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Environmental risk assessment for veterinary medicinal products Part 1. Other than GMO-containing and immunological products First update.

M.H.M.M. Montforts April 1999

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PREFACE

With the finalisation of the EMEA Note for Guidance on the environmental risk assessment for veterinary medicinal products other than GMO-containing and immunological products in January 1997 both manufacturers and authorities were confronted with another field of interest related to veterinary medicines. It seemed the note for guidance has evoked as much questions concerning the ins and outs of the environmental assessment and its procedure as it has provided answers to these matters. I hope this document will prove to be of help to all parties involved in the registration procedure.

The first update was made in response to the availability of more detailed information on the husbandry practice and to comments from FEDESA and RIVM/CSR.

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CONTENTS

ABSTRACT

The EC has issued directive 81/852/EEC that with a request for registration of a veterinary medicinal product information is to be provided to enable an assessment of the safety for the environment.
This document has been written:

- to provide a tool for a uniform risk assessment of veterinary medicinal products.
- to inform other interested parties on the assumptions, default parameters, and model dimensions that are used.
- to provide a basis for the incorporation of the risk assessment into the Uniform System for the Evaluation of Substances.

SUMMARY

The EC has issued directive 81/852/EEC that with a request for registration of a veterinary medicinal product information is to be provided to enable an assessment of the safety for the environment. In this document a risk assessment methodology is presented.

According to the Dutch law a veterinary medicinal product is a substance, whether or not after preparation or processing, with the intention:
a. to cure, relieve or prevent any affection, illness, morbid symptom, pain, injury, or defect of an animal;
b. to remedy, improve, or change the functioning of organs of an animal;
c. to diagnose a disease or defect in animals at application in an animal.
This definition includes pure substances (organic and inorganic) and preparations (including homeopatic products, vaccines, flee-belts), and excludes disinfectants not used on animals (e.g. for cleaning stables).

The risk assessment is an evaluation of the possible fate and effects of the product. As a whole, the risk assessment is structured around the hazard quotient approach used in USES (1994). Predicted environmental concentrations are compared with effect values established in toxicity studies. If reliable exposure data are available, these may replace the predicted values.

Directive 81/852/EEC describes the assessment process in two phases. The first phase (Phase I) shall assess the potential of exposure of the environment to the product, its ingredients, or relevant metabolites. The first phase is thus limited to product identification and exposure assessment. Several exemptions for further testing are given, such as trigger values for predicted environmental concentrations (PECs). When these exemptions do not apply, and trigger values are exceeded, one enters Phase II.

In the second phase (Phase II) the reviewer shall then consider whether further specific investigation of the effects of the product on particular ecosystems is necessary. Phase II is also divided in two parts, Tier A and Tier B. Tier A begins with an elaborate evaluation of the possible fate and effects. If the applicant is unable to demonstrate that exposure is minimised to a level of no concern to the environment, then the effects in the relevant compartments must be adequately investigated in Tier B. The Tier B evaluation is subject to expert judgement and is beyond the scope of this document.

The first section of this report describes the risk assessment model in outline and then in detail. In the second section guidance is given on the actual evaluation of the dossier and preparation of the assessment report.

1. INTRODUCTION

1.1 Scope and objectives of the report.

In the recent past, the environmental impact of veterinary medicinal products has had the interest of Dutch environmental protection and nature conservation organisations (De Roij et al. 1982; Van Gool 1991; Montforts 1997). The major emission source of veterinary medicinal products is the animal husbandry practice. Livestock breeding and rearing is an important industry in the Netherlands (Table 1).
The EC has issued Directive 81/852/EEC that with a request for registration of a veterinary medicinal product information is to be provided to enable an assessment of the safety for the environment.

Table 1. An overview of animal husbandry in the Netherlands (CBS 1996; Kamstra 1995).

Category	number of animal places	number of farms
dairy cows	1,675,000	36,000
cattle	4,550,000	54,400
pigs	14,400,000	21,250
horses and ponies	107,000	20,000
sheep	1,627,000	21,000
goats	100,000	3700
chickens	91,400,000	4500
- broilers	44,000,000	1200
- laying hens	39,500,000	2700
turkeys	1,250,000	140
ducks	860,000	120
other poultry (fowls, quails)	250,000	100
rabbits	470,000	310
minks and foxes	500,000	210
fish	2500 tonnes	50

In this document a risk assessment methodology is presented. The different livestock categories have different characteristics in housing and manure production, but the emission and distribution routes are identical. To ensure an equal assessment of all products a uniform risk assessment methodology is required.
The goals of this document are threefold:

- to provide a tool for a uniform risk assessment of veterinary medicinal products.
- to provide a basis for the incorporation of the risk assessment into the Uniform System for the Evaluation of Substances (USES, 1994).
- to inform interested parties and outsiders on the assumptions, default parameters, and model dimensions that are used to assess the risk for the Dutch environment.

This document forms no legal basis with respect to the admission of veterinary medicinal products in The Netherlands, and no rights can be founded on its contents.

1.2 Framework of the environmental assessment of veterinary medicinal products.

In Commission Directive 81/852/EEC it is included that with a request for registration of a veterinary medicinal product information is to be provided to enable an assessment of the safety for the environment. The directive states that:

"the purpose of the study of environmental safety of a veterinary medicinal product is to assess the potential harmful effects which the use of the product may cause to the environment and to identify any precautionary measures which may be necessary to reduce such risks."

This directive is included in the Dutch law on veterinary medicines ('Diergeneesmiddelenwet' 27 June 1985, Stb. 410, last amendment 10 July 1995), and provides since February 1st, 1997, a formal base to reject a request for registration. An elaboration of this directive is given in the EMEA-documents (EMEA, 1996;1997), issued by The Committee for Veterinary Medicinal Products (CVMP) of the European Agency for the Evaluation of Medicinal Products (EMEA). The EMEA (1997) note is elaborated in this document within the structure of the Uniform System for the Evaluation of Substances (USES 1.0; 1994). The EMEA (1996) note for guidance is not dealt with in this report.

By the direction of the Directorate of Public Health (GZB) of the Ministry of Public Health, Welfare, and Sports (VWS) the Centre for Substances and Risk assessment (CSR) of the National Institute of Public Health and the Environment (RIVM) performs the environmental assessments in charge of the Bureau for the Registration of Veterinary Medicinal Products (BRD). The registration procedure of veterinary medicinal products in the Netherlands is as a whole divided in two rounds. After the first round the applicant has a limited period to respond to questions or calls for more information from the BRD. After the second round the application and evaluation reports are submitted to the Board for the Registration of Veterinary Medicinal Products (CRD), a group of experts on veterinary medicinal products. The CRD advises the responsible minister on the admittance of a veterinary product, based on assessment reports on the various fields of interest (e.g. ecotoxicology, residues, consumer exposure, animal health). The minister decides then on registration.

1.3 The subject of the environmental risk assessment.

According to the Dutch law a veterinary medicinal product is a substance, whether or not after preparation or processing, with the intention:

a. to cure, relieve or prevent any affection, illness, morbid symptom, pain, injury, or defect of an animal;
b. to remedy, improve, or change the functioning of organs of an animal;
c. to diagnose a disease or defect in animals at application in an animal.

This definition includes pure substances (organic and inorganic) and preparations (including homeopatic products, vaccines, flee-belts), and excludes disinfectants not used on animals (e.g. for cleaning stables).
It is not clear whether or not the Dutch law includes all ingredients in a preparation to be taken into account in the environmental risk assessment. The words 'substance' and 'product' are used more or less arbitrarily, or at least interchangeable. However, the EMEA documents (see § 2.3) state explicitely:

"... shall assess the potential of exposure of the environment to the product, its ingredients or relevant metabolites. Metabolites which represent less than 20% of the applied dose are not considered relevant..." (EMEA 1997).

"This assessment must address the risks arising from each of the components of the product, not just the risk from live organisms in vaccines." (EMEA 1996).

The risk assessment is not restricted to the proposed use of the product under consideration. The EMEA-document (1997) states that (page 5):

"The environmental risk assessment should take into consideration other possible use of the active substance contained in the product, in particular when the active substance is used as a pesticide or as an additive to animal feeding stuffs. In such cases, data available from previous evaluations may be cited in the application, including in particular the recommendations/conclusions from other relevant EU bodies (Scientific Committee for Animal Nutrition (SCAN), European Environmental Agency)".

All ingredients in a product are therefore taken into account, as well as all metabolites formed in amounts 20% of the administered dose. The reviewer shall check whether the active substance also is used in The Netherlands as a pesticide[1] or as an additive to animal feeding stuff. In the event that such combinations are found, their contributions to the risks shall be assessed.

Biocides and insecticides intended for use on animals are dealt with as veterinary medicinal products, e.g. products for the disinfection of udders and pour-on anthelmintics and anti-parasitic agents. Because of the division between the Pesticide act and the Veterinary Medicine act, the following uses of disinfectants and insecticides are **not** dealt with as veterinary medicinal products, but as biocides: disinfection of animal housing facilities (including fumigation), fish nurseries, footwear, milk extraction systems, means of transport, hatcheries (Montfoort et al., 1996; Luttik, 1996). Nevertheless, the models presented here may be applied equally for biocides.

Immunological products (vaccines) are not dealt with in this report.

[1] For up to date information see the CTB homepage http://www.ctb.agralin.org

1.4 Readers guide.

On the contents of this document.

This document can be divided in two sections:

Section I (Chapters 1-7).

The first section describes the risk assessment model in outline and then in detail. Chapter 2 describes the structure of the model used for the assessment. The scenarios for emission and distribution are elaborated in Chapters 3, 4, and 5. Chapter 6 is dedicated to effect assessment in relation to the compartment under investigation. In Chapter 7 the principles of hazard identification are worked out.

Section II (Chapters 8-10)

In the second section guidance is given on the actual evaluation of the dossier and preparation of the assessment report. Chapter 8 guides the reviewer through the evaluation process, Chapter 9 gives the report layout and Chapter 10 contains instructions on summarising studies.

A glossary of the abbrevations and definitions used is presented in Appendix I. Appendix II gives detailed information in dung production. Appendix III contains useful information on unit conversion and other background information. Appendix IV gives a list of additional questions to be answered by the notifier. Appendix V presents a list of internationally accepted test guidelines.

On how to evaluate a dossier and make the assessment.

The reader interested in using this document to start from scratch and end with an adequate assessment should start reading Chapters 2.1 and 2.2, and the table of contents, to get an idea of the contents of this document, and should then continue with Chapter 8.

In Chapter 8 guidance is given on how to handle the dossier and this document in order to perform an assessment. One will find references to previous chapters. This enables the reviewer to perform the assessment without having knowledge off all possible models available for all routes of distribution. However, expert judgement remains crucial to make the assessment a success.

This section is followed by Chapter 9, where the format of the assessment report is presented. Finally, chapter 10 gives guidance on summarising and evaluating individual test reports on behaviour and effect of the substances.

2 MODEL DESCRIPTION.

2.1 Structure of the environmental assessment of veterinary medicinal products.

Hazard quotients.
The risk assessment is an evaluation of the possible fate and effects of the product. As a whole, the risk assessment is structured around the hazard quotient approach used in USES (1994) as described in Van Leeuwen and Hermens (1995). Predicted environmental concentrations are compared with effect values established in toxicity studies. If reliable exposure data are available, these may replace the predicted values. This comparison is done using the hazard quotients approach. Hazard quotients indicate the likelihood of adverse effects occurring.

Tiered approach.
Directive 92/18/EEC describes the assessment process in two phases. The first phase (Phase I) shall assess the potential of exposure of the environment to the product, its ingredients, or relevant metabolites. The first phase is thus limited to product identification and exposure assessment. Several exemptions for further testing are given, such as trigger values for predicted environmental concentrations (PECs). When these exemptions do not apply, and trigger values are exceeded, one enters Phase II.

In the second phase (Phase II) the reviewer shall then consider whether further specific investigation of the effects of the product on particular ecosystems is necessary. Phase II is also divided in two parts, Tier A and Tier B. Tier A begins with an elaborate evaluation of the possible fate and effects. If the applicant is unable to demonstrate that exposure is minimised to a level of no concern to the environment, then the effects in the relevant compartments must be adequately investigated in Tier B. The Tier B evaluation is subject to expert judgement and is beyond the scope of this document.

As told, in Phase I several exemptions from further testing are incorporated, but if adverse environmental effects are still anticipated from the use of such products, the further assessment of possible exposure to the environment can be performed.

In Chapter 1.2 the registration procedure was addressed, o.a. the two rounds for application. The two rounds have nothing to do with the two phases. The possibility exists that in the first round the reviewer decides upon the necessity of a phase II assessment, or that in the second round the requested information is delivered to decide that a phase II assessment is not necessary.

2.2 Data requirements.

In order to perform an exposure and effect assessment (describe the substances and their properties) the industry should supply the information. The EMEA-document (1997) states on page 5:

“Applicants are required to submit a complete report which would conclude with an environmental risk assessment based on the characteristics of the product, its potential environmental exposure, environmental fate and effects, and risk management strategies as

appropriate. The report should take into account the pattern of use and administration of the product, the excretion of active substance and major metabolites and the disposal of the product as set out in Directive 81/852/EEC."

The 'complete report' to be submitted to the Dutch authorities should be interpreted as the set of complete individual test reports where it concerns ADME[2]-studies in target animals, studies on (bio)transformation in slurry, soil and water, sorption, ecotoxicity, and contagious capacities of immunological products.

The information needed for the phase I and phase II assessments is discussed in the Evaluation Chapter. All information is evaluated and summarised as to determine its reliability and usefulness.

2.3 Release estimation.

The emission (route and quantity) of the product determines the extent of the assessment (Phase I or Phase II) and the scenario to be used. Emission can take place at any step in the life cycle of the product. Dosage, route of application, type of target animals, excretion, route of entry into the environment, and agricultural practice determine the point of emission:
- at production;
- at application (external application);
- at removal of waste material containing the product (manure, dirty water, fish water);
- by excretion via faeces and urine (grazing animals);
- by contagion (immunological products);
- or at disposal of the containers (empty bottles and flee-belts).

The environmental assessment for veterinary non-immunological medicinal products is only concerned with emission at or after use of the product.

The Phase I assessment is based on a 100% release to the environment (soil, water, manure, dung). When available, data on biotransformation in the animals are taken into account. For the emission of disinfectants used on livestock some default values are used.

Product type, target animal, route of administration, dosage, and excretion are critical for the selection of the emission scenario. The main categories are:
- removal of waste material containing the product (manure, dirty water, fish water);
- excretion via faeces and urine (grazing animals);
- spillage at external application or direct exposure outdoors.

The major routes for internal application of the product are:
- oral,
- intra-ruminal,
- by injection (intra-muscular, sub-cutane).

External applications are dermal: pour-ons, sheep dips, fumigation, udder desinfection, etc. Use of products with external application may result in the product being found in washings from dairy parlours and pig and poultry stables due to cleaning of the pens[3]. If there is no direct route to the manure (spilling, washing), but there is appreciable adsorption through the skin leading to systemic effects, the pathways for internal application should be followed.

[2] ADME stand for Administration, Distribution, Metabolisation and Excretion.

[3] These washings, called 'dirty water' generally contain <3% dry matter, and are made up of water contamintaed by manure, urine, crop seepage, milk, other dairy products and cleaning materials.

This applies especially for insecticides and anthelmintics. Functions and uses not specified here are dealt with on a case by case basis. Based on the husbandry conditions described in Chapter 3.1, the following possible emission routes are identified (Table 2.).

Table 2. Possible emission routes of veterinary medicines.

Livestock category	slurry application	grazing animals	spillage at application and exposure outdoors	emission of waste water and direct entry into water
cattle	X	X		X
pigs	X			X
horses and ponies	X	X		X
sheep	X	X	X	X
goats	X	X		X
chickens	X			X
turkeys	X			X
ducks	X			X
fish farms	X			X

2.4 Environmental distribution.

The emitted product will be distributed in the environment. The route of distribution and the fate in the environment are important for the final exposure concentration or the severity of the effect.
For veterinary medicinal products, the routes of exposure for the terrestrial and aquatic environment are through the application of contaminated manure, dung and urine.
Distribution occurs within exposed compartments and through different compartments.

The terrestrial environment is reached via:
1. direct excretion of dung and urine;
2. direct spillage on the field;
3. spreading of slurry and sludge.

The aquatic environment is reached via:
1. run-off from manured land;
2. overspray from manuring;
3. direct defaecating into water;
4. direct application in water (fish);
5. direct discharge of waste water into surface water (fish);
6. release from Sewage Treatment Plant (fish).

Products used for external application (e.g. sheep dips):
1. are directly accessable to birds;
2. reach the soil (and surface-dwelling invertebrates) after disposal, and
3. also insects in treated fleece are exposed directly.

During distribution the active ingredient can be transformed to metabolites, bound residues and carbon dioxide. Usually metabolites of organic compounds are more hydrophylic than the parent compound, as a result of which they are more susceptible to leaching to the groundwater. In the event no information on metabolism (animal, dung/manure, soil) were provided, we nevertheless can take the formation of hydrophylic metabolites into account when assessing the risk for groundwater contamination.

