for use on cattle in feedlots and on pasture, the applicant would need to provide relevant laboratory studies for

degradation, mobility and accumulation, as well as field dissipation data. For environmental effects data, Environment Australia would require additional data on dung beetles as well as the soil micro-organisms and invertebrates from the base set studies.

Another applicant wants to register a backlining product to control lice on sheep. However, lousicides have implications for the environment when the fleece is scoured, with grease and dirt fractions during scouring discharged in aqueous effluents. The level of environmental exposure obviously depends on the residue level in greasy wool at shearing and on the degree of removal before effluent discharge to the environment. The residue level at shearing will depend on the degradation rate of the chemical in the fleece and the periods between applications and shearing. The applicant will therefore need to provide fleece degradation data to support the proposed wool withholding period, data on the fate of the chemical after scouring, and possibly more extensive environmental effect data for aquatic species.

The type of hazard calculation for each of these examples is explored in greater detail in 7-4.3(c).

For chemicals (and the major degradates) that may persist in the environment (indicated through laboratory studies on hydrolysis, photolysis, metabolism studies, and frequency of application), field dissipation and accumulation studies will be essential, particularly if exposure is high. In this case, the scale of field use (i.e. extensive versus intensive production) cannot be used to justify omission of such data. A chemical might be very persistent, used at high rates and mobile, and therefore of possible concern in its potential to accumulate and/or leach to groundwater, even if used in a part herd application in extensive production.

Any data generated from field dissipation studies, or other studies performed for 'realism' or 'environmental relevance', should use the appropriate formulations

(i.e. those to be used in Australia) to be of most value in the assessment of hazard of the active constituent.

Applicants should also be aware of industry initiatives dealing with the hazard of chemicals on the environment. For example (and especially relevant for the next section (7-4.1(c)), the program by the wool industry to reduce pesticide levels in greasy wool.

If applicants are unclear on data requirements, contact the Manager, Risk Assessment and Policy Section, Environment Australia by phone on (02) 6274 1643 or by fax (02) 6274 1610.

For the two examples in Section 7-3:

The poultry drug would need to address all parts in environmental chemistry and fate, as well as some biodegradation (i.e. metabolism/transformation in the animal and in excreta/soil) studies, especially those performed using a relevant (i.e. soil) test system. A base set of environmental toxicology would be needed, particularly those tests dealing with soil-dwelling micro-organisms and invertebrates because of its high terrestrial (soil) exposure. The applicant might argue if the residues are found to be immobile, however, that minimal aquatic toxicology data are needed.

The gonadotropin use in mares may only need a brief exposure information, including metabolism/transformation (in the animal) studies, due to its potential for biodegradation to 'basic biochemical building blocks' (i.e. amino acids).

(c) Standard of test protocols to fulfil data requirements

Environment Australia generally accepts studies performed using internationally accepted protocols, such as US EPA, EU, Organisation for Economic Co-operation and Development (OECD), or American Society for Testing and Materials (ASTM) pesticide guidelines and other relevant test protocols.

Environment Australia also recognises that several areas are undergoing considerable development. Therefore, other studies will be acceptable if they follow scientifically defensible practice. Such studies should employ sound laboratory procedures, and adhere to good laboratory practice (GLP) or its equivalent. National Association of Testing Authorities (NATA)-approved laboratories should perform tests in Australia where possible.

7-4.2 Assessment of extent of, and potential for, environmental exposure

The applicant should assess the likely extent of, and potential for, environmental exposure, using:

- the estimated quantity of the chemical to be used up to, and including, market maturity;
- the biological, physical and chemical properties of the chemical;
- its method of application and use-patterns; and
- the method of disposal.

The assessment will determine which compartment(s) of the environment (air, soil, water and biota) will be exposed to the chemical, and the likely level of exposure through its use as stated on the proposed product label.

(a) Amount of chemical to be used

The estimated quantity (in tonnes or litres) of chemical/product to be imported, manufactured, formulated or repacked up to, and including, market maturity.

(b) Manufacturing plant (active constituent)¹

Environment Australia considers the chemical in the context of 'cradle-to-grave' (see section 7-3). For those active constituents for which approval is sought, and where the manufacturing plant is located in Australia, the applicant should therefore provide a brief summary² of:

¹ The amount of chemical likely to be released to the environment is a central tenet of environmental hazard assessment. This includes consideration of environmental exposure arising from the manufacture as well as the use of the product. An overview of manufacturing procedures and processes is all that is required.

² Such descriptions need not be elaborate or specific, but should indicate the general procedures that would be followed at such plants and an estimate (e.g. as a percentage of that product) of chemical lost to the environment.

- (i) details of release of the chemical to the environment resulting from manufacture. This will total amounts released to water, air, land, and technology used to minimise release, and
- (ii) proposed means of disposal of waste active constituent arising from manufacturing operations (e.g. spilled material and off-specification batches).

(c) Formulating plant (product)¹

As for (b) above, the applicant should provide a brief summary² of the following for all product formulation and packaging processes taking place in Australia:

- (i) details of release of the chemical to the environment resulting from all formulation and packaging operations (e.g. from disposal of bulk containers and rinsings from cleaning machinery). This will include total amounts released to water, air and land, concentrations in effluent streams, and control technology used; and
- (ii) proposed means of disposal of waste product arising from formulation and packaging operations (e.g. spilled material and off-specification batches).

(d) Use and application

To accurately assess the environmental hazard, the applicant should provide information about label claims (uses) and details of factors affecting transport of the chemical to determine which environmental compartment is the most likely to be exposed to the chemical (see 7-4.1(b), Figure 7-1 and Table 7-3).

Therefore, information is needed on the:

- (i) details of the method of application (e.g. dip, pour-on, drench, injection, tablet and topical cream, etc);
- (ii) details of factors affecting transport of the chemical (e.g. type(s) of systems used to remove dung or faeces containing the material, such as spreading manure or irrigating effluent, or the possible effect of dung beetles burying dung containing the chemical); and

- (iii) fundamental characteristics of the environment which may influence transport and degradation of the chemical (e.g. soil types and range that might receive manure or effluent, rainfall, cropping system and area under cultivation to that crop, etc).

(e) Product disposal

Information should be provided on disposal of:

- (i) empty containers;
- (ii) unused product; and
- (iii) diluted-for-use chemical.

The applicant should consider recent developments in these areas and, in particular, should highlight whether modifications or alternative approaches for disposing of containers of the product under consideration is possible. Such advice might be sought through the Industry Waste Reduction Scheme which targets containers ≥ 1 L or 1 kg and is managed by the Agsafe Office Container Management Project Team. Applicants can contact David Harvest by phone on (02) 6230 6712 or by email on davidh@agsafe.aust.com.