2.5 Exposure module.

In the exposure module the calculated concentrations in the relevant environmental compartments are gathered. These depend on the type of application and the type of target animals selected. See table 3 for the exposed compartments.

Table 3. Primairy and secondary exposed compartments after emission and distribution.

Emission category	manure/ dung	soil	ground water	water	biota
manure application	X	X	X	X	
grazing animals	X	X	X	X	
spillage at application outside residues on fleece		X	X		X
waste water and direct entry into water		X	X	X	

Exposure of birds and mammals through application of veterinary medicinal product residues is possible. Because these non-target species are exposed to the products via their feed and water, calculations are performed to translate concentrations in compartments to concentrations in the feed. Five exemplary food chains will be regarded:

Birds and/or mammals with a diet consisting entirely of worms caught in polluted land or dung;
Birds and/or mammals with a diet consisting entirely of fish caught in polluted water;
Birds and/or mammals exposed through surface water;
Birds and/or mammals exposed through feed (insects in grass and fleece);
Birds exposed through feeding on exposed product (sheep dips and foot baths).

2.6 Effect assessment.

In Phase I no effect studies are required. Phase II is the actual hazard quotient approach and here effect studies are compulsory.
All delivered information shall be summarised and evaluated in order to establish the reliability and usefulness for the assessment. As pointed out in the EMEA (1997) document, studies should be performed according to international accepted guidelines for testing, and Good Laboratory Practices should apply whenever possible.

The standard endpoints for testing are applicable, e.g. mortality, growth and reproduction. In Chapter 10 instructions for summarising and evaluating are given, including the critical decision points.

In the effect assessment a no-effect concentration is derived from experimental toxicity data (PNEC: predicted no-effect concentration) by dividing the experimental L(E)C50 and/or NOEC by an extrapolation factor. This results in PNEC values for a compartment (e.g. soil or water) or ecosystem.

For (dung)-insects, the experimental toxicity result (% effect) is used, as is done in the risk assessment for the registration of pesticides. For birds exposed through sheep dips, the risk is assessed using acute LD50 data, as chronic exposure is not likely.

2.7 Risk characterisation for veterinary medicinal products.

For veterinary medicines several hazard quotients (RCR: risk characterisation ratio) are constructed to account for different types of dispersion. Most frequently the short-term time-scale is observed, and for secondary poisoning the long-term scale is taken into account. The species for which a risk evaluation is carried out are birds, mammals, (ground)water organisms, earthworms, beneficial arthropods, plants and micro-organisms.

For each compartment/ecosystem or species evaluated a separate RCR is calculated, based on the PEC/PNEC concept.

$$RCR_{comp} = \frac{PEC_{comp}}{PNEC_{comp}}$$

input			
PEC_{comp}	predicted environmental concentration in compartment	$[mg_c.kg^{-1}]$ or $[mg_c.l^{-1}]$	O
$PNEC_{comp}$	predicted no effect concentration for compartment	$[mg_c.kg^{-1}]$ or $[mg_c.l^{-1}]$	O
output			
RCR_{comp}	risk characterisation ratio for compartment	[-]	O

As indicated in §2.6, for some species non-extrapolated effect data are used. This yields e.g. “PEC/%effect”. These are denoted as RCR as well.

At this moment no special attention is given to:

- hormones and endocrine disruptors used in medicinal products and possible long-term effects on e.g. fertility of water organisms;
- antibiotics and possible development of resistance.

3. RELEASE ESTIMATION OF VETERINARY MEDICINAL PRODUCTS AT APPLICATION.

In the next chapter the emission and distribution models are presented. In this chapter the routes of emission are introduced, as well as many parameter values. The models and parameters are described according to EUSES (EC 1996) and USES (Linders and Jager, 1997). This means that a lot of modelling language will be used, as this section will be the basis for the computer program version. Firstly we introduce conventions on the use of parameters and units. Parameters and variables are divided into four types :

S	data Set	a value for this parameter must be present in the data entry set.
D	Default	a fixed value. Most default values can be changed by the user.
O	Output	the value is the result of a previous calculation.
P	Pick-list	Parameter value can be chosen from a pick-list with values.
c	closed	Default or output parameter is closed and cannot be changed by the user.

For the parameter symbols, as far as possible, the following conventions are applied:
Parameters are mainly denoted in capitals.
Specification of the parameter is in lower case.
Specification if the compartment for which the parameter is specified is shown as a subscript.

Example: the weight fraction of organic carbon in dung: Foc_{dung}.

All values are expressed in units of the SI system (Système International d'Unités). As a consequence, some parameters have an uncommon unit. Kilograms of chemical are indicated by [kg_c]. Other masses will usually be indicated as wet weight or dry weight ([kg_{wwt}] and [kg_{dwt}] respectively), or by compartment (bodyweight or feed: [kg_{bw}] and [kg_{fd}] respectively) It should be noted that for the dimension 'time' the non-SI units 'days' [d] and 'years' [yr] are used, instead of seconds [s], since these are more relevant units in the framework of this assessment.

In contrast with industrial chemicals, the emission module for veterinary medicines does not usually result in emissions to waste water and air from point sources. Instead, emissions take place to a specific area directly (direct immission into surface water, spillage to soil) or indirectly (spreading with manure or dung).
The emission module which characterises the releases to the environment via manure requires parameters from the distribution module (degradation rates and application intervals), and is therefore incorporated in the distribution chapter.

3.1 Animal husbandry.

The emission routes vary with the target animal to be treated. The animals in the Netherlands can be divided into two major groups: pets, and livestock, poultry and fish. Pets are kept on a small-scale basis, with a limited number of animals at one place. Because with pets no mass medication can be expected, products intended for this group are exempted from further assessment. Horses are part of the animal husbandry group (stock-breeding and -raising industry).
The categories livestock discerned, with their excreta production and the related phosphate production in the Netherlands are based on the index in KWIN (1996; page 62-67).
The faeces of grazing animals in the field is referred to as dung. As the dung is not collected and stored over time, for the hazard assessment the peak concentrations and the drug excretion pattern in time are important. In the field faeces and urine are dispersed separately, whereas in the stable they are mixed. The excreta obtained indoors, referred to as manure, are collected and stored for some time. Slurry is the mixture of faeces, urine, and materials from the housing of animals (e.g. spilled feed, straw, litter, sand, water, down).

The modelling starts with a pick-list of animal categories. Every animal category has its own list of animal-specific parameter values, that will be presented in the chapters below.

Table 4. Pick-list of main animal categories and emission routes.

Livestock main category	**Animal category and defaults**	**Emission route E**			
	see pick list in chapter	spreading of slurry Eslurry	grazing animals Edung	spillage at application pasture $Edirect_{pasture}$	emission of waste water $Elocal_{water}$
cattle	3.2	X	X		
pigs	3.3	X			
horses and ponies	3.4	X	X		
chickens	3.5	X			
turkeys	3.6	X			
ducks	3.7	X			
sheep	3.8		X	X	
goats	3.9				
others	3.10				
fish farms	3.11	X			X

input			
-	livestock main category	[-]	P
output			
E	emission routes	[-]	O
-	picklist animal subcategories and values	[-]	O

The possible inputs and outputs for the environmental assessment of veterinary medicinal products are limited. The general parameters are given below.

Table 5. General parameters for animal categories.

General application inputs		
(averaged) body weight	m_{animal}	[kg_{bw}.animal^{-1}]
input for spreading of slurry		
number of cycli per year	$Ncyclus_{animal}$	[animal.place^{-1}.yr^{-1}]
number of milking days	Tmilking	[d.yr^{-1}]
number of housing days	$Thousing_{animal}$	[d.yr^{-1}]
manure production stable	$Pmanure_{animal}$	[kg_{wwt}.place^{-1}.d^{-1}]
dirty water production stable	$Pdirty\ water_{animal}$	[kg_{wwt}.place^{-1}.d^{-1}]
slurry production stable	$Pslurry_{animal}$	[kg_{wwt}.place^{-1}.d^{-1}]
phosphate production	$P_{P2O5\ animal}$	[kg_{P2O5}.place^{-1}.d^{-1}]
input for grazing		
number of grazing days	Tgrazing	[d.yr^{-1}]
dung production pasture	$Pdung_{animal}$	[kg_{wwt}.animal^{-1}.d^{-1}]
urine production pasture	$Purine_{animal}$	[l.animal^{-1}.d^{-1}]
stocking density pasture	$Nanimal_{ha\ pasture}$	[animal.ha^{-1}]
number of excretions per day	Nexcretion	[d^{-1}]

Some animals are kept at their mature bodyweight, other are reared from a starting weight onwards. For animals in the latter situation the mean bodyweight is the most convenient value. For animals in the former group, the maximum body weight is used. The number of cycles per year is based on the production periods including the days the pens stand empty. For background information on dung production and partitioning see Appendix II. Notice the use of the word dung for the faeces in the field and the words manure and slurry for the mixture of excreta collected in the stable. The specific values for the different animal categories are given below.

3.2 Cattle.

Dairy cows are housed in winter time (175 days) and graze during the rest of the year. During grazing they return to the stable for milking. In spring and autumn they also may return to the stable for the night. Dairy cows are kept on the farm together with yearlings (1-2 years old) and calves (0-1 year old) for replacement in the ratio 100:33:37. The manure production in the stable is 52 - 80 $l.place^{-1}.d^{-1}$ in winter and 11 $l.place^{-1}.d^{-1}$ in summer (KWIN 1996, Berende, 1998b). Dirty water production with dairy cows amounts to 14.6 $l.place^{-1}.d^{-1}$ (Montfoort, 1996).
A suckler cows is kept together with her calf (up to 6 months old) in the same way as dairy cows. Young bulls and heifers are kept for meat production. These animals also are grazed in summer time. These cattle are not used for milk production.
Veal calves are kept indoors: white veal calves live during 0-6 months and are fed milk powder; rose veal calves live during 0-7 months and are fed roughage and concentrate. Currently no specific information on manure production of rose veal calves is available, as this is a newly developing branche. Breeding bulls are also not assessed separately. There are a few artificial insemination farms, and as it concerns healthy full-grown animals, the combination of small-scale husbandry and low medicine use implies a relative low risk on environmental contamination.
Data on manure and dung production are based on KWIN (1996) for housing and Berende (1998b) for grazing.
The following categories of cattle are used in the risk evaluation:

- dairy cows
- suckler cows
- beef cattle
- veal calves

Table 6. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $E_{direct_{pasture}}$	emission of waste water $E_{local_{water}}$
beef cattle		X	X		
suckler cow		X	X		
dairy cow		X	X		
veal calf	X	X			

Table 7. Default settings for cattle.

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,\ cattle}$	[°C]	10
(averaged) body weight	$m_{dairy\ cow}$	$[kg_{bw}.animal^{-1}]$	600
	$m_{suckler\ cow}$	$[kg_{bw}.animal^{-1}]$	600
	$m_{veal\ calf}$	$[kg_{bw}.animal^{-1}]$	140
	$m_{beef\ cattle}$	$[kg_{bw}.animal^{-1}]$	330
number of cycli per year	$Ncyclus_{dairy\ cow}$	$[animal.place^{-1}.yr^{-1}]$	1

parameter	symbol	unit	value
averaged temperature in slurry basin	$t_{slurry,\ cattle}$	[°C]	10
	$Ncyclus_{suckler\ cow}$	[animal.place^{-1}.yr^{-1}]	1
	$Ncyclus_{veal\ calf}$	[animal.place^{-1}.yr^{-1}]	1.8
	$Ncyclus_{beef\ cattle}$	[animal.place^{-1}.yr^{-1}]	0.7
number of housing days cattle excluding veal	$Thousing_{non-veal}$	[d.yr^{-1}]	175
number of housing days veal	$Thousing_{veal\ calf}$	[d.yr^{-1}]	365
number of grazing days	Tgrazing	[d.yr^{-1}]	190
manure production in stable during grazing period	$Pmanure_{dairy\ cow\ grazing}$	[kg_{wwt}.place^{-1}.d^{-1}]	11.2
manure production in stable during housing	$Pmanure_{dairy\ cow\ housing}$	[kg_{wwt}.place^{-1}.d^{-1}]	63.9
	$Pmanure_{suckler\ cow}$	[kg_{wwt}.place^{-1}.d^{-1}]	63.9
	$Pmanure_{veal\ calf}$	[kg_{wwt}.place^{-1}.d^{-1}]	9.9
	$Pmanure_{beef\ cattle}$	[kg_{wwt}.place^{-1}.d^{-1}]	20
dirty water production stable	$Pdirty\ water_{dairy\ cow}$	[kg_{wwt}.place^{-1}.d^{-1}]	14.6
	$Pdirty\ water_{non-dairy}$	[kg_{wwt}.place^{-1}.d^{-1}]	0
phosphate production in stable during grazing period	$P_{P2O5\ dairy\ cow\ grazing}$	[kg_{P2O5}.place^{-1}.d^{-1}]	0.0177
phosphate production during housing	$P_{P2O5\ dairy\ cow\ housing}$	[kg_{P2O5}.place^{-1}.d^{-1}]	0.1123
	$P_{P2O5\ suckler\ cow}$	[kg_{P2O5}.place^{-1}.d^{-1}]	0.1123
	$P_{P2O5\ veal\ calf}$	[kg_{P2O5}.place^{-1}.d^{-1}]	0.0142
	$P_{P2O5\ beef\ cattle}$	[kg_{P2O5}.place^{-1}.d^{-1}]	0.0367
dung production pasture during grazing period	$Pdung_{dairy\ cow}$	[kg_{wwt}.animal^{-1}.d^{-1}]	52
	$Pdung_{suckler\ cow}$	[kg_{wwt}.animal^{-1}.d^{-1}]	52
	$Pdung_{beef\ cattle}$	[kg_{wwt}.animal^{-1}.d^{-1}]	11
stocking density pasture	$Ndairy_{ha\ \ pasture}$	[animal.ha^{-1}]	3.5
	$Nsuckler_{ha\ pasture}$	[animal.ha^{-1}]	3.5
	$Nbeef_{ha\ pasture}$	[animal.ha^{-1}]	9.5
number of excretions per day	Nexcretion	[d^{-1}]	10.5

3.3 Pigs.

Three types of pig-farming are present in the Netherlands: exclusively sows or exclusively fattening-pigs, or a combination of both. On a sow-farm one finds sows with and without piglets. The year-averaged amount of piglets per sow is 2.63, while an average 78% of the sows has suckling piglets and 22% has none. Together they produce 14.8 kg slurry per sow per day. Breeding-boars live ca. 18 months on the farm, but as they perform 130 services a year, they are a minority on the farm. There are a few artificial insemination farms, and as it concerns healthy full-grown animals, the combination of small-scale husbandry and low medicine use implies a relative low risk on environmental contamination.
Pigs may be kept outside, but in the Netherlands the British outdoor-system is not used. Currently there are few farms that breed pigs on pasture land, but on most farms for 'free-ranging pigs' the pigs have the possibility to go outside on a concrete paved floor. Inside straw is present, and both areas are cleaned regularly. This category is not assessed separately in this report.
The Dutch authorities encourage the development of mixed farms to reduce transport of animals. As a sow drops ca. 20 young and there are 2.8 cycles of fattening pigs a year, one needs one sow on every seven fattening pigs. For the moment we take only the segragated farming into consideration. The following categories of pigs are used in the risk evaluation:

fattening pigs
breeding sows including piglets 25 kg.

Table 8. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $Edirect_{pasture}$	emission of waste water $Elocal_{water}$
fattening pig	X	X			
breeding sow	X	X			

Table 9. Default settings for pigs

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,pig}$	[°C]	20
(averaged) body weight	m_{sow}	$[kg_{bw}.animal^{-1}]$	240
	$m_{fattening\ pig}$	$[kg_{bw}.animal^{-1}]$	70
number of cycli per year	$Ncyclus_{sow}$	$[animal.place^{-1}.yr^{-1}]$	1
	$Ncyclus_{fattening\ pig}$	$[animal.place^{-1}.yr^{-1}]$	2.8
number of housing days	$Thousing_{pigs}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{sow}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	14.8
	$Pslurry_{fattening\ pig}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	3.8
phosphate production during housing	$P_{P2O5\ sow}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.0556
	$P_{P2O5\ fattening\ pig}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.0203

3.4 Horses.

Approximatley half of the horses in the Netherlands are privately owned. Private persons and farmers keep some horses for hobby. Terrain-managing institutes keep ponies for grazing. Especially these private animals graze in fields. Donkeys are also kept in the Netherlands, but their number is relatively small compared to horses and ponies. The commercial sector is divers and consists of riding schools, dairy farming, racing centres and stud-farms. Horses for meat production are mainly imported. The commercial animals are stabled most of the time. The manure (slurry) from riding-schools is mostly collected and used for mushroom-cultivation and compost for allotments. The major emission routes are grazing animals, and spreading of manure on allotments and spreading of mushroom-substrate after cultivation. Ponies have a shoulder height <148 cm, horses >148 cm. Horses and ponies come in different sizes and body weights: a full-grown horse is approx. 600 kg (or more); a Halflinger pony 400 kg; and a Shetland approx. 250 kg. Shetlands are kept outside most of the year.
As there were no data available for grazing horses these were manufactured using the data for beef cattle, see Appendix II. Data on slurry production are derived from PR Lelystad.
The following categories of horses are used in the risk evaluation:

horses 600 kg
ponies 250 kg

Table 10. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $E_{direct_{pasture}}$	emission of waste water $E_{local_{water}}$
horses 600 kg	X	X			
ponies 250 kg			X		

Table 11. Default settings for horses.

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,horses}$	[°C]	25
body weight	m_{horse}	$[kg_{bw}.animal^{-1}]$	600
	m_{pony}	$[kg_{bw}.animal^{-1}]$	250
number of cycli per year	$Ncyclus_{horse}$	$[animal.place^{-1}.yr^{-1}]$	1
	$Ncyclus_{pony}$	$[animal.place^{-1}.yr^{-1}]$	1
number of housing days horse	$Thousing_{horse}$	$[d.yr^{-1}]$	365
number of grazing days ponies	$Tgrazing_{pony}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{horse}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	28
phosphate production during housing	$P_{P2O5\ horse}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.034
dung production pasture during grazing period	$Pdung_{pony}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	4.0
stocking density pasture	$Npony_{ha\ pasture}$	$[animal.ha^{-1}]$	5
number of excretions per day	Nexcretion	$[d^{-1}]$	10.5

3.5 Chickens.

Most chickens are kept indoors in cages or on floors. The manure from laying hens in cages is collected on a conveyor-belt. In the broiler industry, after every cycle the manure and litter from the floor is cleaned from the poultry house. Over eighty percent of the manure collected from layers is dried, and this percentage will increase rapidly to 100% in the next few years. The number of chickens kept outdoors is insignificant compared to the other methods of housing. The different stages in the life-cycle (chick, in rearing, parent animal) have different body weights and manure production figures. The following categories of chickens are used in the risk evaluation:

Hens and cockerels of laying breed 18 weeks old
Laying hens kept indoors permanently in cages
Free-ranging laying hens on litter floor, indoors
Hens and cockerels of broilers 19 weeks old
Hens and cocks of broilers
Broilers

Animals in rearing and broilers are non-oviparous. Laying hens, free hens and parent broilers are oviparous.

Table 12. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $Edirect_{pasture}$	emission of waste water $Elocal_{water}$
hen in rearing	X	X			
hen	X	X			
hen free	X	X			
parent broiler in rearing	X	X			
parent broiler	X	X			
broiler	X	X			

Table 13. Default settings for chickens

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,chickens}$	[°C]	25
averaged body weight broilers and hens in rearing (i.r.)	$m_{chicken\ i.r.}$	$[kg_{bw}.animal^{-1}]$	1
body weight adult chickens	$m_{chicken}$	$[kg_{bw}.animal^{-1}]$	2
number of cycli per year	$Ncyclus_{hen\ i.r.}$	$[animal.place^{-1}.yr^{-1}]$	2.7
	$Ncyclus_{hen}$	$[animal.place^{-1}.yr^{-1}]$	0.85
	$Ncyclus_{hen\ free}$	$[animal.place^{-1}.yr^{-1}]$	0.84
	$Ncyclus_{parent\ broiler\ i.r.}$	$[animal.place^{-1}.yr^{-1}]$	2.4
	$Ncyclus_{parent\ broiler}$	$[animal.place^{-1}.yr^{-1}]$	1.05
	$Ncyclus_{broiler}$	$[animal.place^{-1}.yr^{-1}]$	7
number of housing days	$Thousing_{chicken}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{hen\ i.r.}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.026
	$Pslurry_{hen}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.072
	$Pslurry_{hen\ free}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.081
	$Pslurry_{parent\ broiler\ i.r.}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.038

parameter	symbol	unit	value
averaged temperature in slurry basin	$t_{slurry,chickens}$	[°C]	25
	$Pslurry_{parent\ broiler}$	[$kg_{wwt}.place^{-1}.d^{-1}$]	0.060
	$Pslurry_{broiler}$	[$kg_{wwt}.place^{-1}.d^{-1}$]	0.030
phosphate production during housing	$P_{P2O5\ hen\ i.r.}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00055
	$P_{P2O5\ hen}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00137
	$P_{P2O5\ hen\ free}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00137
	$P_{P2O5\ parent\ broiler\ i.r.}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00068
	$P_{P2O5\ parent\ broiler}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00203
	$P_{P2O5\ broiler}$	[$kg_{P2O5}.place^{-1}.d^{-1}$]	0.00066

3.6 Turkeys.

Turkeys in the Netherlands are mainly kept for meat. Parent animals can be divided into three groups. The animals are kept indoors like ducks and broilers. The following categories of turkeys are used in the risk evaluation:

Parent animals in rearing 0-6 weeks old
Parent animals in rearing 6-30 weeks old
Parent animals
Turkeys for meat production.

Animals in rearing and turkeys for meat production are non-oviparous. Parent turkeys are oviparous.

Table 14. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $Edirect_{pasture}$	emission of waste water $Elocal_{water}$
turkey in rearing 0-6 weeks	X	X			
turkey in rearing 6-30 weeks	X	X			
parent turkey	X	X			
beef turkey	X	X			

Table 15. Default settings for turkeys.

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,turkeys}$	[°C]	25
averaged body weight parent animals in rearing 0-6 weeks	$m_{turkey\ i.r.\ 0\text{-}6}$	$[kg_{bw}.animal^{-1}]$	2
averaged body weight parent animals in rearing 6-30 weeks	$m_{turkey\ i.r.\ 6\text{-}30}$	$[kg_{bw}.animal^{-1}]$	7.5
body weight parent animals	$m_{parent\ turkey}$	$[kg_{bw}.animal^{-1}]$	14
averaged body weight turkeys for meat	m_{turkey}	$[kg_{bw}.animal^{-1}]$	7
number of cycli per year	$Ncyclus_{turkey\ i.r.\ 0\text{-}6}$	$[animal.place^{-1}.yr^{-1}]$	7.4
	$Ncyclus_{turkey\ i.r.\ 6\text{-}30}$	$[animal.place^{-1}.yr^{-1}]$	2.2
	$Ncyclus_{parent\ turkey}$	$[animal.place^{-1}.yr^{-1}]$	1
	$Ncyclus_{turkey}$	$[animal.place^{-1}.yr^{-1}]$	2.7
number of housing days	$Thousing_{turkey}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{turkey\ i.r.\ 0\text{-}6}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.037
	$Pslurry_{turkey\ i.r.\ 6\text{-}30}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.126
	$Pslurry_{parent\ turkey}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.195
	$Pslurry_{turkey}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.125
phosphate production during housing	$P_{P2O5\ turkey\ i.r.\ 0\text{-}6}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.00071
	$P_{P2O5\ turkey\ i.r.\ 6\text{-}30}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.00040
	$P_{P2O5\ parent\ turkey}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.00548
	$P_{P2O5\ turkey}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.00216

3.7 Ducks.

Ducks in the Netherland are mainly kept for meat. The number of parent animals is relatively low compared to the number of the ducks kept for meat. Ducks are kept in stable on litter floors, although at some farms they are kept (partly) outside. The following categories of ducks are used in the risk evaluation:

ducks for meat.

Table 16. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $E_{direct_{pasture}}$	emission of waste water $E_{local_{water}}$
ducks	X	X			

Table 17. Default settings for ducks.

parameter	**symbol**	**unit**	**value**
averaged temperature in slurry basin	$t_{slurry,ducks}$	[°C]	25
averaged body weight ducks for meat	m_{duck}	$[kg_{bw}.animal^{-1}]$	1.6
number of cycli per year	$Ncyclus_{duck}$	$[animal.place^{-1}.yr^{-1}]$	7.4
number of housing days	$Thousing_{duck}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{duck}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	0.214
phosphate production during housing	$P_{P2O5\ duck}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.00164

3.8 Sheep.

Most sheep are only put up between mid-February and mid-April to lamb. Over the year they spend 10.5 months in field and 1.5 months indoors. One ewe raises an average 1.7 lamb (range 1.33-2.80 (KWIN 1996)). The lamb and ewe are turned out ca. three weeks after lambing, and the lamb is slaughtered after 6 months when it reached a weight of 40-45 kg. A mature ewe weighs an average 82 kg (Berende, 1998a). The ewes may be treated for diseases when they are put up, and approximately one week after lambing the animals are treated with anthelmintics. This latter treatment is repeated in May-June and September-October. The body weight and dung production of the lambs is therefore chosen at 32 calender weeks (end of May) and averaged for ewes and rams, single and twins (Berende, 1998a).
Sheep can also be dipped or substances can be applied topically in high volumes. The following categories of sheep are used in the risk evaluation:

sheep on pasture, >1 year old, including lambs 45 kg.

Table 18. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $E_{direct_{pasture}}$	emission of waste water $E_{local_{water}}$
sheep			X	X	

Table 19. Default settings for sheep.

parameter	**symbol**	**unit**	**value**
body weight ewe	m_{ewe}	$[kg_{bw}.animal^{-1}]$	82
body weight lamb	m_{lamb}	$[kg_{bw}.animal^{-1}]$	36
number of cycli per year	$Ncyclus_{ewe}$	$[animal.place^{-1}.yr^{-1}]$	1
number of housing days	$Thousing_{ewe}$	$[d.yr^{-1}]$	0
number of grazing days ewe	$Tgrazing_{ewe}$	$[d.yr^{-1}]$	320
number of grazing days lamb	$Tgrazing_{lamb}$	$[d.yr^{-1}]$	160
dung production pasture during grazing period ewe	$Pdung_{ewe}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	1.025
dung production pasture during grazing period lamb	$Pdung_{lamb}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	1.758
stocking density pasture ewe	$Newe_{ha\ pasture}$	$[animal.ha^{-1}]$	15
stocking density pasture lamb	$Nlamb_{ha\ pasture}$	$[animal.ha^{-1}]$	25
number of excretions per day	Nexcretion	$[d^{-1}]$	10.5

3.9 Goats.

Because of the modest scale of this branche compared to dairy cows and sheep, goats are not separately assessed in the Phase I and Phase II Tier A assessments.
Goats are kept for dairy production like cows. On every dairy goat 0.25 lamb is reared on a year's basis. The production of dirty water for cleaning of milking equipment etc. is not documented, therefore the figures for dairy cows may be applied. Goats are milked 300 days a year. On may assume they are treated like dairy cows: housing 175 days a year, grazing 190 days a year.

3.10 Fur-bearing animals, rabbits, ostriches and other poultry.

Minks make up 98% of the number of fur-bearing animals. In 1995 fox-farms were prohibited by law, and before the year 2005 all fox-farms will have terminated their activities. Minks are kept in cages and the manure is collected in gutters and pits. In general, little or no medicinal products are used in this sector (personal communication IKC-L, V.d. Kerkhof).
Rabbits are kept in cages. Rabbit body weights differ greatly between sexes and ages. As an estimate the average rabbit weighs 2 kg (personal communication IKC-L, V.d. Kerkhof).
In the Netherlands poultry like ostriches, emoes, nandoes, guinea-fowl, quails, and geese are kept. As their numbers are relatively small compared to other poultry (chickens and turkeys), they are not dealt with separately in this document.

3.11 Fish.

Fish medicines are mostly added to the water, after which the circulation is stopped. Some antibiotics can be added to the feed.

The scale of fish cultivation for commercial purposes is limited in the Netherlands (Kamstra et al., 1995). In 1994 in total 26 and 10 companies were involved in cultivating eel and catfish, respectively. Rainbow trout is cultivated on a small scale in flow-through and in landbased systems, in which the water body fulfils a role in water treatment. Several trout nurseries use flow-through systems: surface water is lead through the fish basin over a settling tank back into the surface water system. There is one place in the province Zeeland where Salmonidae are kept in cages in the estuaria. There are no cage systems in fresh surface water. Finally, there are occasional projects in the cultivation of tarbot, tilapia, and sturgeon.
Most nurseries use recirculation systems, that recycle the water after a (biological) water treatment (filtration). Catfish nurseries discharge on the Sewage Treatment Plants (STP), but 40% of the eel nurseries discharge directly on surface water. The number of companies that discharge the fish water untreated is negligible, as most have some way of water treatment (filters, settlement basins, ponds) before the water is discharged. The recycling systems and the settlement tanks before discharge remove virtually all undissolved particles. Many nurseries collect the sludge from this treatment and sell or use it as fertiliser.

The following scenarios are proposed, based on information given in Kamstra et al. (1995) and USES1.0 (1994). The scenarios are based on a fish farm that breeds 50 tonnes eel a year, the median production.
a) continuous treatment; with recirculation/filtration, followed by settlement tank and STP;
b) continuous treatment; without recirculation/filtration, followed by settlement tank;
c) occasional treatment (4 times a year), without recirculation/filtration before discharge on the settlement tank and STP;
d) occasional treatment (4 times a year), without recirculation/filtration before discharge on the settlement tank.

On a yearly basis an eel farm discharges 200-1900 m^3 water per tonne fish, depending on the water use. An average 250 m^3 per tonne fish is used here, resulting in a turnover rate of 35 $m^3.d^{-1}$. It is assumed the total water volume of the nursery[4] is 70 m^3. After the settlement tank the water fraction is discharged, while the sludge (2% dry matter) in the tank (and filters) is used as soil fertiliser. Per tonne fish 13 kg P (equivalent to 60 kg P_2O_5) is removed in the sludge. The load from the settlement tank and recirculation system will be expressed in terms of kg chemical per day, and it is assumed that this load is equally spread over 25 days in case of occasional treatment (c.f. USES mushrooms module).

The recirculation/filtration system and the settlement tank both have an estimated removal efficiency of 50% of the dose from the water, but this amount is added to the dosage in the sludge used for spreading on the land[5].

[4] Based on a feed/growth factor of 1.7, a growth of 50 tonnes per year, and 0.3 m^3 system water per kg feed.
[5] The removal percentage of 50% is based on the assumption that removal will be correlated with sorption and degradation properties of the substance, but also with dimensions of the tank and the overflow of sludge into the water.

Table 20. Pick-list of animal subcategories and emission routes.

Livestock subcategory	**Emission route E**				
	spreading of slurry Eslurry grassland	spreading of slurry Eslurry arable land	grazing animals Edung	spillage and direct exposure at application pasture $Edirect_{pasture}$	emission of waste water $Elocal_{water}$
fish	X				X

Table 21. Default settings for fish.

parameter	**symbol**	**unit**	**value**
phosphate production per day	$P_{P2O5\ fish}$	$[kg_{P2O5}.\ yr^{-1}]$	3000
fraction retention in sludge with filtration	$F_{ret,\ filtration}$	[-]	0.75
fraction retention in sludge without filtration	F_{ret}	[-]	0.5
number of application continuous treatment	$Nappl_{con.}$	$[yr^{-1}]$	365
number of application occasional treatment	$Nappl_{occ.}$	$[yr^{-1}]$	4
volume of waste water continuous treatment	$Vwaste\ water_{con.}$	[l]	35000
volume of waste water occasional treatment	$Vwaste\ water_{occ.}$	[l]	70000
dilution factor recieving water continuous treatment	$DILUTION_{fish\ ,con.}$	[-]	5
dilution factor receiving water occasional treatment	$DILUTION_{fish\ ,occ.}$	[-]	3
emission period for discharge to STP	$Temission_{stp}$	[d]	25

3.12 Agricultural manuring practice in the Netherlands.

The Dutch agricultural practice is characterised by:

- restricted manure spreading periods for grassland and arable land in specified area's;
- phosphate immission standards; nitrate immission standards are not used;
- injection of slurry into the grassland soil to ca. 5 cm depth.
- spreading of slurry onto arable land, immediately followed by a tillage operation;
- phosphate production standards per type of animal.

The periods in which the spreading of manure (i.e. stable manure, slurry and sludge) is allowed are different for indicated and non-indicated areas. For indicated areas this period is February 1-August 31 for grassland and arable land. For non-indicated areas this period is February 1-September 15 for grassland and the whole year for arable land (KWIN 1996).
We assume that on grassland the phosphate immission standard is filled in four events, and on arable land in one event, in spring before the maize grows. The manure for spreading on arable land is stored for 152 days and spread on February 1. The manure for grassland is stored in winter (152 days), and during three intervals (71 days) in summer.
A worst-case estimation would be that the medicine is excreted the day before the manure is spread. A best-case estimation is that the manure is spread one year after the medicine is excreted. Probably the truth is in the middle. We need to take into account the number of treatments per place per year. A treatment that is repeated every cycle is given twice a year to veal, but eight times to broilers. On grassland the manure is spread in four events. In veal manure only in one or two events the medicine is present, but with broilers probably in all manure the medicine is present. We therefore calculate an averaged concentration in the manure, based on the intervals between spreading. The longest interval is 152 days, the shortest 71 days. For the calculation of the highest concentration in the soil these scenarios result in three spreading intervals of 71 days for grassland, and for arable land no spreading interval is accounted for. During the interval the residues can dissipate from the soil, which lowers the final concentration at the end of the season.

Table 22. Default settings for spreading of veterinary medicinal product residues on grassland and arable land.