The applicant, in adhering to Good Product Stewardship, should ensure the user of the product is able to deal appropriately with excess diluted-for-use material, unused product, and residues from cleaning of equipment. The applicant should consider whether the excess and other residues could be avoided, re-used or recycled, minimised, or treated, and methods to achieve this; avoidance and re-use would have the greater environmental benefit and would be preferred.

The applicant should ensure that the container disposal statement appearing on the proposed product label is consistent with the information given in the application. This information should advise of suitable techniques for disposal of empty containers.

Any label statement should follow the *Vet Labelling Code: Code of Practice for Labelling Veterinary Chemical Products* (NRA, 1997).

(f) Accidental release

Environment Australia will review the material safety data sheet (MSDS) for the active constituent and product to determine whether the stated measures for clean-up are adequate to protect the environment. The applicant should consider recent developments in these areas, and in particular should highlight whether modifications or alternative approaches for dealing with spillage of the product under consideration are possible.

7-4.3 Assessment of environmental hazard

The aim of the assessment is to determine the potential impact of the chemical on the environment. The applicant is encouraged to conduct an assessment of environmental hazard by considering environmental exposure data and then the relevant environmental toxicity data for those species most at risk from exposure. Environment Australia uses the quotient method (7-4.3(a)) and threshold values for standard aquatic scenarios. This is an iterative process and is discussed in detail Appendix 7-1. For veterinary chemical products, it is expected that exposure of the soil compartment to the chemical will be of great concern in the majority of cases. Calculation of hazard for various industry models is given in 7-4.3(b), both for soil and for the aquatic compartment.

(a) The quotient method

To predict environmental hazard as accurately as possible, a number of simple calculations can be performed. For example, in agreement with overseas assessment agencies (e.g. US EPA), Environment Australia uses the quotient approach (Urban and Cook, 1986). The quotient (Q) of the estimated environmental concentration (EEC) and the relevant toxicity concentration (lethal concentration for 50% of a population, LC₅₀ or lowest-observed-effect concentration, LOEC) acts as a trigger for further scrutiny (see examples below).

The Q-value provides a measure of the risk to the organism concerned. Chronic data (LOEC) give a greater assurance of long-term environmental protection than acute data (LC₅₀). If the Q-value is very

low and is based on a LOEC, the risk of long-term adverse effects is low.

Environment Australia is now formalising ratios of concern on an assessment-by-assessment basis, particularly for aquatic hazard (see Appendix 7-1). The following gives some guidance on how Environment Australia will use the Q-value in an assessment, although this may vary depending on the level of information and data available for the chemical.

For establishing hazard under standard scenarios (i.e. direct overspray and 10% spray-drift), with adequate fate and toxicity data, if:

- $Q > 0.5$ then hazard is unacceptable,
- $0.1 \leq Q \leq 0.5$ hazard may be able to be mitigated by some form of risk management, such as label restraints for a specific use and an identified hazard arising from that use, and
- $Q < 0.1$, hazard is considered low (and may or may not require some form of risk management, such as general label restraints).

Although Environment Australia does not use application or safety factors, if an acute (lethal) end-point is used, Environment Australia will more rigorously review the resultant Q-value when considering the potential for the chemical to have medium to long-term effects.

If applicants are unclear on the assessment of hazard, contact the Manager, Risk Assessment and Policy Section (see section 7-4.1(b) for contact details).

(b) Guidance notes to establish hazard using various industry models

Exposure of non-target organisms mainly depends on the route of administration of the veterinary chemical product, whether external (e.g. for treating wounds) or internal (e.g. endoparasiticides). Therefore, the method of application (e.g. backlining, dipping, drenching, injecting, bathing, oral administration; number of animals; and type of husbandry practices) is a starting point to assess the risk to the environment.

Metabolism data (Part 4, Metabolism and Kinetics) are taken into account to assess the environmental risk because, unlike agricultural chemicals, veterinary chemical products are usually not directly released to the environment and the main exposure pathway is through excretion, often unchanged, in urine and faeces (see Table 7-1, section 7.1.8(c)).

An estimated environmental concentration (EEC) is calculated for the relevant compartment (e.g. soil, water column, sediment and air) and compared with the relevant effects data. For chemicals administered internally, the EEC is calculated as:

- a function of the type and degree of biotransformation (e.g. 10% of the drug converted to a less toxic, more water soluble metabolite versus activation of 50% of the drug to the active constituent form) and
- other pharmacokinetic properties of the active constituent (e.g. half-life, time to first appearance of drug in faeces or urine, time for complete depletion).

For chemicals externally applied, EEC is calculated by taking into account the potential transport of residues to other media (e.g. lousicides in effluent after processing of wool).

The information given in submissions needs to be sufficiently detailed so Environment Australia can adequately review the claims made. It should include metabolism data that will clarify the potential environmental levels of the chemical (or its metabolites), even though this might already have been submitted in Part 4, Metabolism and Kinetics (see Table 7-1, section 7.1.8(c)).

The following examples describe, step-by-step, the calculations of an EEC for various categories of veterinary chemical products. Their aim is to give some specific guidance for different use patterns, transport pathways and pharmacological properties. In addition, they demonstrate how EECs can be more realistic when using appropriate data.

These examples are designed to help applicants both understand which fate

and environmental toxicity tests may be relevant and to provide a variety of hazard calculations. Applicants will need to adapt these examples appropriately.

(i) Veterinary chemical products used in cattle

The applicant will need to consider the proposed application and use-pattern carefully, and subsequent effects on rate of metabolism and excretion, and concentration of residues in excreta (assuming minimal loss by other routes, e.g. milk). The applicant will also need to determine the likely hazard of the chemical according to husbandry practices (e.g. feedlot versus free-range).

For instance, the applicant will need to consider such questions as:

- Will the type of formulation affect rate of metabolism?
- Is the chemical being applied to feedlot cattle or cattle on pasture (or both)?
- To what extent will the chemical be metabolised and excreted?
- Are the metabolites still likely to be toxic to non-target organisms?
- With which excreta are residues associated: urine or faeces?
- What are the residue levels in excreta, and their time course (that is, half-life, time to first appear, time for complete depletion, etc)?
- How do management practices affect these residue levels: are animals continuously dosed or do they receive consecutive treatments in the shed?
- How are residues, in excreta, managed: are they collected and pooled, left in situ where they fall, etc (either state the 'worst case' or use one which seems the most relevant)?

Example of an endoparasiticide

Wonderwormer is a new endoparasiticide of a class of chemicals not previously registered. It is highly lipophilic and appears to strongly bind to the organic fraction, being totally excreted with the faeces (up to 75% is not metabolised).