Parameter	**symbol**	**unit**	**value**
mixing depth grassland[6]	$DEPTH_{grassland}$	[m]	0.05
mixing depth arable land	$DEPTH_{arable\ land}$	[m]	0.20
phosphate immission standard grassland	$Q_{P2O5\ grassland}$	$[kg_{P2O5}.ha^{-1}.yr^{-1}]$	135
phosphate immission standard arable land	$Q_{P2O5\ arable\ land}$	$[kg_{P2O5}.ha^{-1}.yr^{-1}]$	110
application interval manure on grassland	$T_{interval,grassland}$	[d]	71
application interval manure on arable land	$T_{interval,arable\ land}$	[d]	152
storage time slurry before spreading on grassland	$T_{storage,grassland}$	[d]	71
storage time slurry before spreading on arable land	$T_{storage,arable\ land}$	[d]	152
number of spreading events on grassland	$Nspreading_{grassland}$	$[yr^{-1}]$	4
number of spreading events on arable land	$Nspreading_{arable\ land}$	$[yr^{-1}]$	1

[6] Based on the EMEA/CVMP/055/96-final agreements.

4. EMISSION AND DISTRIBUTION MODELS.

The models are presented in the order:

- introduction	text
- default values	table with borders: parameter, symbol, unit, value, restriction
- calculations	formula
- parameters	table without borders: symbol, parameter, unit, value, type, restriction
- input values	
- intermediate results	
- output values	

The following models are presented:

4.1 Concentration in slurry and dung.

In the event the product reaches the slurry after internal or external application, or direct exposure, the environment is exposed by spreading of slurry. In the event the product is excreted after internal or external application by grazing animals, the environment is exposed via urine and dung.
The first step in the hazard assessment is the calculation of the concentration in slurry before spreading onto land, or in fresh dung, because these are trigger values in Phase I.

The concentration in slurry for animals that are housed their whole life can be based on the averaged yearly production of slurry. Cattle, except for veal, are housed in winter and are grazed in summer, and dairy cows return to the housing for milking. This is reflected in the manure production per day for these periods.The concentration in the slurry depends a.o. on the dirty water production. The dirty water production for dairy cows is quantified separately from the manure production. For all other animals the dirty water production is integrated in the slurry production.

Table 23. Default settings for the calculation of the concentrations in slurry.

animal category	**dirty water production ($P_{dirty\ water}$)**	**unit**
dairy cow	14.6	[$kg_{wwt}.place^{-1}.d^{-1}$]
other animals	0	[$kg_{wwt}.place^{-1}.d^{-1}$]

4.1.1 Direct entry into manure (external applications).

4.1.1.1 Disinfection of udders.

Udders of dairy cows are disinfected after milking. The quantity of active ingredient used to disinfect udders depends on the quantity product ($Q_{product}$) and the concentration of a.i.. Although the remainder of the disinfectant should be considered as dangerous waste, it is assumed that it will end up in the slurry storage system. The emission to the slurry storage system depends on the quantity active ingredient used and the fraction released to the slurry storage. The concentration in slurry during the summer period, when the dairy cows are grazed, is supposed to be the most critical. Therefore only the slurry production during the grazing period and the spreading on grassland are taken into consideration. Cows are milked 2-3 times a day but here one application per day is assumed.

Table 24a. Default settings of the module for udder disinfection.

parameter	**symbol**	**unit**	**value**
fraction chemical released to slurry storage	F_{slurry}	[-]	0.2
application interval	$T_{interval}$	[d]	1
number of applications before spreading of slurry	Nappl	[-]	71
half-life time for biodegradation in slurry	$DT50deg_{slurry}$	[d]	1e6
manure production in stable during grazing period	$Pmanure_{dairy\ cow\ grazing}$	[$kg_{wwt}.place^{-1}.d^{-1}$]	9.3
dirty water production	$Pdirty\ water_{dairy\ cow}$	[$kg_{wwt}.place^{-1}.d^{-1}$]	14.6
dairy cattle; storage time slurry	$T_{storage}$	[d]	71

The model takes a daily treatment regime during one slurry storage period into account, as well as the degradation in the manure during the storage period. The last day after treatment it will take an average half day before the slurry is removed and spread.

$$PIECslurry = \frac{Q_{product} \cdot C_c \quad F_{slurry}}{Pslurry \cdot T_{storage}} \cdot \frac{1 - F_{rsl}^{Napplications}}{1 - F_{rsl}} \cdot e^{-k deg_{slurry} \cdot T\text{interval}/2}$$

$$Pslurry = Pmanure + Pdirty\ water$$

$$F_{rsl} = e^{-k\,\deg_{slurry} \cdot T_{\text{interval}}}$$

$$k\,deg_{slurry} = \frac{ln\,2}{DT50\,deg_{slurry}}$$

input			
$Q_{product}$	quantity product used	[kg.animal^{-1}.d^{-1}]	S
C_c	concentration a.i. in product	[mg$_c$.kg^{-1}]	S
F_{slurry}	fraction released to slurry storage	[-]	D
$T_{interval}$	time between two applications	[d]	D
$Pmanure_{dairy\ cow\ grazing}$	manure production in stable during grazing period	[kg$_{wwt}$.place^{-1}.d^{-1}]	D
$T_{storage}$	storage time slurry	[d]	D
$Pdirty\ water_{dairy\ cow}$	dirty water production	[kg$_{wwt}$.place^{-1}.d^{-1}]	D
Napplications	number of applications during storage period	[-]	D
$DT50deg_{slurry}$	half-life time for biodegradation in slurry	[d]	S/D
intermediate results			
$kdeg_{slurry}$	rate constant for biodegradation in slurry	[d^{-1}]	O
Pslurry	production of slurry	[kg$_{wwt}$.place^{-1}.d^{-1}]	O
F_{rsl}	fraction of the concentration remaining in slurry after time $T_{interval}$	[-]	O[c]
output			
PIECslurry	predicted initial concentration in slurry before spreading	[mg$_c$. kg$_{wwt}$ $^{-1}$]	O

4.1.1.2 Disinfection of stables.

Disinfection of stables is no part of the environmental assessment of veterinary medicinal products, but of pesticides. Above mentioned module however can be easily adapted for this use.

4.1.1.3 Spillage from external application.

Substances used for topical application (spraying or pour-on) on animals may reach the slurry directly due to spillage (drift from spraying) and rubbing off. Initially, a calculation is performed where it is assumed that the dosage reaches the slurry completely. This can be calculated using the model in § 4.1.2.1 and using $Q_{excreted}$ as the dosage per animal. Should the trigger for slurry be exceeded, a refined calculation is made, assuming spillage, uptake and excretion.

Table 24b. Default settings for the calculation of the concentration in slurry by direct exposure.

product type	**symbol**	**unit**	**value**
spray	$Fslurry_{spillage}$	[-]	0.2
pour-on	$Fslurry_{spillage}$	[-]	0

Sprays are supposed to spill 20% of the dosage. The $Q_{excreted}$ in §4.1.2.1 is corrected with (1-$Fslurry_{spillage}$) and $F_{excreted}$ and finally the concentration in slurry caused by the $Fslurry_{spillage}$ is added. Table 24a shows that the refined assessment for pour-ons can be performed with § 4.1.2.1 alone, because no spillage is assumed.

4.1.2 Entry into slurry and dung after uptake and excretion.

4.1.2.1 Calculation of the concentration in slurry after uptake and excretion.

The concentration in the slurry is given by the excreted amount of substance per cycle, the degradation during the interval time between the cycles (which equals the T_{cyclus}, but is never longer than $T_{storage}$), the number of cycles (and thus of treatments) and the time remaining before the slurry is spread, in which the substance can degrade further (T_{rest}). This T_{rest} is maximally the difference between the total duration of complete cycli within the storage period and the $T_{storage}$, and might be zero days (excretion into slurry just before the slurry is spread).
The effective time degradation can take place cannot be calculated mathematically, but it is obvious that any duration between zero days and T_{rest} has an equal chance. For the time degradation can take place the value of one half T_{rest} is chosen, a the value that gives the most averaged result.
For the model calculations it is assumed that the excretion of residues into slurry takes place in one single event (in reality excretion is spread over several days).

Table 25. Default settings of the module for the calculation of the concentration in slurry after uptake and excretion

parameter	symbol	unit	value
fraction of dosage chemical excreted in manure	$F_{excreted}$	[-]	1
half-life time for biodegradation in slurry	$DT50deg_{slurry}$	[d]	1e6
cattle except veal; average storage time slurry	$T_{storage}$	[d]	152
sheep; average storage time slurry	$T_{storage}$	[d]	0
veal, horses, pigs, poultry; average storage time slurry[7]	$T_{storage}$	[d]	71

Given $T_{storage}$ the maximum number of applications (Napplications) possible within the storage period is:

grassland $T_{storage}$ 71 days			arable land $T_{storage}$ 152 days		
$Ncyclus_{animal}$	$Tcyclus_{animal}$	$N_{application}$	$Ncyclus_{animal}$	$Tcyclus_{animal}$	$N_{application}$
5.1	71	1	2.4	152	1
5.2- 10.1	36-71	2	2.5-4.7	77-151	2
10.2- 15.2	23-35	3	4.8-7.2	51-76	3
			7.3-9.4	39-50	4
			9.5-11.8	31-38	5

Model for calculating the concentrations in slurry before spreading as a result of excretion.

$$Q_{excreted} = Q_{product} \,.\, C_c \,.\, T_{treatment} \,.\, F_{excreted} \,.\, m_{animal}$$

$$PIEC_{slurry} = \frac{Qexcreted}{Pslurry \,.\, T_{storage}} \,.\, \frac{1 - F_{rsl}^{Napplication}}{1 - F_{rsl}} \,.\, e^{-k\,deg_{slurry} \cdot T_{rest}/2}$$

$$F_{rsl} = e^{-kdeg_{slurry} \cdot Tcyclus_{animal}}$$

$$k\,deg_{slurry} = \frac{ln2}{DT50\,deg_{slurry}}$$

$$T_{rest} = T_{storage} - (Napplication - 1) \,.\, T_{cyclus}$$

$$T_{cyclus} = 365 \,/\, Ncyclus_{animal}$$

$$Pslurry = Pmanure + Pdirty\ water$$

[7] See 4.2.1 The concentration in soil after spreading.

input			
$Q_{product}$	dosage product used	[$kg.kg_{bw}^{-1}.d^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
$T_{treatment}$	duration of treatment per cycle	[d]	S
m_{animal}	(averaged) body weight	[$kg_{bw}.animal^{-1}$]	D
$F_{excreted}$	fraction of dosage chemical excreted in manure	[-]	S/D
$Pmanure_{animal}$	manure production animal in stable	[$kg_{wwt}.place^{-1}.d^{-1}$]	O
Pdirty water	dirty water production	[$kg_{wwt}.place^{-1}.d^{-1}$]	D
$DT50deg_{slurry}$	half-life time for biodegradation in slurry	[d]	S/D
$T_{storage}$	storage time slurry	[d]	D
Napplication	number of applications per storage period	[-]	O
$Ncyclus_{animal}$	number of cycli per year	[$animal.place^{-1}.yr^{-1}$]	O
intermediate results			
$kdeg_{slurry}$	rate constant for biodegradation in slurry	[d^{-1}]	O
$Q_{excreted}$	amount substance excreted	[$mg_c.place^{-1}.yr^{-1}$]	O
Pslurry	production of slurry	[$kg_{wwt}.place^{-1}.d^{-1}$]	O
T_{cyclus}	duration of cyclus	[d]	O
F_{rsl}	fraction of the concentration remaining in slurry after time $T_{interval}$	[-]	O
T_{rest}	duration of storage after last treatment	[d]	O
output			
PIECslurry	predicted initial concentration in slurry	[$mg_c.kg_{wwt}^{-1}$]	O

4.1.2.2 Calculation of the concentration in dung after uptake and excretion.

Treated animals that graze in the field excrete drug residues in the urine and faeces. Relevant environmental compartments that are exposed directly are the dung, the soil, and the surface water.

We assume that in the event the herd need a remedy that takes several treatments over a few days, the animals are housed or stabled. Therefore the model has to take only single-application products into account. We need a reasonable maximum concentration in dung, which preferably is determined in ADME-experiments, as this concentration is a trigger value for phase II.

When this information is not delivered, we calculate a worst-case maximum. If useful information on excretion is available, this can be used to calculate a better estimation of the concentration in the dung.

Use the factors in table 24b to adjust the dosage of products with external application. In addition, sheep are supposed to rubb off 20% of the dosage they receive from dipping.

Table 26. Default settings for the module for the calculation of the maximum concentration in dung.

parameter	**symbol**	**unit**	**value**
duration of treatment	$T_{treatment}$	[d]	1
highest fraction excreted in dung in one day	$F_{max.\ excreted\ dung}$	[-]	1
number of dung excretion events per day	Nexcretion	[d^{-1}]	10.5

Model for the calculation of the maximum concentration in dung if PEC_{dung} is not available from the dossier:

$$PECdung = \frac{Q_{product} \,.C_c \,.m_{animal} \,.T_{treatment} \,.F_{max.excreted.dung} \,.Nexcretion}{Pdung_{animal}}$$

input			
$Q_{product}$	dosage product used	[$kg.kg_{bw}^{-1}.d^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
m_{animal}	(averaged) body weight	[$kg_{bw}.animal^{-1}$]	S/D
$T_{treatment}$	duration of treatment	[d]	D
$F_{max.\ excreted\ dung}$	highest fraction excreted in dung in one day	[-]	S/D
$Pdung_{animal}$	dung production animal in field	[$kg_{wwt}.animal^{-1}.d^{-1}$]	O
Nexcretion	number of dung excretion events per day	[d^{-1}]	D
output			
PECdung	predicted (maximum) concentration in dung	[$mg_c.kg_{wwt}^{-1}$]	O/S

4.2 Concentrations in soil.

The soil can be reached by direct and indirect exposure:
- spreading of slurry and sludge;
- leaching from dung on the pasture;
- direct excretion with urine on the pasture;
- emission of (high volume) topical application fluids.

4.2.1 The concentration in soil after spreading of slurry.

The concentration in the soil depends on a number of factors. One has to consider the number of applications of slurry on land (in one year), the relation between the moments the substance is excreted into the slurry and the moments the slurry is removed from the basin, the time the substance is in the slurry, and the time the substance is in the soil. The maximum concentration in the soil may be reached at the end of the year, but may also be reached in the event in one storage period a maximum number of excretions takes place.
The effective time degradation can take place in slurry and in soil cannot be calculated mathematically. Given the number of cycli per year, and assuming the time between the applications in the cycli is constant, one can search for the worst case and best case combinations of slurry storage time and soil storage time. However, this largely depends on the substance properties. Therefore arbitrary values will be given for every livestock category of interest to simulate an average situation.
The amount of slurry spread depends on the phosphate immission standard and the phosphate content of the slurry. It is therefore more convenient to calculate the concentration in the slurry based on phosphate production. For the model calculations it is assumed that the excretion of residues into slurry takes place in one single event (in reality the excretion could takes several days).

Table 27. Pick list for the target field.

animal category	**target fields**	**Model (main category)**
cattle udder disinfection	grassland	model for grassland
cattle except veal	arable land	model for arable land
veal, pigs, poultry	arable land grassland	model for arable land model for grassland

input			
animal category		[-]	S
output			
target field		[-]	O
model (main category)	model for calculation of concentration in soil	[-]	O

Table 28. Pick list for the spreading of slurry.

target field	**Nspreading (yr^{-1})**	**Q_{P2O5} (kg_{P2O5}. $ha^{-1}.yr^{-1}$)**	**DEPTHfield (m)**
arable land	1	110	0.2
grassland	4	135	0.05

input			
target field		[-]	O
output			
Nspreading	number of slurry spreading events per year	[yr^{-1}]	O
Q_{P2O5}	phosphate immission standard	[kg_{P2O5}. $ha^{-1}.yr^{-1}$]	D
DEPTHfield	mixing depth with soil	[m]	O

Table 29. Default settings of the module for the calculation of the concentration in soil after spreading of slurry.

parameter	**symbol**	**unit**	**value**
fraction of dosage chemical excreted in manure	$F_{excreted}$	[-]	1
half-life time for biodegradation in slurry	$DT50deg_{slurry}$	[d]	1e6
half-life time for biodegradation in soil	$DT50deg_{soil}$	[d]	1e6
bulk density of soil	RHOsoil	[$kg.m^{-3}$]	1500
conversion factor for the area agricultural field	$CONV_{area\ field}$	[$m^2.ha^{-1}$]	10000

Models for the calculation of the concentration in soil after spreading of slurry. General formulas.

$$Q_{e,creted} = Q_{product} \,.\, C_c \,.\, T_{treat\ ent} \,.\, F_{e,creted} \,.\, m_{ani\ al}$$

$$k\,deg_{slurry} = \frac{ln2}{DT50\,deg_{slurry}}$$

$$k\,deg_{soil} = \frac{ln2}{DT50\,deg_{soil}}$$

Models for arable land.