Environmental exposure to *Wonderwormer* will mainly occur in soil

that receives residues of the drug in cattle dung. Significant aquatic contamination would not be expected because of the strong affinity of the drug for organic matter.

Wonderwormer will be available as a pour-on for use on cattle in feedlots and on pasture, although only the feedlot situation will be considered in detail here. The dose is 0.25 mg *Wonderwormer* (as active constituent) per kilogram body weight. If it were also available as an injectable formulation, then similar arguments would be used.

In the feedlot situation, the highest residues in manure would be generated by beef production. Thus, a 300 kg animal would receive 75 mg of *Wonderwormer* before entering the feedlot, and excrete about 20 kg manure (containing about 90% water) daily during a 70 day stay (a total of 1400 kg). Data from the Queensland Department of Primary Industries (QDPI) may be used to estimate residue levels (Watts, 1991). The QDPI model assumes that scraped manure removed from the feedlot has undergone 30% degradation and retains only 30% water.

The maximum concentration of *Wonderwormer* in the soil can be calculated by considering the ploughing of scraped manure to a depth of 15 cm at 15 tonnes per hectare (the highest rate recommended by NSW Department of Agriculture).

For a soil density of 1.2 g.mL⁻¹, the EEC in the soil is calculated as:

- Wet manure production (90% water) = 1400 kg
- Dry manure production (30% water) = 560 kg
(i.e. implies 60% reduction in water volume of the 1400 kg,
i.e. 1400 - (60% X 1400 kg) = 560 kg)
- Scraped manure (30% degradation of organic matter) = 518 kg
(i.e. total organic matter in 1400 kg was 10% of 1400 kg = 140 kg;
30% of organic matter = 30% X 140 kg = 42 kg;

for dry manure, reduction in mass =
560 kg - 42 kg = 518 kg)

- Total *Wonderwormer* residues (no degradation) = 75 mg
- *Wonderwormer* concentration in scraped manure = 0.145 ppm
(i.e. 75 mg/518 kg = 0.145 mg.kg⁻¹ or 0.145 ppm)
- Mass of 1 ha soil (15 cm depth) = 1800 tonnes
(i.e. 10⁴ cm X 10⁴ cm X 15 cm X 1.2 g.cm⁻³ = 1.8 X 10⁹ g or 1800 t)
- *Wonderwormer* concentration in soil (scraped manure applied at 15 t.ha⁻¹)
EEC = 1.2 ppb (i.e. (0.145 ppm X 15 t)/1800 t = 1.2 X 10⁻³ ppm or 1.2 ppb)

The EEC is then compared to appropriate environmental toxicity data to determine a Q-value (see more fully worked aquaculture example (v) below).

For free range cattle, the highest residues of *Wonderwormer* will be in fresh dung, although the situation is a little more problematic (i.e. spatial and temporal distribution, exposure of dung, availability to dung beetles because of their important role in breaking down cowpats, etc). The applicant would therefore need to consider potential levels in field situations, and subsequent effects on the ecology of non-target fauna to better estimate the environmental impact of routine (e.g. prophylactic/seasonal) and non-routine (e.g. disease outbreak) treatments.

(ii) Veterinary chemicals used in poultry

Intensive production is likely to give rise to the concentration of veterinary chemical products in the excreta when applied to the whole poultry lot. The use of chicken manure as a fertiliser should be considered as a case for environmental risk. The manure may be used as such or in commercial products (i.e. pellets). Broad-acre application of the manure is probably rarer than application in horticulture and in home gardens. The applicant should consider various cases of application. It is possible that simple management practices, such as allowing

some period of degradation prior to use as manure, will significantly reduce the level of the chemical.

Thus, an EEC should be established by taking into account:

- timing and frequency of application of the chemicals to animals,
- metabolism and route of excretion of the chemicals,
- frequency of removing litter from sheds, and
- latter use of the manure.

An EEC is calculated for some amount of excreta incorporated into some amount of soil (see previous example). A Q is then calculated using the environmental toxicity data on appropriate sensitive species (e.g. terrestrial organisms). A more fully worked example is given below for a coccidiostat, *Cocc-cup*, applied to control coccidiosis in poultry.

Hazard to soil invertebrates from the application of chicken manure

The main route for environmental release of *Cocc-cup* would appear to be through disposal of chicken excreta on farmland. Residue levels in manure were measured to be about 2 ppm.

Chicken manure is generally applied at 10–12.5 t.ha⁻¹ in the outer Sydney region although rates may be as high as 16.8 t.ha⁻¹ on occasion.

For a soil density of 1.5 g.mL⁻¹, the EEC in the soil is calculated as:

- Concentration of *Cocc-cup* in all manure applied to land is 2 ppm
- Amount applied at rate of 16.8 t.ha⁻¹ = 33.6 mg.m⁻² of *Cocc-cup* (i.e. 2 mg.kg⁻¹ X 16.8 t.ha⁻¹ = 33.6 g.ha⁻¹ or 33.6 g/10000 m² = 3.36 mg.m⁻²)
- Mass of 1 ha of soil (10 cm depth) = 1800 tonnes (i.e. 10⁴cm X 10⁴cm X 10cm X 1.5 g.cm⁻³ = 1.5 X 10⁹g or 1500t)
- *Cocc-cup* residue concentration in soil (manure applied at 16.8 t.ha⁻¹) EEC = 22 ppb (i.e. (2 ppm X 16.8 t)/1500 t = 22.4 X 10⁻³ ppm or 22 ppb).

The EEC is then compared to appropriate environmental toxicity data to determine a Q-value (see more fully worked aquaculture example (v) below). Also, residues in the manure will be diluted by the litter used in the sheds, as well as mixed with manure from untreated birds, potentially lowering the EEC. Any mitigating factors, like further degradation mobility (or lack of mobility, i.e. adsorption to organics) should also be considered.

Environment Australia recognises that the assessment of the environmental risk to soil organisms is a developing area and encourages applicants to submit relevant data for scientific evaluation using test protocols available from various jurisdictions. For a more complete discussion of this area, the applicant can refer to Carruthers (1994) or approach Environment Australia for advice.

(iii) Veterinary chemicals used in piggeries

For a chemical used to treat pigs housed in intensive piggeries, the applicant should consider:

- how and when the chemical is applied,
- how the chemical is metabolised and excreted by the pig (degradation pathways and metabolites), and
- the method of treatment of piggery effluent and possible transport pathways of the chemical.