The phosphate immission standard is filled in one spreading event in spring. Given $T_{storage}$ the maximum number of applications (Napplication) within the winter storage period is:

Table 30a. Pick list for the calculation for arable land.

arable land $T_{storage}$ 152 days		
$Ncyclus_{animal}$	$Tcyclus_{animal}$	$N_{application}$
2.4	152	1
2.5-4.7	77-151	2
4.8-7.2	51-76	3
7.3-9.4	39-50	4
9.5-11.8	31-38	5

input			
$Ncyclus_{animal}$	number of cycli per year	[animal.place^{-1}.yr^{-1}]	D
output			
T_{cyclus}	duration of cyclus	[d]	O
Napplication	number of applications per storage period	[-]	O

$$C_{P2O5} = \frac{Q_{excreted}}{T_{storage} . P_{P2O5}} . \frac{1 - F_{rsl}^{\ Napplication}}{1 - F_{rsl}} . e^{-k\deg_{slurry} T_{rest}/2}$$

$$F_{sl} = e^{-\ slurry \cdot cyclus_{animal}}$$

$$T_{s} = T_{s\ a} - (Napplication - 1) . T_{cyclus}$$

$$T_{cyclus} = 365 / Ncyclus_{animal}$$

$$PIECsoil = \frac{C_{P2O5} . Q_{P2O5}}{RHOsoil . CONV_{area\ field}\ DEPTHfield}$$

Models for grassland.

There are four storage periods for slurry in a year: one time 152 days and three times 71 days. The phosphate immission standard is filled in four spreading events. We here discern six models for the calculation of the concentration in soil. The models are based on daily application of udder disinfectans, and on administration of medicinal products in one, two, three, seven, and eight cycli per year. In the table below one can find what models applies to what animal category.

Table 30b. Pick list for the choice of calculation model for grassland.

animal category	**Ncyclus$_{animal}$**	**Model with .. applications per year**	**Model (subcategory) number**
dairy cow	-	udder disinfection	1
beef cattle	0.7	1	2
hen	0.85	1	2
hen free	0.84	1	2
dairy cow	1	1	2
suckler cow	1	1	2
sow	1	1	2
horse	1	1	2
pony	1	1	2
parent turkey	1	1	2
parent broiler	1.05	1	2
veal	1.8	2	3
turkey i.r. 6-30	2.2	3	4
parent broiler i.r.	2.4	3	4
turkey	2.7	3	4
hen i.r.	2.7	3	4
fattening pig	2.8	3	4
broiler	7	7	5
duck	7.4	8	6
turkey i.r. 0-6	7.4	8	6

input			
animal category		[-]	S
Ncyclus$_{animal}$	number of cycli per year	[animal.place^{-1}.yr^{-1}]	D
output			
model (subcategory)	model for calculation of concentration in soil	[-]	O

1. In case of **udder disinfection** the concentration in soil is calculated using the slurry collected during summer. The final concentration is reached after three spreading events of slurry. The concentration in slurry is spread three times with regular interval of 71 days. The time between applications is one day, and so is the time between the last application and the moment of spreading.

Table 24. Default settings of the module for udder disinfection.

parameter	symbol	unit	value
fraction chemical released to slurry storage	F_{slurry}	[-]	0.2
application interval	$T_{interval}$	[d]	1
number of applications before spreading of slurry	Napplication	[-]	71
half-life time for biodegradation in slurry	$DT50deg_{slurry}$	[d]	1e6
manure production in stable during grazing period	$Pmanure_{dairy\ cow\ grazing}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	9.3
dirty water production	$Pdirty\ water_{dairy\ cow}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	14.6
dairy cattle; storage time slurry	$T_{storage}$	[d]	71

$$C_{P2O5} = \frac{Q_{excreted}}{T_{storage} . P_{P2O5}} \cdot \frac{1 - F_{rsl}^{\ Napplication}}{1 - F_{rsl}} \cdot e^{-k\deg_{slurry} \cdot T_{rest}/2}$$

$$F_{rsl} = e^{-kdeg_{slurry} \cdot 1}$$

$$T_{rest} = 1$$

$$PIECsoil = \frac{0.25 . Q_{P2O5} \quad C_{P2O5}}{RHOsoil . CONV_{area\ field} \quad DEPTHfield} \cdot \frac{1 - F_{rs}^{\ (Nspreading-1)}}{1 - F_{rs}}$$

$$F_{rs} = e^{-kdeg_{soil} \cdot T\,interval\ spreading}$$

2. In case of **one animal cyclus per year**, we assume the treatment coincides with the shortest storage period (71 days).

$$C_{P2O5} = \frac{Q_{excreted}}{T_{storage} \cdot P_{P2O5}} \cdot e^{-k\,deg_{slurry} \cdot T_{rest}/2}$$

$$T_{rest} = T_{storage}$$

$$PIECsoil = \frac{C_{P2O5} \cdot 0.25 \cdot Q_{P2O5}}{RHOsoil \cdot CONV_{area\ field} \cdot DEPTHfield}$$

In case of two or more animal cycles per year, the residue present in the soil from previous applications has to be taken into account. The moment the first treatment is given (e.g. in the beginning of the winter storage period) determines the moment the second treatment is given, etc.

3. Two animal cycles per year. As long as the Tcyclus is more than 183 days and less than 213 days the two treatments can be in two summer storage periods. Every treatment finally results in a concentration that is spread onto land; C_A after the first treatment and C_B after the last treatment. The concentration in the soil after the last treatment is calculated, taking degradation in the soil into account.

$$C_{P2O5\,A} = \frac{Q_{excreted}}{71 \cdot P_{P2O5}} \cdot e^{-k\,deg_{slurry} \cdot 71}$$

$$C_{P2O5\,B} = \frac{Q_{excreted}}{71 \cdot P_{P2O5}} \cdot e^{-k\,deg_{slurry} \cdot 10}$$

$$PIECsoil = \frac{0.25 Q_{P2O5} (C_{P2O5\,A} \cdot e^{-k\,deg_{soil} \cdot 142} + C_{P2O5\,B})}{RHOsoil \cdot CONV_{area\ field} \cdot DEPTHfield}$$

4. In case of **3 animal cycles per year** one treatment (A) takes place during the winter storage period and two (B and C) during two summer storage periods. Every storage period finally results in a concentration that is spread onto land; C_A after the first period, C_B after the second period and C_C after the third period. The concentration in the soil after the last treatment is calculated, taking degradation in the soil into account.

$$C_{P2O5\,A} = \frac{Q_{excreted}}{152 \,.\, P_{P2O5}} \,.\, e^{-k\,\deg_{slurry} \cdot 91}$$

$$C_{P2O5\,B} = \frac{Q_{excreted}}{71 \,.\, P_{P2O5}} \,.\, e^{-k\,\deg_{slurry} \cdot 18}$$

$$C_{P2O5\,C} = \frac{Q_{excreted}}{71 \,.\, P_{P2O5}} \,.\, e^{-k\,\deg_{slurry} \cdot 15}$$

$$PIECsoil = \frac{0.25 Q_{P2O5} (C_{P2O5\,A} \,.\, e^{-k\,deg_{soil} \cdot 213} \quad C_{P2O5\,B} \quad e^{-k\,deg_{soil} \cdot 142} \quad \cdots \quad C_{P2O5\,C})}{RHOsoil \,.\, CONV_{area\ field} \quad DEPTHfield}$$

5. In case of 7 **animal cycles per year,** two treatments (A) may take place during the winter storage period and five (B, C, D) during the three summer storage periods. Every storage period finally results in a concentration that is spread onto land; C_A after the first period, C_B after the second period, etc. The concentration in the soil after the last treatment is calculated, taking degradation in the soil into account.

$$C_{P2O5\,A} = \frac{Q_{excreted} (e^{-k\,deg_{slurry} \cdot 104} + e^{-k\,deg_{slurry} \cdot 52})}{152 \,.\, P_{P2O5}}$$

$$C_{P2O5\,B} = \frac{Q_{excreted} (e^{-k\,deg_{slurry} \cdot 71} + e^{-k\,deg_{slurry} \cdot 19})}{71 \,.\, P_{P2O5}}$$

$$C_{P2O5\,C} = \frac{Q_{excreted}}{71 \,.\, P_{P2O5}} \,.\, e^{-k\,deg_{slurry} \cdot 38}$$

$$C_{P2O5\,D} = \frac{Q_{excreted} (e^{-k\,deg_{slurry} \cdot 57} + e^{-k\,deg_{slurry} \cdot 5})}{71 \,.\, P_{P2O5}}$$

$$PIECsoil = \frac{0.25Q_{P2O5}(C_{P2O5A}.e^{-k\,deg_{soil}\cdot 213} + C_{P2O5B}\ e^{-k\,deg_{soil}\cdot 142} + C_{P2O5C}\ e^{-k\,deg_{soil}\cdot 71} + C_{P2O5D}) + }{RHOsoil.CONV_{area\ field}\ DEPTHfield}$$

6. In case of **8 animal cycles per year**, three or four treatments (A) may take place during the winter storage period and four to five (B, C, D) during the three summer storage periods. Every storage period finally results in a concentration that is spread onto land; C_A after the first period, C_B after the second period, etc. The concentration in the soil after the last period is calculated, taking degradation in the soil into account.

$$C_{P2O5A} = \frac{Q_{excreted}(e^{-k\,deg_{slurry}\cdot 140} + e^{-k\,deg_{slurry}\cdot 91} + e^{-k\,deg_{slurry}\cdot 42})}{152.P_{P2O5}}$$

$$C_{P2O5B} = \frac{Q_{excreted}(e^{-k\,deg_{slurry}\cdot 64} + e^{-k\,deg_{slurry}\cdot 15})}{71.P_{P2O5}}$$

$$C_{P2O5C} = \frac{Q_{excreted}}{71.P_{P2O5}}.e^{-k\,deg_{slurry}\cdot 34}$$

$$C_{P2O5D} = \frac{Q_{excreted}(e^{-k\,deg_{slurry}\cdot 59} + e^{-k\,deg_{slurry}\cdot 10})}{71.P_{P2O5}}$$

$$PIECsoil = \frac{0.25Q_{P2O5}(C_{P2O5A}.e^{-k\,deg_{soil}\cdot 213} + C_{P2O5B}\ e^{-k\,deg_{soil}\cdot 142} + C_{P2O5C}\ e^{-k\,deg_{soil}\cdot 71} + C_{P2O5D}) + }{RHOsoil.CONV_{area\ field}\ DEPTHfield}$$

Input-output list of the models for the calculation of the concentration in soil after uptake and excretion into slurry.

input			
$Q_{product}$	dosage product used	[$kg.kg_{bw}^{-1}.d^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
$T_{treatment}$	duration of treatment	[d]	S
m_{animal}	(averaged) body weight	[$kg_{bw}.animal^{-1}$]	O
$F_{excreted}$	fraction excreted in faeces and urine	[-]	S/D
$Ncyclus_{animal}$	number of cycli per year	[$animal.place^{-1}.yr^{-1}$]	O
$P_{P2O5\ animal}$	phosphate production animal in stable	[$kg_{P2O5}.place^{-1}.d^{-1}$]	O
$DT50deg_{slurry}$	halflife time in slurry	[d]	S/D
$DT50deg_{soil}$	halflife time in soil	[d]	S/D
$T_{storage}$	average storage time slurry grassland/arable land	[d]	O
Nspreading	number of slurry spreading events in a year	[yr^{-1}]	O
$T_{interval\ spreading}$	spreading interval	[d]	O
Q_{P2O5}	phosphate immission standard	[$kg_{P2O5}.\ ha^{-1}.yr^{-1}$]	D
RHOsoil	bulk density of soil	[$kg.m^{-3}$]	D[c]
DEPTHfield	mixing depth with soil	[m]	O
$CONV_{area\ field}$	conversion factor for the area of the agricultural field	[$m^2.ha^{-1}$]	D[c]
Napplication	number of applications per storage period	[-]	O
intermediate results			
$kdeg_{slurry}$	reaction constant transformation in manure	[d^{-1}]	O
$kdeg_{soil}$	reaction constant transformation in soil	[d^{-1}]	O
F_{rs}	fraction of the concentration remaining in soil after time $T_{interval}$	[-]	O
F_{rsl}	fraction of the concentration remaining in slurry after time $T_{interval}$	[-]	O
$Q_{excreted}$	amount substance excreted	[$mg_c.place^{-1}.yr^{-1}$]	O
C_{P2O5}	concentration in phosphate	[$mg_c.kg_{P2O5}^{-1}$]	O
T_{cyclus}	duration of cyclus	[d]	O
T_{rest}	duration of storage after last treatment	[d]	O
output			
PIECsoil	highest concentration in the soil	[$mg_c.kg_{soil}^{-1}$]	O

4.2.2 The concentration in soil by spreading of urine and leaching from dung.

Substances that are taken up and are excreted by grazing animals reach the soil. Urine is spread in several events per day and penetrates the soil. Residues might leach from dung into the soil. We assume that the water fraction in the dung is transferred to the soil (e.g. when raining) and that the residues are evenly distributed in the top 5 cm throughout the field.

Substances with external application on grazing animals have a fraction of the dosage that is spilled ($Fsoil_{spillage}$). See § 4.2.4 for more information.

A pick-list with information on dung volume fractions is given in Appendix II.

Table 31. Default settings for the module for spreading of urine and leaching from dung.

parameter	**symbol**	**unit**	**value**
duration of treatment	$T_{treatment}$	[d]	1
fraction excreted in urine	$Fexcreted_{urine}$	[-]	1
bulk density of soil	RHOsoil	[$kg.m^{-3}$]	1500
mixing depth with soil	DEPTHfield	[m]	0.05
conversion factor for area of the agricultural field	$CONV_{area\ field}$	[$m^2.ha^{-1}$]	10000
density of dung solids	$RHOsolid_{dung}$	[$kg.m^{-3}$]	1675
density of water	RHOwater	[$kg.m^{-3}$]	1000
weight fraction of organic carbon in dung	Foc_{dung}	[$kg.kg^{-1}$]	0.44
fraction leached from dung	$F_{leached\ dung}$	[-]	0

Model for calculation of the concentration in soil after spreading of urine and leaching from dung.

$$Q_{excreted\ urine} = Q_{product} \,.\, C_c \,.\, m_{animal} \,.\, F_{excreted\ urine} \,.\, T_{treatment}$$

$$Q_{leached.dung} = Q_{product} \,.\, C_c \,.\, m_{animal} \,.\, F_{excreted\ dung} \,.\, F_{leached.dung} \,.\, T_{treatment}$$

$F_{excreted\ dung} = 1 - F_{excreted\ urine}$ unless experimentally measured.

$$F_{leached.dung} = \frac{Fwater_{dung}}{K_{dung-water}}$$

$$K_{dung-water} = Fwater_{dung} + Fsolid_{dung} \,\frac{Kp_{dung}}{1000}\, RHOsolid_{dung}$$

$$Kp_{dung} = Foc_{dung} \,.\, Koc$$

$$PIECsoil = \frac{\left(Q_{excreted\ urine} + Q_{leached\ dung}\right) Nanimal_{field}}{RHOsoil\ .CONV_{area\ field}\ \ DEPTHfield}$$

input			
$Q_{product}$	dosage product used	[kg.kg bw^{-1}.d^{-1}]	S
C_c	concentration a.i. in product	[mg$_c$.kg^{-1}]	S
m_{animal}	(averaged) body weight	[kg$_{bw}$.animal^{-1}]	P
$T_{treatment}$	duration of treatment	[d]	D
$F_{excreted\ urine}$	fraction excreted in urine	[-]	S/D
$Nanimal_{field}$	stocking density animals	[animal.ha^{-1}]	P
RHOsoil	dry bulk density of soil	[kg.m^{-3}]	D[c]
DEPTHfield	mixing depth with soil	[m]	D[c]
$CONV_{area\ field}$	conversion factor for the area of the field	[m^2.ha^{-1}]	D[c]
$RHOsolid_{dung}$	density of dung solids	[kg.m^{-3}]	D[c]
RHOwater	density of water	[kg.m^{-3}]	D[c]
$Fwater_{dung}$	fraction water in dung	[m^3.m^{-3}]	P
$Fsolid_{dung}$	fraction solids in dung	[m^3.m^{-3}]	P
Foc_{dung}	weight fraction of fraction organic carbon in dung	[kg.kg^{-1}]	D[c]
Koc	partition coefficient organic carbon - water	[dm^3.kg^{-1}]	S/O
intermediate results			
$Q_{excreted\ urine}$	quantity a.i. excreted with urine	[mg$_c$.animal^{-1}]	O
$Q_{leached\ dung}$	quantity a.i. leached with dung	[mg$_c$.animal^{-1}]	O
$F_{excreted\ dung}$	fraction excreted in dung	[-]	O/S
$F_{leached\ dung}$	fraction leached from dung	[-]	O
$K_{dung\text{-}water}$	partition coefficient solids and water in dung	[m^3.m^{-3}]	O
Kp_{dung}	partition coefficient solids and water in dung	[dm^3.kg^{-1}]	O
output			
PIECsoil	highest concentration in the soil	[mg$_c$.kg$_{soil}$$^{-1}$]	O

In case of sustained release preparations the degradation in soil can be taken into account using the term $(1\text{-}F^N)/(1\text{-}F)$ from the formula Models for Arable land, that introduces the disappearance of the substance during the treatment intervals (i.e. one day). The duration of treatment has to be set at 1 day, but the number of applications is the duration of the release.