For instance, State legislation requires that piggery effluent not pollute waterways. Piggeries will therefore use waste management catchment systems like runoff storage ponds. In most animal sheds, wastes are flushed into channels beneath slatted floors, then combined with wastes from all sheds and treated in anaerobic and aerobic ponds. Pond effluents are used to irrigate and fertilise pastures and crop lands.

Environmental exposure may occur through waste products from treated pigs:

- when chemicals enter the soil environment from waste pond effluent used as fertiliser on pasture or crop land, and

- when chemicals enter aquatic habitats because of runoff from fertilised lands, leaching to ground water (e.g. highly hydrophilic chemicals).

Establishing a 'worst case' estimated environmental concentration

The following example aims to describe the steps to calculate a 'worst case' EEC.

A moderately water soluble (12 g.L^{-1}) hypothetical drug, *Oinkmentin*, (active constituent) is to be added in food.

- *Oinkmentin* is used on weaners weighing about 15 kg,
- *Oinkmentin* is used once every 6 months in the piggery (although not important in this example, the frequency of application relative to the frequency of disposal would also need to be considered),
- weaners consume $1.2 \text{ kg feed.d}^{-1}$,
- *Oinkmentin* is administered at $200 \text{ mg active ingredient}\cdot\text{kg}^{-1}$ feed, and
- the treatment period is 21 days.

Metabolism data indicate that:

- 20% of the active constituent is metabolised by pigs in simple and non-toxic metabolites;
- 70% of *Oinkmentin* is excreted unchanged in urine; and
- 10% of *Oinkmentin* is excreted unchanged in faeces.

Metabolism data giving the amount excreted in urine and faeces are important to adjust the EEC for different husbandry practices.

The average pig will excrete about 4.1 kg wet manure (urine, faeces) per day and a minimum of 47 L of water per pig will be used to flush the pen.

We will assume:

- because of its solubility, *Oinkmentin* partitions to water rather than sediment (and all of the drug excreted in the faeces partition to water when collected in ponds),
- no further dilution (e.g. by non-treated pigs), and

- no other abiotic or biotic degradation over 21 days,

Under the previous conditions:

- each pig would receive a dose of $5.04 \text{ g Oinkmentin per pig}$ i.e. $1.2 \text{ kg feed}\cdot\text{day}^{-1} \times 200 \text{ mg active ingredient}\cdot\text{kg}^{-1} \text{ feed} \times 21 \text{ days} = 5.04 \text{ g active ingredient per pig}$,
- the daily slurry of faeces and water is $51.1 \text{ kg waste slurry}\cdot\text{day}^{-1}$, i.e. $4.1 \text{ kg wet manure}\cdot\text{day}^{-1} + 47 \text{ L} = 51.1 \text{ kg waste slurry}\cdot\text{day}^{-1}$,
- the total amount produced over a 21-day treatment period is about 1000 kg i.e. $21 \text{ days} \times 51.1 \text{ kg waste slurry}\cdot\text{day}^{-1} = 1073 \text{ kg}$ or about 1000 kg, and
- the concentration of *Oinkmentin* in 1 kg of waste slurry at the end of a 21-day treatment period would therefore be about 4 mg i.e. 80% (due to 20% being metabolised) of $5.0 \text{ g Oinkmentin} \div 1,000 \text{ kg waste slurry} = 4 \text{ mg Oinkmentin}\cdot\text{kg waste slurry}^{-1}$.

Environmental hazard is then determined by comparing the EEC *Oinkmentin* in waste slurry with relevant environmental toxicity data (see more fully worked aquaculture example (v) below).

Terrestrial environmental toxicity studies and/or aquatic environmental toxicity studies may be required depending on the disposal of the slurry.

For instance, is the water used for irrigation and what is the rate and frequency of irrigation? What is the solids content of the irrigated water? When, and to where, are solids removed from settling ponds? How much of the chemical will be associated with the water and solid phase? What is its fate when applied to pastures? If the chemical remains in the water phase, all of it will have the potential to be applied to pastures and may move to groundwater or with surface water. If the chemical remains with the solids (and partitioning data would need to be provided to substantiate this claim), the fate of these solids would need to be considered (e.g. to landfill, as a manure application). Appropriate information from degradation, mobility, and field

studies (Table 7-1) will substantiate claims.

(iv) Applications of ectoparasiticides to sheep

Backlining is a convenient method for farmers to apply ectoparasiticides to sheep. However, ectoparasiticides have implications for the environment when the fleece is scoured.

Fate of Ectoparasiticides in Greasy Wool

Most pesticide residues are removed with grease and dirt fractions during scouring and then discharged in aqueous effluents. In general, Environment Australia assumes the aqueous fraction to contain $\leq 20\%$ of total fleece residues for lipophilic pesticides ($\log P > 4$) and $\geq 80\%$ for hydrophilic pesticides ($\log P < 2$) (see example below). Pesticides of intermediate lipophilicity will be treated on a case-by-case basis (see example below). Data should be provided to substantiate these assumptions whenever possible.

The level of environmental exposure depends on the residue level (R) in greasy wool at shearing and on the degree of removal before effluent discharge to the environment. The residue level at shearing will depend on the degradation rate of the chemical in the fleece and the periods between applications and shearing. The applicant will need to provide fleece degradation data to support the proposed wool withholding period, according to the protocol described below. Ideally, fleeces should be sampled at sufficient intervals in order to determine the decay curve. In addition, the total fleece weight should be estimated at each sampling point. Band sampling (70 mm handpiece) around the girth of the animal is preferred as

experience indicates this method to give the most accurate results, short of extracting the entire fleece. An alternative approach is to obtain a mass balance for residues in pilot scale (1 tonne) scouring trials on wool for which the history of pesticide application is well defined.

Assuming discharge of 10 L aqueous effluent per kg greasy wool, an initial fleece residue of R mg.kg⁻¹ will leave residues in scouring effluent of $\leq 0.02R$ mg.L⁻¹ for lipophilic pesticides and $\geq 0.08R$ mg.L⁻¹ for hydrophilic pesticides.

Residues in sewage effluent are reduced further through dilution by other waste streams.

A model has been developed to estimate maximum mean residues across the Australian clip that would generate a non-toxic effluent at the outfall. The model is based on scouring at Geelong where primary treated effluent from 50 tonnes of wool is discharged daily through the Geelong sewerage system (daily flow 50 ML) to the Black Rock ocean outfall. Primary treatment (wax recovery) at the scour is estimated to remove 30% of lipophilic pesticides and 0% of hydrophilic pesticides.

Acute LC_{50s} are used as target concentrations as considerable dilution occurs in receiving waters. For simplicity, the calculation begins with a fleece residue of 1 mg/kg greasy wool. As 50 tonnes wool contains 50 g pesticide, 35 g of lipophilic pesticide would be discharged to sewer after scouring (50 g for the hydrophilic compound). The following table lists concentrations at the outfall, target concentrations, and maximum wool residues.

Pesticide	synthetic pyrethroid	insect growth regulator	organo-phosphate	hydrophilic compound
Removal by sewage treatment	95%	80%	50%	0%
Amount discharged (g)	1.75	7	17.5	50
Outfall concentration (ng/L)	35	140	350	1000
Target concentration (ng/L)	50	1000	1000	93 x 10 ⁶
Max fleece residue (mg/kg)	1.5	7	3	93000

Analysis based on chronic endpoints is indicated for ectoparasiticides that persist in the receiving environment (half-life greater than 6 weeks). For analysis based on chronic exposure, an additional dilution factor of 150 is assumed.

Ectoparasiticides that exhibit a morphological rather than toxic mode of action (e.g. an insect growth regulator) also merit special consideration. Testing of such substances must include at least one moult of the test organisms.

Applicants may, however, challenge the assumptions in the model by providing data or scientific argument. For example, some organophosphate products may undergo greater than 50% removal during sewage treatment.

Knowledge of market share and degradation kinetics on the fleece allows estimation of a shearing withholding period to meet the above residue requirements. The applicant will need to provide information on the residues likely to be found in fleece at shearing and, if possible, the kinetics of degradation in fleece. The applicant should also provide data describing the likely fate of residues following discharge to the marine environment.

Hazard Assessment of Pesticide Residues in Greasy Wool

Aquatic organisms are therefore generally the focus of hazard assessment because of their likely exposure and sensitivity to these residues. For non-persistent chemicals, hazard calculations may be based on acute data whereas persistent chemicals would best be assessed on the basis of chronic endpoints.

The hazard is assessed by comparing the EEC with the appropriate effects concentrations (LC₅₀, LOEC—see more fully worked aquaculture example (v) below). Environment Australia may recommend a longer withholding period if the predicted exposure concentration is close to the effects concentration.

Applicants should also be mindful of the *Guidelines for Sewerage Systems* issued jointly by the Agricultural and Resource Management Council of Australia and New Zealand (ARMCANZ) and ANZECC in

November 1994, which specify an acceptance guideline (i.e. on entry to sewage plant) of 1 mg.L⁻¹ for pesticides in general. This may be varied, with appropriate scientific justification, by local sewerage authorities. For example, some organophosphates have specific guidelines of 0.1 mg.L⁻¹. To satisfy this requirement, it will be necessary to ensure residues in scouring effluent ($\leq 0.02R$ mg.L⁻¹ for lipophilic pesticides and $\geq 0.08R$ mg.L⁻¹ for hydrophilic pesticides) will remain below this threshold.

(v) **Veterinary chemicals used in aquaculture**

Chemicals used in aquaculture are of concern when used in large volumes in, or released to, open waters. In comparison, when restricted in use (e.g. for use on brood stock where the number of animals treated is much smaller) and with restricted release of the chemical to the environment (e.g. due to the chemical being directly injected into the fish where it may be metabolised), these chemicals are, potentially, of much less concern to the environment.

General Concerns

It is essential the applicant address the following general concerns and provide:

- relevant physico-chemical properties;
- a full description of use pattern;
- any other relevant studies that will help determine the likely fate of the drug when applied according to the label directions; and
- appropriate environmental toxicity studies of a range of species.

Provide relevant physico-chemical properties

This information is essential as it gives information as to the potential behaviour of the chemical in the environment (albeit the behaviour may be modified by the use of excipients, which the applicant should consider).

For example, persistent chemicals have the potential for greater environmental impact due to an obvious longer effect period, as well as their potential for bioaccumulation. The degree to which

they threaten the environment from bioaccumulation will also depend on other factors, like the lipophilicity, molecular weight and size, solubility in water, type of chemical bonds and chemical reactivity (Connell 1989). It is important therefore that the applicant satisfies Environment Australia, through either laboratory studies or a thorough literature search (which may include chemical modelling like quantitative structure analysis relationships), of the chemical's stability, lipophilicity and solubility.

If the chemical is to be applied in sea water, then its solubility and stability in sea water should be provided.

Provide a full description of use pattern

The applicant must provide enough information to enable Environment Australia to determine the likely environmental fate of the chemical. The use pattern might be relatively safe for the environment (i.e. single injection) or it might have some environmental consequences (i.e. a series of applications to a large number of animals as for medicated feed to fish in sea cages). The route of administration of the chemical, the husbandry practices, the number of animals to be treated, the location of application (i.e. closed ponds, open rivers) are important in assessing the likely environmental fate of the chemical.

The applicant should consider:

• **Use-pattern:**

- Is the chemical applied by dipping or bathing in solution, as an injection, or given with feed (either pre-mixed or as part of a prepared food; hand dispersed, auto-bin etc)?
- Is it advised that any adjuvant be added to ensure even dosing (e.g. even mixing and sorption to food, or adequate solubility as a solution)?
- Is the dose rate different for size class, sex, freshwater or saltwater, etc (state the 'worst case' or argue one case)?

• **Husbandry practices:**

- Are the animals to be treated quarantined prior to application, or

managed in any other way that is different to normal husbandry practices?

- If the chemical is applied as a medicated feed, is the chemical given at a level below the normal feeding rate, and what is the feeding/dosing rate?
- What size cages are to be used and are the cages in a larger containment structure or natural feature (e.g. freshwater pond or bay or estuary)?
- What is the stocking rate (i.e. number of animals in a given volume and average weight of the animal if dosed according to weight)?

• **Environmental conditions:**

- Are there any environmental conditions that will modify dose rate (e.g. temperature, rain event)?
- Are the cages or containment structures likely to contain the chemical when deposited with particulate matter? What is the fate of this particulate matter (e.g. accumulated as sludge, left to oxidise between crops while pond empty and potentially used as an organic source to initiate the next algal bloom for food for the next crop)?
- Do the cages or containment structures have the potential for soluble chemicals to move freely from them (e.g. as overflow from earthen ponds or due to sea currents moving through them)?
- Are there any other environmental conditions that will modify dispersal of the chemical (e.g. tidal flushing, ocean currents, rain events, river flow in the receiving waters)?

Provide any other relevant studies that will help determine the likely fate of the drug when applied according to the label directions

As well as providing relevant physicochemical degradation, biodegradation and mobility studies as outlined in Table 7-1, studies on the metabolism of the chemical (Part 4,

Metabolism and Kinetics) in the fish should be provided if relevant.