4.2.3 The concentration in soil by spreading of sludge from fisheries.

It is assumed the sludge is removed four times a year and is only spread on grassland. See chapter 4.1.2.1 for more information on the chosen formulas.

Table 32. Default settings of the module for the calculation of the concentration in soil after spreading of sludge.

parameter	symbol	unit	value
bulk density of soil	RHOsoil	[kg.m^{-3}]	1500
conversion factor for the area of the agricultural field	$CONV_{area\ field}$	[m^2.ha^{-1}]	10000
phosphate production per year	$P_{P2O5\ fish}$	[kg_{P2O5}. d^{-1}]	8.22
half-life time for biodegradation in soil	$DT50deg_{soil}$	[d]	1e6
number of spreading events on grassland	$Nspreading_{grassland}$	[yr^{-1}]	4
mixing depth in soil	DEPTHfield	[m]	0.05

Table 33. Pick list for the default settings of the fraction of retention in sludge, treatment time and volume of waste water.

type of treatment	type of water treatment	F_{ret} [-]	Napplication	Vwaste water [l]	model
continuous treatment	filtration and settlement tank	0.75	equals Tstorage	35000	1
continuous treatment	settlement tank	0.5	equals Tstorage	35000	1
occasional treatment	settlement tank	0.5	4 per year	70000	2

input			
type of treatment		[-]	S
type of water treatment		[-]	S
output			
F_{ret}	fraction of chemical retained	[-]	O
Napplication	number of applications	[-]\[yr^{-1}]	O
Vwaste water	volume of waste water	[l]	O
model	model for calculation of concentration in soil	[-]	O

Models for the calculation of the concentration in soil after spreading of sludge.
General formulas

$$Q_{emitted} = Q_{product} \,.\, C_c \,.\, Vwaste\ water \,.\, F_{ret}$$

1. Continuous treatment:

$$C_{P2O5} = \frac{Q_{emitted}}{T_{storage} \,.\, P_{P2O5}} \,.\, \frac{1 - F_{rsl}^{\ Napplication}}{1 - F_{rsl}} \,.\, e^{-k\deg_{slurry}\ T_{rest}/2}$$

$$F_{rsl} = e^{-kdeg_{slurry} \cdot 1}$$

$$T_{rest} = 1$$

2. Occasional treatment:

$$C_{P2O5} = \frac{Q_{emitted}}{T_{storage} \cdot P_{P2O5}} \cdot e^{-k\deg_{slurry} \cdot T_{rest}/2}$$

$$T_{rest} = 36$$

C_{P2O5A} for Tstorage = Napplication = 152.

C_{P2O5B} for Tstorage = Napplication = 71.

$$PIECsoil = \frac{0.25 Q_{P2O5}}{RHOsoil \cdot CONV_{area\ field} \cdot DEPTHfield} \cdot \left(C_{P2O5_A} \cdot e^{-k\,deg_{soil} \cdot 213} + C_{P2O5_B} \cdot \frac{1 - F_{rs}^3}{1 - F_{rs}} \right)$$

$$F_{rs} = e^{-kdeg_{soil} \cdot 71}$$

input			
$Q_{product}$	dosage product used	[kg.l^{-1}]	S
C_c	concentration a.i. in product	[mg$_c$.kg^{-1}]	S
Vwaste water	volume of waste water discharged	[l]	O
F_{ret}	fraction of retention in sludge	[-]	O
$P_{P2O5\ fish}$	phosphate production per year	[kg$_{P2O5}$. yr^{-1}]	D
$DT50deg_{soil}$	halflife time in soil	[d]	S/D
$N_{application}$	number of applications per storage period	[-]	O
T_{rest}	time remaining after last treatment	[d]	D
Q_{P2O5}	phosphate immission standard	[kg$_{P2O5}$. ha^{-1}.yr^{-1}]	D
RHOsoil	bulk density of soil	[kg.m^{-3}]	D[c]
DEPTHfield	mixing depth with soil	[m]	D
$CONV_{area\ field}$	conversion factor for the area of the agricultural field	[m^2.ha^{-1}]	D[c]
intermediate results			
$kdeg_{soil}$	reaction constant transformation in soil	[d^{-1}]	O
F_{rs}	fraction of the concentration remaining in soil after time $T_{interval}$	[-]	O
F_{rsl}	fraction of the concentration remaining in sludge after time $T_{interval}$	[-]	O
$Q_{emitted}$	amount of substance emitted	[mg$_c$.d^{-1}]	O
C_{P2O5}	concentration in phosphate	[mg$_c$.kg$_{P2O5}^{-1}$]	O
output			
PIECsoil	highest concentration in the soil	[mg$_c$.kg$_{soil}^{-1}$]	O

4.2.4 The concentration in soil by direct exposure.

Substances used for topical application (spraying or pour-on) on grazing animals may reach the environment directly due to spillage (drift from spraying), washing off by rain and rubbing off. Initially, a calculation is performed where it is assumed that the dosage for the entire heard reaches the soil completely. This can be calculated using the model in § 4.2.2 and using $F_{excreted\ urine} = 1$. Should the trigger for soil be exceeded, a refined calculation is made, assuming spillage, uptake and excretion.

Table 34a. Default settings for the calculation of the concentration in soil by direct exposure.

product type	**symbol**	**unit**	**value**
spray	$Fsoil_{spillage}$	[-]	0.2
pour-on	$Fsoil_{spillage}$	[-]	0

Sprays are supposed to spill 20% of the dosage. The $Q_{product}$ in §4.2.2 is corrected with (1-$Fsoil_{spillage}$) and finally the concentration in soil caused by the $Fsoil_{spillage}$ is added. Table 34a shows that the refined assessment for pour-ons can be performed with § 4.2.2 alone, because no spillage is assumed.

Discharge of sheep dips may be regulated by instructions induced by law or by good agricultural practice. When the remaining dip should be spread over the land as if it were slurry, than this scenario should be used for calculations.
In the events these specific instructions are lacking, a worst-case scenario is used. The concentration in soil after discharge of dipping fluids on the land depends on the concentration of the product in the fluid. The area and volume of soil that will be contaminated depends on the volume of the fluid discharged and soil structure. Soil has a volume fraction of solids of 0.6. The fluid will take maximally 40% v/v of the soil volume by superseding the air and the present soil porewater.

Table 34. Default settings for the module for discharge of sheep dips.

parameter	**symbol**	**Unit**	**value**
bulk density of soil	RHOsoil	[$kg.m^{-3}$]	1500
fraction of the product remaining in dip after treatments	F_{rd}	[-]	0.8
volume fraction of solids in soil	$Fsolids_{soil}$	[m^3. m^{-3}]	0.6

Model for calculation of the concentration in soil after discharge of sheep dips.

$$PIECdip = \frac{D_{product} \,.\, C_c}{Vdilution\ water}$$

$$PIECsoil = \frac{PIECdip \,.\, F_{rd} \,.\, (1 - Fsolids_{soil})}{RHOsoil}$$

input			
$D_{product}$	dosage product used	[kg] or [l]	S
C_c	concentration a.i. in product	$[mg_c.kg^{-1}]$ or $[mg_c.l^{-1}]$	S
F_{rd}	fraction of the product remaining in dip after treatments	[-]	D/S
$Fsolids_{soil}$	volume fraction of solids in soil	$[m^3. m^{-3}]$	D[c]
Vdilution water	volume of dilution water prescribed	$[m^{-3}]$	S
intermediate results			
PIECdip	initial (prescribed) concentration in dip fluid or foot bath	$[mg_c.m^{-3}]$	O
output			
PIECsoil	highest concentration in the soil	$[mg_c.kg_{soil}^{-1}]$	O

4.3 The concentration in ground water.

The concentration in ground water depends on the concentration in the soil and the capacity of the substance to adsorb to the organic material in the soil. In Phase I the EU-approach[8] is used, where the concentration in the ground water is set equal to the concentration in the porewater.

Table 35. Default settings of the module for ground water.

parameter	symbol	unit	value
bulk density of fresh soil (not dry soil!)	RHOsoil	[kg.m^{-3}]	1700
density of soil solids	RHOsolid$_{soil}$	[kg.m^{-3}]	2500
fraction air in soil	Fair$_{soil}$	[m^3.m^{-3}]	0.2
fraction water in soil	Fwater$_{soil}$	[m^3.m^{-3}]	0.2
fraction solids in soil	Fsolid$_{soil}$	[m^3.m^{-3}]	0.6
weight fraction organic carbon in soil	Foc$_{soil}$	[kg.kg^{-1}]	0.02
temperature at air-water interface	TEMP	[K]	285
gas constant	R	[Pa. m^3.mol^{-1}.K^{-1}]	8.314

Model for calculation of the concentration in ground water.

$$PIECgw = PIECporewater$$

$$PIECporewater = \frac{PIECsoil \,.\, RHOsoil}{K_{soil-water} \,.\, 1000}$$

$$K_{soil-water} = Fair_{soil} \cdot K_{air-water} + Fwater_{soil} + Fsolid_{soil} \cdot \frac{Kp_{soil}}{1000} \cdot RHOsolid$$

$$Kp_{soil} = Foc_{soil} \,.\, Koc$$

$$K_{air-water} = \frac{VP \,.\, MOLW}{SOL \,.\, R \,.\, TEMP}$$

We prefer a K_{oc} experimentally determined in a test with at least three soil types (OECD106), but it may be estimated from the octanol-water partition coefficient (Kow) (RIVM, 1994):

$$Koc = 0.411 \,.\, Kow$$

With this calculation one should take the limitations of these structure-activity relations into account: they apply for organic compounds that do not dissociate.

[8] Chapter 2.3.8.6 (p. 312) (ECB, 1996).

input			
PIECsoil	highest concentration in the soil	[$mg_c.kg_{soil}^{-1}$]	O
RHOsoil	fresh bulk density of soil	[$kg.m^{-3}$]	D
RHOsolid	density of soil solids	[$kg.m^{-3}$]	D
$Fair_{soil}$	fraction air in soil	[$m^3.m^{-3}$]	D
$Fwater_{soil}$	fraction water in soil	[$m^3.m^{-3}$]	D
$Fsolid_{soil}$	fraction solids in soil	[$m^3.m^{-3}$]	D
Foc_{soil}	fraction organic carbon in soil (w/dw)	[$kg.kg^{-1}$]	D
Koc	partition coefficient organic carbon - water	[$dm^3.kg^{-1}$]	S/O
VP	vapour pressure	[Pa]	S
MOLW	molar mass	[$g.mol^{-1}$]	S
SOL	water solubility	[$mg.l^{-1}$]	S
TEMP	temperature at air-water interface	[K]	D
R	gas constant	[$Pa.\ m^3.mol^{-1}.K^{-1}$]	D
intermediate results			
$K_{soil\text{-}water}$	partition coefficient solids and water in soil (v/v)	[$m^3.m^{-3}$]	O
Kp_{soil}	partition coefficient solids and water in soil (v/w)	[$dm^3.kg^{-1}$]	O
$K_{air\text{-}water}$	partition coefficient air and water in soil	[$m^3.m^{-3}$]	O
PIECporewater	predicted initial concentration in porewater	[$mg_c.l^{-1}$]	O
output			
PIECgw	predicted initial concentration in ground water	[$mg_c.l^{-1}$]	O

4.4 The concentration in surface water.

Surface water can be reached by direct and indirect exposure:

run-off.
direct excretion into surface water;
emission of waste water from fisheries;

Run-off is not considered to be an important distribution factor in the Netherlands. An exposure assessment of surface water through run-off is not considered necessary in case the Koc is >500 l/kg.

4.4.1 Run-off from agricultural soil.

Substances not adsorbed to soil particles may be present in the soil water and thus be prone to run-off during rainfall events. The concentration in the surface water will be influenced by the amount of rainfall relative to the interstitial pore water and subsequent dilution by the receiving water. It is assumed that catchment areas tend to be proportional in size to the receiving stream therefore no account is taken of the size of the catchment or receiving water. Further dilution occurs on entry of run-off water into receiving water (a factor 10 is chosen).

Table 36. Default settings for concentration in surface water due to run-off.

parameter	**symbol**	**unit**	**value**
Dilution factor for run-off water reaching the surface water	$DILUTION_{run\text{-}off}$	[-]	10

Calculation for concentration in surface water due to run-off.

$$PIECsw_{run-off} = \frac{PIECgw}{DILUTION_{run-off}}$$

input			
PIECgw	predicted initial concentration in ground water	$[mg_c.l^{-1}]$	O
$DILUTION_{run\text{-}off}$	dilution factor for run-off water reaching the surface water	[-]	D
output			
$PIECsw_{run\text{-}off}$	highest concentration in surface water	$[mg_c.l^{-1}]$	O

The result may be used for a calculation with the Sloot.box model in USES (1994) to calculate long-term concentrations as a result of adsorption to suspended matter in the water.

4.4.2 Direct excretion into surface water by grazing livestock.

This section applies to treatments of animals in grazing pastures with products that are subsequently excreted in dung, and where residues have insecticidal activity (see Chapter 6 Effect assessment). The model is based on the following assumptions:

that livestock roam freely over pasture and do not spend a greater proportion of time in any one area, including any stream passing through the field;

that excretion is as likely to occur into the stream as into the pasture

that a hectare of pasture contains a slow-flowing stream 100 m long, 1 m wide and 0.3 m deep.

It is assumed that 1% of the dosage per hectare is excreted into the stream.

Table 37. Default settings of the module for concentration in surface water due to direct excretion.

parameter	**symbol**	**unit**	**value**
duration of treatment	$T_{treatment}$	[d]	1
volume of the surface water per hectare	Vsurface water	[$l.ha^{-1}$]	30000
fraction excreted into surface water	$F_{excreted}$	[-]	0.01

Calculation for concentration in surface water due to direct excretion.

$$PIECsw_{excr.} = \frac{Q_{product} \,.\, C_c \,.\, m_{animal} \,.\, T_{treatment} \,.\, Nanimal_{field} \,.\, F_{excreted}}{Vsurface\ water}$$

input			
$Q_{product}$	dosage product used	[$kg.kg_{bw}^{-1}.d^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
m_{animal}	(averaged) body weight	[$kg_{bw}.animal^{-1}$]	P
$T_{treatment}$	duration of treatment	[d]	D
$Nanimal_{field}$	stocking density animals	[$animal.ha^{-1}$]	P
Vsurface water	volume of the surface water per hectare	[$l.ha^{-1}$]	D
$F_{excreted}$	fraction excreted into surface water	[-]	D
output			
$PIECsw_{excr.}$	highest initial concentration in surface water	[$mg_c.l^{-1}$]	O

The result may be used for a calculation with the Sloot.box model in USES (1994) to calculate long-term concentrations as a result of adsorption to suspended matter in the water.

4.4.3 Fisheries waste water.

The water is either dicharged on surface water or into the STP. The emission to the STP waste water is the input parameter for the STP module in USES (1994). This module is not described here and the reader is referred to USES (1994) and Linders and Jager (1997). Due to the settlement tank the total amount emitted is equally spread out over 25 days, which of course will have no effect on the surface water concentration in case of continuous treatment.

Table 38. Default settings of the module for emission to waste water

parameter	**symbol**	**unit**	**value**
emission period for discharge to STP	$Temission_{stp}$	[d]	25

Table 39. Pick list for the default settings of the fraction of retention in sludge, treatment time and volume of waste water.

type of treatment	**type of water treatment before STP**	**F_{ret} [-]**	**$N_{application,\ year}$ [yr^{-1}]**	**Vwaste water [l]**	**$DILUTION_{fish}$ [-]**
continuous	filtration and settlement tank	0.75	365	35000	5
continuous	settlement tank	0.5	365	35000	5
occasional	settlement tank	0.5	4	70000	3

input			
type of treatment		[-]	S
type of water treatment		[-]	S
output			
F_{ret}	fraction of chemical retained	[-]	O
Napplication, year	number of applications per year	[yr^{-1}]	O
Vwaste water	volume of waste water	[l]	O
$DILUTION_{fish}$	dilution factor for fish waste water reaching the surface water	[-]	O

Model for the calculation of the emission to waste water during episode.

$$Q_{.m\ \ .d} = Q_{produc}\ .C_c\ .Vwaste\ water$$

$$Elocal_{water} = \frac{Q_{emitted}\ .(1 - F_{ret})}{Temission_{stp}}$$

$$Temission = Temission_{stp}\ .Napplication,\ year$$

input			
$Q_{product}$	dosage product used	[$kg.l^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
Vwaste water	volume of waste water discharged	[l]	P
F_{ret}	fraction of retention in sludge	[-]	P
$Temission_{stp}$	emission period for discharge to STP	[d]	D
$N_{application,\ year}$	number of applications in one year	[yr^{-1}]	P

intermediate results			
$Q_{emitted}$	amount of substance emitted	[$mg_c.d^{-1}$]	O
output			
$Elocal_{water}$	emission to waste water during episode	[$mg_c.d^{-1}$]	O
Temission	number of emission days	[d]	O

In case of direct discharge on surface water, the $Elocal_{water}$ is used for calculation.