Modelling, or data on local conditions from field observations, might also demonstrate possible dispersal pathways. For instance, hydrological data might demonstrate that rapid dilution might be achieved for a water soluble chemical because of an expected high water turnover due to coastal currents. This type of data might also indicate possible deposition zones if the chemical shares the fate of uneaten food.

Experience gained from well designed overseas field studies might provide some useful data, providing the results are not closely tied to site-specific characteristics.

Provide appropriate environmental toxicity studies of a range of species

If the applicant expects the chemical to partition mainly to water, then environmental toxicity studies should deal with non-target aquatic organisms; marine or freshwater as relevant. In contrast, if the chemical is expected to partition to sediment, perhaps because it adsorbs to food material, then the environmental toxicity studies should also deal with non-target sediment-dwelling (benthic) organisms; marine or freshwater as relevant.

Calculating a 'worst case' estimated environmental concentration

Example 1: a fungicide applied as a bath

This example gives a calculation of an EEC for a very water soluble (100 g.L^{-1}), hypothetical fungicide, *Mycokiller*, in a 'worst case' situation after application using a dip bath.

Individual brood stock fish are caught with a dip net then removed to a bath containing a concentrated solution of *Mycokiller* (2% active ingredient solution, w/v). The fish are held in the solution for one minute then returned to their tank. The volume of the bath is 100 L. The bath solution is renewed monthly, with the spent solution disposed of by flushing to a drain. This drain discharges to the local river, 1 km upstream from the river mouth situated on a well-flushed bay. The river flow is seasonal with a minimum flow

rate of $1 \text{ m}^3.\text{s}^{-1}$. The drain discharges into the river at a minimum of 100 L.s^{-1} with the bath contents diluted by at least 100:1 with overflow from holding tanks, etc.

Clearly, this example illustrates that the bath contents are very well diluted by the time it reaches the bay, by several orders of magnitude: 100:1 dilution 'in house' from other discharges, then a 1000:1 dilution when the drain discharges to the river, and further possible dilution with tidal flushing and further river flow after the pulse passes. For a discharge made only monthly, dilution would appear to be adequate, although if it were a continuous stream the concentration of *Mycokiller* in the river would be in the low microgram per litre range. The environmental consequences of this level of *Mycokiller* would then depend on the actual dilution achieved with tidal flushing (and the worst case might mean considering neap tides that occur twice monthly) and the relevant ecotoxicological data from tests performed with marine water column species.

Example 2: a herbicide applied to an earthen pond to control cyanobacteria

This example gives a calculation of an EEC for a poorly water soluble ($4 \text{ }\mu\text{g.L}^{-1}$), hypothetical herbicide, *Bloominell*, in a 'worst case' situation after spray application to ponds used for rearing native estuarine crustacean species.

Typical of its class, *Bloominell* has a moderate log octanol/water partition coefficient (K_{ow}) of 2.6, is relatively persistent in (fresh) water with a half-life of about 30 days. It adsorbs to clays and tends to move while sorbed to soil particles rather than as the free chemical. It can be persistent in soils, with a half-life ranging from 60–250 days, although some microbial degradation is evident in soils with high organic content. Exposure to light causes some degradation in both (fresh) water and soil. The class of chemicals *Bloominell* belongs to is known to contaminate groundwater supplies because of its high application rate and persistence, despite its low (fresh) water solubility. *Bloominell's* proposed extension for use in aquaculture

is therefore of some concern because of the possibility of adding to this contamination, as well as its direct application to the aquatic environment. Also, its behaviour in brackish salt water is not well understood compared to that in freshwater.

Bloominell is applied at about 4 kg active ingredient.ha⁻¹ to give a concentration of 5 mg.L⁻¹ in a 2 m deep pond. Exchange rates for a pond might be 30–40% per day although over the whole farm exchange rates might average out to be only 4–5% per day. Water exchange is either by pump or channel: growers prefer channel irrigation because of lower cost. Water is held for a week and then released directly to the sea. The ponds achieve at least a 10-fold dilution with water currents moving along the coast in the direction from the inlet to the outlet (to ensure flushing and avoid contamination of inlet water).

The situation is obviously more complex than the example above with the monthly release of chemical to a drain, and where dilution was easily achieved. In this situation, the worst case scenario would be for ponds that are fed from channels at high tide, with all ponds emptying to a common drain which then drains slowly as the tide recedes.

On release, the pond water containing *Bloominell* would be expected to be diluted by at least 30%, giving a concentration of 3 mg.L⁻¹. Further dilution would be achieved in the common drain but would appear to be negligible. A 10-fold dilution in the receiving water implies an EEC of 0.3 mg.L⁻¹. The applicant provided data indicating that other algae and macrophytes would show effects at around or below these levels, and therefore a potential hazard exists with the proposed use for these farms.

Example 3: an antibiotic applied to a sea cage

This example gives a calculation of an EEC for a slightly water soluble (4 g.L⁻¹), hypothetical *Pisceoffmyacin* in a 'worst case' situation after application, in food, to pens where:

- stocking rate of fish in pens is about 5000 fish per 500 m³,

- average weight of fish in pens approx. 250 g,
- if 5000 fish per 500 m³ then stocking rate is equivalent to 2.5 kg fish/m³, and
- chemical (taken as active constituent) is to be applied at 40 mg.kg⁻¹ of fish.day⁻¹ for 10 days.

Then assuming:

- because of its solubility, it partitions to water rather than sediment,
- no dilution due to currents,
- no degradation over 10 days, and
- no metabolism by fish, and even if all consumed, all of *Pisceoffmyacin* is excreted unchanged.

This implies:

- dosing water at 100 mg.m³ or 0.1 ppm each day, and
- over the 10 day application period, the final concentration (EEC_{water}) would be 1.0 ppm.

A similar calculation could be made for a chemical that partitioned to sediment (solubility = 5 mg.L⁻¹, log K_{ow} = 5.3), where it was incorporated to a depth of 10 cm. The surface area of the pen is 500 m² and the depth is 10 m.

From this information,

- volume in pen is 5000 m³ with 50,000 fish,
- 200 kg of chemical added in feed.

Then assuming:

- no degradation over 10 days,
- no metabolism by fish, and even if all consumed, all of *Pisceoffmyacin* is excreted unchanged and remains with faeces,
- faeces containing *Pisceoffmyacin* settles evenly immediately beneath the pen, and
- sediment has a density of 1.3 kg.L⁻¹,

This implies:

- 200 kg *Pisceoffmyacin* per 500 m² (5x10⁶ cm²) in 10 cm of sediment,

- $200/(5 \times 10^6 \times 10 \times 1.3) = 3 \times 10^{-6}$ kg *Pisceoffmyacin*.kg sediment (i.e. 3 ppm) from one day's treatment, and
- over a 10 day treatment period, the final concentration (ECC_{sediment}) would be 30 ppm.

These scenarios illustrate the importance of determining the extent of dilution, degradation, partitioning and metabolism of the chemical. If the chemical has the potential to bioaccumulate, then bioaccumulation studies would also be needed.

Example of hazard calculation on limited data

In the above example, hazard can now be estimated using the quotient method for each compartment and the EEC.

The following toxicity data provided for the *Pisceoffmyacin* are:

- water column species:
 - prawn LC_{50} was $200 \mu\text{g.L}^{-1}$ (i.e. 200 ppb) and LOEC (growth) was $10 \mu\text{g.L}^{-1}$ (i.e. 10 ppb)
 - fish LC_{50} was 1mg.L^{-1} (i.e. 1 ppm) and LOEC (reproduction) was $50 \mu\text{g.L}^{-1}$ (i.e. 50 ppb)
- sediment (benthic) species:
 - oligochaete worm LC_{50} was 200mg.kg^{-1} (i.e. 200 ppm) and LOEC (reproduction) was 5mg.kg^{-1} (i.e. 5 ppm)

- amphipod (crustacean) LC_{50} was 1mg.kg^{-1} (i.e. 1 ppm)

The Q value for the water phase can therefore be calculated using the prawn LOEC (the most appropriate sensitive water column species using the most sensitive endpoint):

$$Q = ECC_{\text{water}}/LOEC_{\text{(growth)}} = 1000 \mu\text{g.L}^{-1}/10 \mu\text{g.L}^{-1} = 100$$

Q is clearly of concern since the EEC is two orders of magnitude greater than the observed effects. However, the EEC might be able to be refined further by considering the assumptions and modifying the EEC calculation with new data. For example, additional studies might indicate significant metabolism of *Pisceoffmyacin* to non-toxic metabolites, a very high consumption of food, and/or considerable dilution by water exchange due to ocean currents.

The Q value for the sediment phase can be calculated using the amphipod LC_{50} (the most appropriate sensitive benthic species, even when using an acute endpoint):

$$Q = EEC_{\text{sediment}}/LC_{50} = 30 \text{mg.L}^{-1}/1 \text{mg.L}^{-1} = 30$$

Q is also of concern since the EEC is an order of magnitude greater than the observed acute effects. If a chronic endpoint value was used, the EEC is likely to exceed the effect concentration by at least two orders of magnitude.

Appendix 7-1

General principles in assessing hazard

The following is taken from the *Ag Requirements Series* Part 7, section 7-4.3(b). While it may deal with matters of a more agricultural nature (e.g. spray drift), the general principles are the same.

When assessing hazard, every case cannot be accounted for, so the applicant can follow an iterative process (see also Figure A1) by considering:

- a 'worst case' scenario, and, if needed,
- a series of refinements which account for other factors and results in setting more realistic scenarios at each step.

The worst case should identify the sensitive environmental compartment(s) most at risk from exposure to the chemical (Scenario 1, Figure A1). If these environmental compartments are not at risk (i.e. the Q-value is acceptable), then no other assessment is needed.

If the Q-value is not acceptable (or close to the cut-off limit), then the process is gradually refined in a number of steps, initially making some simple assumptions. For example, possible risk management strategies (e.g. label restraints) or other mitigating factors (e.g. degree of adsorption) might be considered (Scenario 2, Figure A1). This refined case may or may not be the 'typical case'. If the Q-value still indicates unacceptable hazard to the environment, the refined case can

then be further modified making more sophisticated or complex assumptions (i.e. the process is then repeated for each subsequent refinements (Scenario 3, Figure A1). In each subsequent refinement, the assessment may then consider still further how:

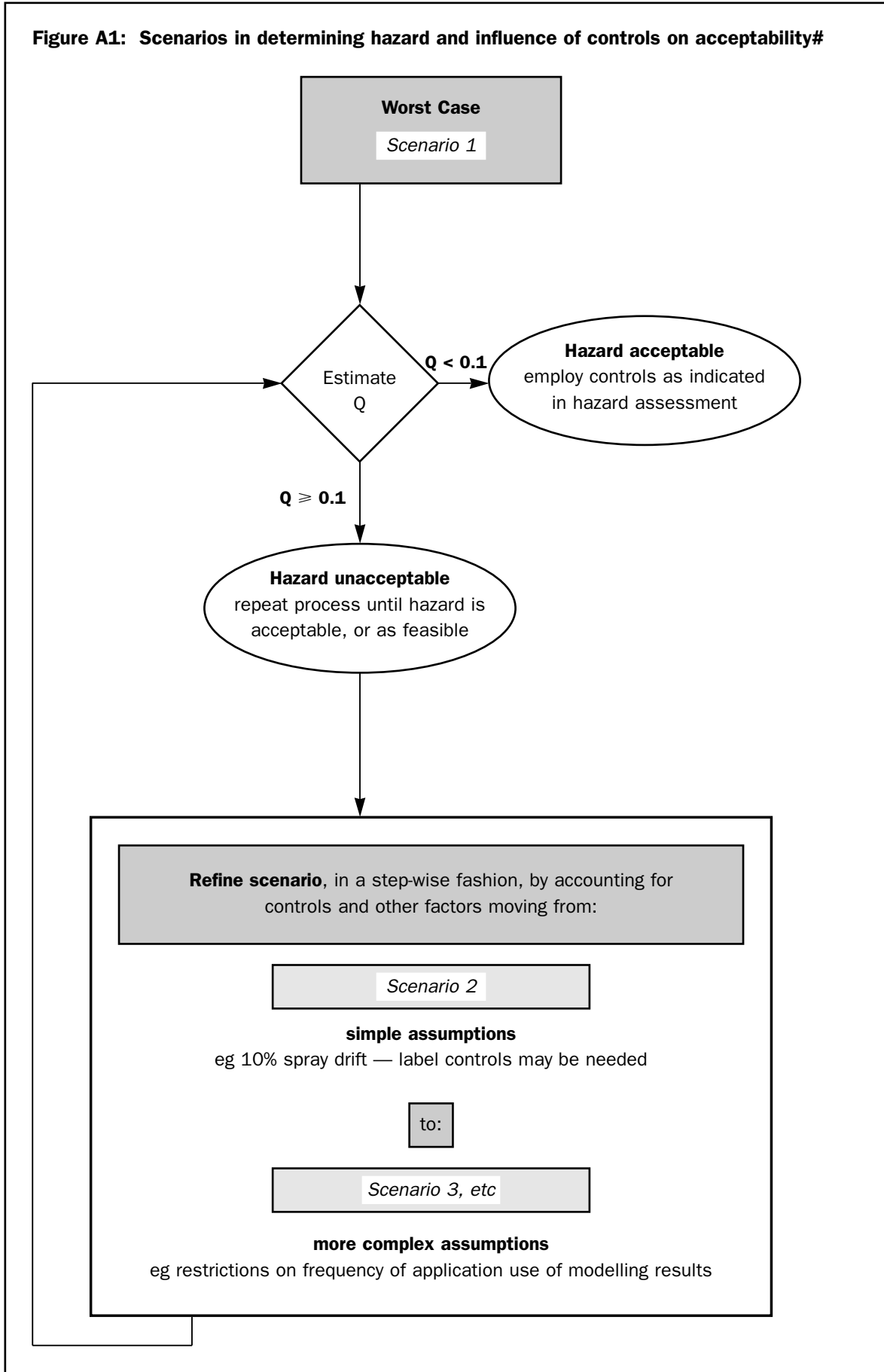
- other constraints (e.g. constraints placed on proposed use such as restrictions on the frequency of application, retention of first flush of storm-water from irrigation channels on farm, restriction on aerial spraying if this was proposed, etc) or
- other data (e.g. results of modelling)