Model for the calculation of the concentration in surface water after direct discharge from fish settlement tank.

$$PIECsw_{fish} = \frac{Elocal_{water}}{DILUTION_{fish}}$$

input			
$Elocal_{water}$	emission to waste water during episode	[$mg_c.d^{-1}$]	O
$DILUTION_{fish}$	dilution factor for fish waste water reaching the surface water	[$l.d^{-1}$]	O
output			
$PIECsw_{fish}$	highest initial concentration in surface water	[$mg_c.l^{-1}$]	O

The result may be used for a calculation with the Sloot.box model in USES (1994) to calculate long-term concentrations as a result of adsorption to suspended matter in the water.

4.5 The concentration in sediment.

Concentrations in sediment are determined by the concentrations in water and the sediment-water partitioning coefficient. This coefficient is estimated from Koc and Foc_{ditch}.

Table 40. Default settings of the module for concentration in sediment.

parameter	symbol	unit	value
fresh bulk density sediment in ditch	RHOsed	$[kg_{wwt}.m^{-3}]$	1300
volume fraction solids in sediment ditch	$Fsolid_{sed}$	$[m^3.m^{-3}]$	0.2
bulk density of solids	RHOsolid	$[kg.m^{-3}]$	2500
weight fraction organic carbon in sediment ditch	Foc_{ditch}	$[kg.kg^{-1}]$	0.05

Model

$$CONV_{sed} = \frac{RHOsed}{Fsolid_{sed} \,.RHOsolid}$$

$$PIECsed = \frac{Foc_{ditch} \,.Koc\,.PIECsw}{CONV_{sed}}$$

input			
PIECsw	concentration in surface water	$[mg_c.l^{-1}]$	O
RHOsed	fresh bulk density sediment in ditch	$[kg_{wwt}.m^{-3}]$	D
$Fsolid_{sed}$	volume fraction solids in sediment ditch	$[m^3.m^{-3}]$	D
RHOsolid	bulk density of solids	$[kg.m^{-3}]$	D
Foc_{ditch}	weight fraction organic carbon in sediment ditch	$[kg.kg^{-1}]$	D
Koc	organic carbon partitioning coefficient substance	$[l.kg^{-1}]$	S
intermediate results			
$CONV_{sed}$	conversion factor for sediment concentrations: wwt to dwt	$[kg_{wwt}.kg_{dwt}^{-1}]$	O[c]
output			
PIECsed	predicted initial concentration in sediment	$[mg_c.kg_{wwt}^{-1}]$	O

Instead of an acute concentration in water an average concentration can be used, e.g. an average concentration over a certain period, or after several years of emission. The PECsed derived from this is then to be compared to a NOEC respectively an MPC for sediment dwelling organisms.
For further information see Linders and Jager (1997).

4.6 The concentration in air.

Exposure of air is possible. Substances with a vapour pressure (VP) lower than 1e-4 Pa or a Henry's law constant (H, equal to $K_{air\text{-}water}$) lower than 1e-5, are classified as very slightly volatile (from water) and are not further assessed.

The concentration in air as a result from evaporation from soil can be calculated using the EUSES model (1996). This route is not further assessed in this report.

5. EXPOSURE MODULE.

In the exposure module, exposure levels for predating birds and mammals are estimated. Birds and mammals are likely to be exposed to the veterinary medicinal product or its metabolites in the event the contaminated compartment still supports the development of worms, insects, and fish. Insects in the fleece of treated animals or in the grass where products (dips) have been disposed of will carry residues in the range of 2.7 - 29 times the application rate (see Table 41). The assessment of secondary poisoning of birds and mammals considers exposure through fish and earthworms. Bioconcentration may be of concern for lipophylic organic chemicals. Insects and worms in dung and soil can accumulate the residues and carry them over when they are eaten. The bioconcentration factor (BCF) between the compartment and the feed are needed. When an experimental BCF is not available, the BCF for the earthworms can be estimated using the logKow and the sorption coefficient of the substance (EC, 1996). The following food chains are assessed.

Direct food chains:

- Birds exposed through exposed product (sheep dips and foot baths);
- Birds and/or mammals exposed through drinking water;
- Birds and/or mammals exposed through feed (insects in grass and fleece);

Indirect food chains:

- Birds and/or mammals with a diet consisting of worms caught in polluted land;
- Birds and/or mammals with a diet consisting of worms caught in polluted dung;
- Birds and/or mammals with a diet consisting of fish caught in polluted water.

5.1 The concentration in sheep dips and footbaths.

The concentration in sheep dips or foot baths follows directly from the usage instructions.

Model

$$PIECdip = \frac{D_{product} . C_c}{Vdilution\ water}$$

input			
$D_{product}$	dosage product used	[kg] or [l]	S
C_c	concentration a.i. in product	$[mg_c.kg^{-1}]$ or $[mg_c.l^{-1}]$	S
Vdilution water	volume of dilution water prescribed	$[m^{-3}]$	S
output			
PIECdip	initial (prescribed) concentration in dip fluid or foot bath	$[mg_c.m^{-3}]$	O

5.2 Exposure of birds and mammals due to contaminated feed.

Initial concentrations in grass and insects after dipping (fleece) or after disposal of dips and foot baths (grassland) can be estimated with the table given below. Hoerger and Kenega (1972) have described a method which estimates the concentration of a pesticide on various types of feed after exposure. It gives a relation by which the mean and maximal concentration directly after an application with a certain dosage can be determined. It must be noted, however, that measured data on feed concentrations is always preferable. Only mean concentrations will be used.
If the diet of birds or mammals consists of various kinds of crops or insects, this can be taken into account for the calculation of the C_{food} by manually calculating the feed concentration from the various sources given in the next table.

Table 41. Initial concentration in feed for birds and mammals.

Type of feed	**Mean concentration on feed (C_{food}; in $kg_c.kg_{food}^{-1}$)**	**Maximal concentration on feed (C_{food}; in $kg_c.kg_{food}^{-1}$)**
short grass	$112 \times DOSE_{max} \times 10^{-2}$	$214 \times DOSE_{max} \times 10^{-2}$
tall grass	$82 \times DOSE_{max} \times 10^{-2}$	$98 \times DOSE_{max} \times 10^{-2}$
seeds & small insects	$29 \times DOSE_{max} \times 10^{-2}$	$52 \times DOSE_{max} \times 10^{-2}$
pods & large insects	$2.7 \times DOSE_{max} \times 10^{-2}$	$11 \times DOSE_{max} \times 10^{-2}$

Input			
$DOSE_{max}$	apparent maximum dosage	$[kg_c.m^{-2}]$	O
-	type of food for the bird species of choice	[-]	P
-	type of food for the mammalian species of choice	[-]	P
Output			
$Cfood_{bird}$	initial concentration in bird food	$[kg_c.kg_{food}]$	S/O
$Cfood_{mammal}$	initial concentration in mammalian food	$[kg_c.kg_{food}]$	S/O

The concentration in feed has to be calculated over 5 days for evaluating acute toxicity and over a longer period of time (depending on the exposure period in the toxicity test for the species) for chronic toxicity. For this calculation it is necessary that the half-life time of the pesticide in crops or insects ($DT50_{food}$) is known. The half-life time should preferably be determined from residue data on crops and insects. If $DT50_{food}$ is unknown, no disappearance of the substance is assumed.

$$k_{food} = \frac{\ln 2}{DT50_{food}}$$

if $DT50_{food}$ is not given:

$$Cfood_{x-5} = Cfood_{Tx} = Cfood_x$$

$$Cfood_{bird\text{-}5} = \frac{Cfood_{bird}}{k_{food} \ldots 5} \ldots \left(1 - e^{-k_{food} \cdot 5}\right)$$

$$Cfood_{Tx} = \frac{Cfood_x}{k_{food} \ldots T_x} \ldots\left(1 - e^{-k_{food} T_x}\right)$$

$$x \geq \{bird, mammal\}$$

Input			
k_{food}	first order disappearance rate of pesticide in food	[d^{-1}]	O
$Cfood_{bird}$	initial concentration in food for birds	[$kg_c.kg_{food}^{-1}$]	S/O
$Cfood_{mammal}$	initial concentration in food for mammals	[$kg_c.kg_{food}^{-1}$]	S/O
$DT50_{food}$	DT50 in food	[d]	S
T_{bird}	duration of chronic toxicity test for birds	[d]	S
T_{mammal}	duration of chronic toxicity test for mammals	[d]	S
Output			
$Cfood_{bird\text{-}5}$	mean concentration in birds food over 5 days	[$kg_c.kg_{food}^{-1}$]	O
$Cfood_{Tbird}$	mean concentration in food over T_{bird} days	[$kg_c.kg_{food}^{-1}$]	O
$Cfood_{Tmammal}$	mean concentration in food over T_{mammal} days	[$kg_c.kg_{food}^{-1}$]	O

5.3 Secondary poisoning.

5.3.1 Bioconcentration in earthworms

This BCF should preferably be derived experimentally. If no experimentally obtained data are available, it can be estimated by means of the Quantitative Structure Activity Relationship (QSARs) given below. BCF worm has to be calculated for the specific properties of the compartment.

$$C_{worm\text{-}Tx} = BCF_{worm} \cdot PECcomp_{Tx} \quad x \geq \{bird, mammal\}$$

Input			
$PECcomp_{Tbird}$	mean concentration in compartment over T_{bird} days	$[mg_c.kg^{-1}]$	O
$PECcomp_{Tmammal}$	mean concentration in compartment over T_{mammal} days	$[mg_c.kg^{-1}]$	O
BCF_{worm}	bioconcentration factor for earthworms	$[kg_{soil}.kg_{wwt}^{-1}]$	O
Output			
$C_{worm\text{-}Tbird}$	mean concentration in earthworms in birds	$[mg_c.kg_{wwt}^{-1}]$	O
$C_{worm\text{-}Tmammal}$	mean concentration in earthworms for mammals	$[mg_c.kg_{wwt}^{-1}]$	O

Table 42. Pick-list for the bioconcentration in worms

compartment	**Foc_{comp}** [9] **($kg.kg^{-1}$)**	**$RHOsolid_{comp}$ ($kg.m^{-3}$)**	**RHOcomp ($kg_{wwt}.m^{-3}$)**	**$Fsolids_{comp}$ ($m^3.m^{-3}$)**	**$Fwater_{comp}$ ($m^3.m^{-3}$)**
soil	0.02	2500	1700	0.6	0.2
dung cattle	0.18	1675	1030	0.09	0.88
dung horses	0.18	1675	900	0.17	0.62
dung sheep	0.18	1675	1090	0.26	0.67

input			
-	compartment	[-]	P
output			
Foc_{comp}	fraction organic carbon in compartment	$[kg.kg^{-1}]$	O
$RHOsolid_{comp}$	density dry matter in compartment	$[kg.m^{-3}]$	O
RHOcomp	density compartment	$[kg_{wwt}.m^{-3}]$	O
$Fsolid_{comp}$	volume fraction dry matter in compartment	$[m^3.m^{-3}]$	O
$Fwater_{comp}$	volume fraction water in compartment	$[m^3.m^{-3}]$	O

Table 43. Default setting for the module to calculate the BCF worm-compartment.

parameter	**symbol**	**unit**	**value**
density of earthworm	RHOworm	$[kg_{wwt}.m^{-3}]$	1000

[9] The fraction organic carbon in dung is in fact 0.44. However, because the accumulation-sorption relationships expressed in the QSAR used is no longer valid at high (>30% o.m.) organic matter contents, the value 0.18 is used for the Foc in dung. See Appendix III.

Model for the calculation of the bioconcentration factor worm-compartment.

$$BCF_{worm} = \frac{K_{worm-water} \,.\, RHOcomp}{K_{comp-water} \,.\, RHOworm}$$

$$K_{comp-water} = Fwater_{comp} + Fsolid_{comp} \,.\, \frac{Kp_{comp}}{1000} \,.\, RHOsolid_{comp}$$

$$Kp_{comp} = Foc_{comp} \,.\, Koc$$

$$K_{worm-water} = 0.25 \,.\, Kow \,.\, 0.16$$

We prefer a K_{oc} experimentally determined in a test with at least three soil types (OECD106), but it may be estimated from the octanol-water partition coefficient (Kow) (RIVM, 1994):

$$Koc = 0.411 \,.\, Kow$$

With this calculation one should take the limitations of these structure-activity relations into account: they apply for organic compounds that do not dissociate.

input			
Koc	partition coefficient organic carbon - water	[$dm^3.kg^{-1}$]	S/O
Kow	octanol-water partition coefficient a.i.	[-]	S
RHOcomp	density of compartment	[$kg.m^{-3}$]	O
$RHOsolid_{comp}$	density of compartment solids	[$kg.m^{-3}$]	O
RHOworm	density of earthworm	[$kg_{wwt}.m^{-3}$]	D
$Fwater_{comp}$	fraction water in compartment	[$m^3.m^{-3}$]	O
$Fsolid_{comp}$	fraction solids in compartment	[$m^3.m^{-3}$]	O
Foc_{comp}	weight fraction of organic carbon in compartment	[$kg.kg^{-1}$]	O
intermediate results			
$K_{worm-water}$	partition coefficient worm and water	[$m^3.m^{-3}$]	O
$K_{comp-water}$	partition coefficient between compartment and water	[$m^3.m^{-3}$]	O
Kp_{comp}	partition coefficient between solids and water in compartment	[$dm^3.kg^{-1}$]	O
output			
BCF_{worm}	bioconcentration factor worm-compartment	[$kg_{comp}.kg_{worm}^{-1}$]	O

We assume that the bioconcentration factor for insects and insect larvae and pupae is equal to the BCF for earthworms.

5.3.2 Bioconcentration in fish.

The uptake of pesticides by water organisms is calculated by means of the bioconcentration factor (BCF). If no experimentally derived BCF is available, the QSAR-calculation given below can be used.

$$C_{fish\text{-}Tx} = BCF_{fish} \cdot Cwater_{Tx} \quad x \geq \{bird, mammal\}$$

Input			
$Cwater_{Tbird}$	mean concentration in water over T_{bird} days	[$kg_c.m^{-3}$]	O
$Cwater_{Tmammal}$	mean concentration in water over T_{mammal} days	[$kg_c.m^{-3}$]	O
BCF_{fish}	bioconcentration factor for fish	[$m_{water}^3.kg_{wet\ fish}^{-1}$]	O
Output			
$C_{fish\text{-}Tbird}$	mean concentration in fish for birds	[$kg_c.kg_{wet\ fish}^{-1}$]	O
$C_{fish\text{-}Tmammal}$	mean concentration in fish for mammals	[$kg_c.kg_{wet\ fish}^{-1}$]	O

The methods that estimate a BCF for fish from log *Kow* are widely used and, in general, the most reliable. The following combination of QSARs is advised in Chapter 4 of the TGD (ECB, 1996). Domain of physico-chemical properties: log *Kow* 1 to 10 (outside this range the minimum or maximum *Kow* is used), molecular weight less than 700 g/mol. For chemicals with a molecular weight of more than 700 g/mol, the BCF tends to decrease but in lack of experimental data, the QSAR can be used as an initial worst-case estimate.

if log *Kow* 6 then:

$$\log BCF_{fish} = 0.85 \cdot \log Kow - 0.70 - 3$$

if log *Kow* > 6 then:

$$\log BCF_{fish} = -0.20 \ldots(\log Kow)^2 + 2.74 \ldots \log Kow - 4.72 - 3$$

Input			
Kow	octanol-water partition coefficient	[$m^3.m^{-3}$]	S
Output			
BCF_{fish}	bioconcentration factor for fish	[$m^3.kg_{wwt}^{-1}$]	O

6. EFFECT ASSESSMENT.

6.1 Deriving PNEC.

6.1.1 Aquatic compartments: surface water and ground water.

Depending on the available toxicity data for aquatic organisms, assessment factors are selected for extrapolating single-species toxicity tests to a PNEC for the water compartment. If intermittent release is identified for a stage of the life cycle, only short-term effects need to be considered for risk characterisation of that stage (only for the aquatic compartment). The following trophic levels are distinguished:

algae (primary producers);
Daphnia (primary consumers);
fish (secondary consumers);
other species (e.g. decomposers).

$$LC50\,aqua_{min} = \min\left(LC50\,aqua_i \right)$$

$$NOECaqua_{min} = \min\left(NOECaqua_i \right)$$

Available data	**Additional criteria**	**TOXaqua**	**AFaqua**
1-3 LC50s		$LC50aqua_{min}$	1000
3 LC50s (independent of avail. NOECs)	If intermittent release is identified for a stage of the life cycle	$LC50aqua_{min}$	100
	Same taxonomic group as $LC50aqua_{min}$?		
1 NOEC additional (not algae!)	yes no $LC50aqua_{min}/1000 < NOECaqua_{min}/100$ no $LC50aqua_{min}/1000 \quad NOECaqua_{min}/100$	$NOECaqua_{min}$ $LC50aqua_{min}$ $NOECaqua_{min}$	100 1000 100
2 NOEC additional	yes no	$NOECaqua_{min}$ $NOECaqua_{min}$	50 100
3 NOEC algae, *Daphnia* and fish		$NOECaqua_{min}$	10
3 NOEC *not* algae, *Daphnia* and fish	yes no	$NOECaqua_{min}$ $NOECaqua_{min}$	10 50

$$PNEC_{water} = \frac{TOXaqua}{AFaqua}$$

Input			
$LC50aqua_i$	LC50 for aquatic organisms, trophic level *i*	$[kg_c.m^{-3}]$	S
$NOECaqua_i$	NOEC for aquatic organisms, trophic level *i*	$[kg_c.m^{-3}]$	S
Output			
TOXaqua	toxicological data used for extrapolation of PNEC	$[kg_c.m^{-3}]$	O
AFaqua	assessment factor applied in extrapolation of PNEC	[-]	O
$PNEC_{water}$	PNEC for aquatic organisms (surface water r groundwater)	$[kg_c.m^{-3}]$	O^c

6.1.2 Sediment compartment.

Toxicity data for sediment-dwelling organisms will be scarce. At the moment no standardised test methods or assessment factors have been agreed upon. Therefore, only the equilibrium-partitioning approach is suggested. It should be noted that the equilibrium partitioning method must depart from the PNEC based on chronic effects and not the PNEC derived from LC50s.

$$PNEC_{sed,ep} = \frac{K_{sed\text{-}water}}{RHO_{sed}} \quad PNEC_{water}$$

$$PNEC_{sed} = PNEC_{sed,ep}$$

EPsed = 'yes'

Input			
$PNEC_{water}$	PNEC for aquatic organisms	$[kg_c.m^{-3}]$	O^c
$K_{sed\text{-}water}$	sediment-water partition coefficient	$[m^3.m^{-3}]$	O^c
RHO_{sed}	bulk density of sediment	$[kg_{wwt}.m^{-3}]$	O^c
$PNEC_{sed,ep}$	PNEC for sediment-dwelling organisms derived by eq. part.	$[kg_c.kg_{wwt}^{-1}]$	O^c
Output			
EPsed	equilibrium partitioning used for PNEC in sediment?	[yes/no]	O^c
$PNEC_{sed}$	PNEC for sediment-dwelling organisms	$[kg_c.kg_{wwt}^{-1}]$	O

6.1.3 Micro-organisms.

Depending on the toxicity data available for micro-organisms, assessment factors are selected for extrapolating results from toxicity tests to a PNEC for the sewage treatment plant or soil micro-organisms.