might influence the hazard, and how practical, realistic or uncertain these might be.

The process is therefore necessarily iterative and will depend on the complexity of the assessment (e.g. number of sensitive environments, number of proposed crops, applications and application methods, degree of toxicity of the active constituent, persistence of the active constituent, etc).

If applicants are unclear on the assessment of hazard contact the Manager, Risk Assessment and Policy Section, Environment Australia by phone on (02) 6274 1643 or by fax (02) 6274 1610.

Figure A1: Scenarios in determining hazard and influence of controls on acceptability#



The threshold used is based on $Q = 0.1$ as unacceptable and $Q < 0.1$ acceptable—this is done for simplicity.

Glossary

Active constituent The substance or substances in a formulated product, that is/are primarily responsible for the biological or other effects that make the product a veterinary chemical product.

Acute toxicity testing There is no easily agreed definition for 'acute' when used to describe the exposure period in ecotoxicity testing. However, it generally refers to some very short period (eg < 10%) in relation to the organism's typical expected life span. Acute toxicity testing generally has lethal effects as the end-points. For example, an acute *Daphnia* test would be performed over 48 h, with the end-point being immobilisation (an EC₅₀ would be determined), or a fish test would be performed over 96 h with the end-point being death (an LC₅₀ would be determined).

ANZECC Australian and New Zealand Environment and Conservation Council aims to provide a forum for consultation and co-ordination between the State, Territory and Commonwealth governments of Australia and the Government of New Zealand on environmental and conservation issues.

AVCARE Avcare Ltd (formerly AVCA, Agricultural and Veterinary Chemicals Association) is the National Association for Crop Protection and Animal Health. The affiliated companies are engaged in the manufacture, formulation, distribution, and servicing of crop protection and health products.

Chronic toxicity testing There is no easily agreed definition for 'chronic' when used to describe the exposure period in toxicity testing. However, it generally refers to a substantial period (eg >90%) in relation to the organism's typical expected life span. Chronic toxicity testing normally has sub-lethal effects as the end-point. For example, a chronic *Daphnia* test would be performed over 21–28 days, with the end-point being reproduction (NOEC and LOEC would be determined for number of young, etc), or an algae test would be performed over

72 h or 96 h with the end-point being growth rate or number of cells (an EC₅₀ and/or NOEC and LOEC would be determined).

Ectoparasiticide A veterinary chemical product that is administered or applied to an animal by any means for the control, treatment or prevention of infestations with arthropod parasites.

Estimated Environmental Concentration (EEC) Normally the EEC is derived from set parameters, such as the concentration in water if a still water body (or soil) of 15 cm depth was sprayed at the label rate, unless evidence (use pattern, research etc) indicates otherwise (e.g. the product is incorporated to a depth of 5 cm soil).

Good Product Stewardship A companies' initiated program to promote responsible manufacture, use and disposal of the product.

LC₅₀ The concentration of a substance that produces death in 50 per cent of a population of experimental organisms within a specified period. It is usually expressed in milligrams per litre (mg.L⁻¹) or milligrams per kilogram (mg.kg⁻¹) as a concentration in food, water or air.

LD₅₀ The dose of a substance that produces death in 50 percent of a population of experimental organisms within a specified period. It is usually expressed in milligrams per kilogram (mg.kg⁻¹) of body weight.

Lowest-observed-effect concentration (LOEC) The lowest test concentration in a concentration series which is statistically significantly different from the control value within a specified time period. The measured effect (i.e. endpoint) is normally the result of chronic or sub-chronic testing. The LOEC is most meaningful when stated in relation to the NOEC. If the LOEC is the lowest test concentration of the test concentration series, then it should be stated as 'LOEC ≤ lowest test concentration'.

Material safety data sheet (MSDS) Data sheets produced by manufacturers/

importers which provide the information needed to allow the safe handling of hazardous substances used at work.

No-observable-effect-concentration (NOEC) The next lowest concentration in the concentration test series from LOEC. The measured effect (i.e. endpoint) is normally the result of chronic or sub-chronic testing. The NOEC is most meaningful when stated in relation to the LOEC. If the NOEC is the highest test concentration of the test concentration series, then it would be stated as 'NOEC is \geq highest test concentration'.

Product A formulation containing one or more active constituent(s), and possibly non-active constituent(s), which is intended for application, with or without dilution prior to use, and which is labeled with directions for use.

Q The potential hazard of the chemical to the environment can be determined by dividing the estimated environmental concentration by the relevant toxicity concentration. The resulting quotient, Q, then provides a measure of the risk to the organism concerned.

Sub-chronic toxicity testing The exposure period described between acute and chronic (eg 10% < sub-chronic < 90%). Sub-chronic testing normally has sub-lethal effects such as reproductive effects (eg decreased brood size), growth, or behavior (e.g. reaction to light) as end-points. For example, a fish early life stage test may have embryos exposed up until the time of hatching and 32 days post-hatching, with number hatched, time to hatching and growth as end-points.

Use-pattern The combination of all factors involved in the use of a formulated product, including the concentration of active constituent in the preparation being applied, rate of application, method of application, frequency and duration of treatments, additives recommended and other directions which determine total quantity applied, timing of treatment and withholding period.

Veterinary chemical product A substance or mixture of substances that fits the legal definition in the *Agricultural and Veterinary Chemicals Code Act 1994*. This definition appears in the *Vet Manual* Module A.

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