Available ecotox. data	**Specific bacterial population? (e.g. nitrifying bacteria or *P. putida*)**	**TOXmicro**	**AFmicro**
$EC50_{micro}$	yes no	$EC50_{micro}$	10 100
$EC10_{micro}$	yes no	$EC10_{micro}$	1 10
$NOEC_{micro}$	yes no	$NOEC_{micro}$	1 10

If more than one toxicity value is given, the lower of the resulting PNECs is used.

$$PNEC_{micro\text{-}organisms} = \frac{TOXmicro}{AFmicro}$$

Input			
$EC50_{micro}$	EC50 for STP or soil micro-organisms	$[mg_c.l^{-1}]$ or $[mg_c.kg^{-1}]$	S
$EC10_{micro}$	EC10 for STP or soil micro-organisms	$[mg_c.l^{-1}]$ or $[mg_c.kg^{-1}]$	S
$NOEC_{micro}$	NOEC for STP or soil micro-organisms	$[mg_c.l^{-1}]$ or $[mg_c.kg^{-1}]$	S
Output			
TOXmicro	toxicological data used for extrapolation of PNEC	$[mg_c.l^{-1}]$ or $[mg_c.kg^{-1}]$	O
AFmicro	assessment factor applied in extrapolation of PNEC	[-]	O
$PNEC_{micro\text{-}organisms}$	PNEC for STP or soil micro-organisms	$[mg_c.l^{-1}]$ or $[mg_c.kg^{-1}]$	O^c

6.1.4 Earthworms.

Depending on the toxicity data available for earthworms, assessment factors are selected for extrapolating results from toxicity tests to a PNEC.

Available ecotox. data	**TOXearthworm**	**AFearthworm**
$EC50_{earthworm}$	$EC50_{earthworm}$	100
$NOEC_{earthworm}$	$NOEC_{earthworm}$	10

If more than one toxicity value is given, the lower of the resulting PNECs is used.

$$PNEC_{earthworms} = \frac{TOXearthworm}{AFearthworm}$$

Input			
$EC50_{earthworm}$	EC50 for earthworm	$[mg_c.kg^{-1}]$	S
$NOEC_{earthworm}$	NOEC for earthworm	$[mg_c.kg^{-1}]$	S
Output			
TOXmicro	toxicological data used for extrapolation of PNEC	$[mg_c.kg^{-1}]$	O
AFmicro	assessment factor applied in extrapolation of PNEC	[-]	O
$PNEC_{earthworm\ s}$	PNEC for earthworms	$[mg_c.kg^{-1}]$	O^c

6.1.5 Plants

Depending on the toxicity data available for plants, assessment factors are selected for extrapolating results from toxicity tests to a PNEC

Available ecotox. data	**TOXplant**	**AFplant**
$EC50_{plant}$	$EC50_{plant}$	100
$NOEC_{plant}$	$NOEC_{plant}$	10

If more than one toxicity value is given, the lower of the resulting PNECs is used.

$$PNEC_{plant} = \frac{TOXplant}{AFplant}$$

Input			
$EC50_{plant}$	EC50 for plant	$[mg_c.kg^{-1}]$	S
$NOEC_{plant}$	NOEC for plant	$[mg_c.kg^{-1}]$	S
Output			
TOXmicro	toxicological data used for extrapolation of PNEC	$[mg_c.kg^{-1}]$	O
AFmicro	assessment factor applied in extrapolation of PNEC	[-]	O
$PNEC_{plant}$	PNEC for plants	$[mg_c.kg^{-1}]$	O^c

6.1.6 Secondary poisoning

The results of mammalian repeated-dose toxicity test(s) are used to assess secondary poisoning effects. Toxicity data for birds may also be present. Extrapolation from such test results gives a predicted no-effect concentration in food that should be protective of other mammalian and avian species. Acute lethal doses LD50 (rat, bird) are not acceptable for extrapolation to chronic toxicity, as these tests are not dietary tests. Acute effect concentrations (LC50, 5-day avian dietary studies) for birds are acceptable for extrapolation. The results of these tests may be expressed as a concentration in the food (mg/kg) or a dose (mg/kg body weight/day) causing no effect. For the assessment of secondary poisoning, the results are converted to the concentration in food (kg_c/kg food). NOECs converted from NOAELs have the same priority as direct NOECs. The table below gives some conversion factors for laboratory species.

Bird toxicity tests are not usually given for the test durations specified below (T_{bird}). This test duration is however only used to arrive at a representative assessment factor. The user therefore has to decide whether a longer-term bird toxicity test is comparable to 90 day or chronic mammal test.

Available ecotox. data	Duration of (sub-)chronic test	TOXoral	AForal
$LC50_{bird}$ only		$LC50_{bird}$	1000
$NOEC_{bird}$	28 days 90 days chronic	$NOEC_{bird}$	100 30 10
$NOEC_{mammal,food,chr}$	28 days 90 days chronic	$NOEC_{mammal,food,chr}$	100 30 10

If an NOEC for both birds and mammals is given, the lower of the resulting PNECs is used.

$$PNEC_{oral} = \frac{TOXoral}{AForal}$$

Input			
$LC50_{bird}$	LC50 in avian dietary study (5 days)	$[kg_c.kg_{food}^{-1}]$	S
$NOEC_{bird}$	NOEC for birds	$[kg_c.kg_{food}^{-1}]$	S/O
$NOEC_{mammal,food,chr}$	NOEC for mammals	$[kg_c.kg_{food}^{-1}]$	S/O
T_{bird}	duration of (sub-)chronic test with birds	[d]	P
T_{mammal}	duration of (sub-)chronic test with mammals	[d]	P
Output			
TOXoral	toxicological data used for extrapolation of PNEC	$[kg_c.kg_{food}^{-1}]$	O
AForal	assessment factor applied in extrapolation of PNEC	[-]	O
$PNEC_{oral}$	PNEC for secondary poisoning of birds and mammals	$[kg_c.kg_{food}^{-1}]$	O[c]

If toxicity data are given as NOAEL only (see also § 6.5):

$$NOEC_{bird} = NOAEL_{bird} \quad CONV_{bird}$$

$$NOEC_{mammal,food,chr} = NOAEL_{mammal,oral,chr} \quad CONV_{mammal}$$

Input			
$NOAEL_{bird}$	NOAEL for birds	$[kg_c.kg_{bw}.d^{-1}]$	S
$NOAEL_{mammal,oral,chr}$	NOAEL for mammals	$[kg_c.kg_{bw}.d^{-1}]$	S/O
$CONV_{bird}$	conversion factor from NOAEL to NOEC	$[kg_{bw}.d.kg_{food}^{-1}]$	S
$CONV_{mammal}$	conversion factor from NOAEL to NOEC	$[kg_{bw}.d.kg_{food}^{-1}]$	P/S
Output			
$NOEC_{bird}$	NOEC for birds	$[kg_c.kg_{food}^{-1}]$	S/O
$NOEC_{mammal,food,chr}$	NOEC for mammals	$[kg_c.kg_{food}^{-1}]$	S/O

Table 44. Conversion factors from NOAEL to NOEC for several mammalian species.

Species	**Conversion factor (BW/DFI) $CONV_{mammal}$ [$kg_{bw}.d.kg_{food}^{-1}$]**
Canis domesticus	40
Macaca spp.	20
Microtus spp.	8.3
Mus musculus	8.3
Oryctolagus cuniculus	33.3
Rattus norvegicus (> 6 weeks)	20
Rattus norvegicus (6 weeks)	10
Gallus domesticus	8

6.2 Insecticidal properties.

According to the EMEA (1997) note for guidance it should be established whether or not the product has insecticidal properties. This is relevant for the exposure of surface water by direct defaecation into water grazing animals. Where there is no information a test should be conducted if any of the following apply:

where residues of drug and/or metabolites are likely to be present in excreta excreted on pasture; inversely, if a substance is not excreted, there is no exposure of dung or surface water, and no further assessment is needed.
where residues of used high volume topical application are likely to be spread onto land;
where residues of high volume topical application are likely to be present in fleece.

The following may be used as evidence of insecticidal activity:

product indications may include activity against arthropod species;
other compounds in the same chemical group may have been shown to have activity against arthropod species;
drug screening data show activity against arthropod species;
other evidence, e.g. in the literature, indicating insecticidal activity.

The following information may be used as evidence of lack of activity against arthropod species:

related compounds may have been shown to have a lack of activity against arthropod species.

6.3 Bodyweight of birds and mammals.

If the bodyweight is not given in the data set, the user can choose between some species given in the table.

Table 45. Bodyweight of birds and mammals.

Species	Range in body weight (g)	Mean body weight (g)
Birds:		
Quail	-	102
Common Partridge	-	375
Common Pheasant	-	1200
Turtle Dove	-	152
Collared Dove	-	195
Woodpigeon	-	440
Chaffinch*	-	22
Goldfinch	-	15
Common Redpoll	-	14
House Sparrow	-	25
Mammals:		
Hedgehog	400-1000	700
Mole	65-135	100
Woodshrew	6-13	9.5
Hare	2500-6500	4500
Rabbit	1300-2500	1900
Fieldmouse*	14-40	27
Woodmouse	14-35	24.5
Brown rat	240-500	370
Badger	7500-15000	11250

* Organism is used as default

Input

-	bird species of concern	[-]	P
-	mammalian species of concern	[-]	P

Output

BW_{bird}	Mean bodyweight of bird species of concern	[kg]	S/O
BW_{mammal}	Mean bodyweight of mammalian species of concern	[kg]	S/O

6.4 Daily food intake for birds and mammals.

If the daily food intake (DFI) is not given in the data set, it can be estimated. The DFI of birds and mammals is strongly correlated to the body weight (BW). Nagy (1987) has derived the relationships presented here.

All birds

$$\log(DFI_{bird} \quad 1000) = -0.188 + 0.651 \quad \log(BW_{bird} \quad 1000)$$

Passerines

$$\log(DFI_{bird} \quad 1000) = -0.4 + 0.85 \quad \log(BW_{bird} \quad 1000)$$

Non passerines

$$\log(DFI_{bird} \quad 1000) = -0.521 + 0.751 \quad \log(BW_{bird} \quad 1000)$$

All mammals

$$\log(DFI_{mammal} \quad 1000) = -0.629 + 0.822 \quad \log(BW_{mammal} \quad 1000)$$

Input			
BW_{bird}	mean bodyweight of bird species of concern	[kg]	S/O
BW_{mammal}	mean bodyweight of mammalian species of concern	[kg]	S/O
Output			
DFI_{bird}	daily food intake for bird species of concern	$[kg_{food}.d^{-1}]$	S/O
DFI_{mammal}	daily food intake for mammalian species of concern	$[kg_{food}.d^{-1}]$	S/O

6.5 Daily water intake of birds and mammals.

If no value is known, it is assumed that birds with a mean body weight of less than 100 g have a daily water intake (DWI) of at most 30% of their bodyweight per day. For birds with a mean body weight higher than 100 g this is at most 10% per day. Degradation of the pesticide is not taken into consideration.

if BW_x <= 0.1 kg then:

$$DWI_x = 0.30 \,.\, BW_x \,.\, 0.001$$

if BW_x > 0.1 kg then:

$$DWI_x = 0.10 \,.\, BW_x \,.\, 0.001$$

$$x \geq \{\text{bird,mammal}\}$$

Input			
BW_{bird}	mean bodyweight of bird species of concern	[kg_{bw}]	S/O
BW_{mammal}	mean bodyweight of mammalian species of concern	[kg_{bw}]	S/O
Output			
DWI_{bird}	daily water intake of bird species of choice	[$m_{water}^3.d^{-1}$]	O^c
DWI_{mammal}	daily water intake of mammalian species of choice	[$m_{water}^3.d^{-1}$]	O^c

6.6 Derivation of the NOEC from NOAEL

If only a NOAEL is given in the input, a NOEC can be converted using the daily food intake and the bodyweight.

$$NOEC_{bird} = \frac{NOAEL_{bird} \quad BW_{bird}}{DFI_{bird}}$$

$$NOEC_{mammal,food,chr} = \frac{NOAEL_{mammal,oral,chr} \quad BW_{mammal}}{DFI_{mammal}}$$

Input			
$NOAEL_{bird}$	NOAEL for birds	$[kg_c.kg_{BW}^{-1}.d^{-1}]$	S
$NOAEL_{mammal, oral}$	NOAEL for mammals	$[kg_c.kg_{BW}^{-1}.d^{-1}]$	S
BW_{bird}	mean bodyweight of bird species of concern	[kg]	S/O
BW_{mammal}	mean bodyweight of mammalian species of concern	[kg]	S/O
DFI_{bird}	daily food intake for bird species of concern	$[kg_{food}.d^{-1}]$	S/O
DFI_{mammal}	daily food intake for mammalian species of concern	$[kg_{food}.d^{-1}]$	S/O
Output			
$NOEC_{bird}$	NOEC for birds in food	$[kg_c.kg_{food}^{-1}]$	O
$NOEC_{mammal,food,chr}$	NOEC for mammals in food	$[kg_c.kg_{food}^{-1}]$	O

7. HAZARD ASSESSMENT.

In hazard assessment, exposure levels are compared to suitable no-effect levels to yield so-called Risk Characterisation Ratios (RCR) for each protection goal. For the environmental end-points, this generally is the ratio of PEC to PNEC or L(E)C50.

7.1 RCR for birds and mammals exposed through grass and insects.

Hazard for birds and mammals eating insects from fleece and insects and grass on land after disposal of dips and foot baths will be assessed using acute exposure only. The short-term concentration in food is directly compared to the LC50. With the daily food intake (DFI) of the species and its bodyweight, LD50s if present, can be translated to LC50s in food.

$$RCRfood_{bird\text{-}1} = \frac{Cfood_{bird} \quad DFI_{bird} \quad 1}{LD50_{bird} \quad BW_{bird}}$$

$$RCRfood_{bird\text{-}5} = \frac{Cfood_{bird\text{-}5}}{LC50_{bird}}$$

The *1* in the formula above is the number of feeding days assumed to be representative with respect to the single dose toxicity value (LD50) used.

$$RCRfood_{mammal\text{-}1} = \frac{Cfood_{mammal} \quad DFI_{mammal} \quad 1}{LD50_{mammal,oral} \quad BW_{mammal}}$$

Input			
$LD50_{bird}$	LD50 for birds	$[mg_c.kg_{BW}^{-1}]$	S
$LC50_{bird}$	LC50 in food for birds	$[mg_c.kg_{food}^{-1}]$	S
$LD50_{mammal,\ oral}$	LD50 for mammals	$[mg_c.kg_{BW}^{-1}]$	S
DFI_{bird}	daily food intake for bird species of concern	$[kg_{food}.d^{-1}]$	S/O
DFI_{mammal}	daily food intake for mammalian species of concern	$[kg_{food}.d^{-1}]$	S/O
$Cfood_x$	initial concentration in food for *x*	$[mg_c.kg_{food}^{-1}]$	S/O
$Cfood_{x\text{-}5}$	mean concentration in food for *x* over 5 days	$[mg_c.kg_{food}^{-1}]$	O
BW_{bird}	mean bodyweight of bird species of concern	[kg]	S/O
BW_{mammal}	mean bodyweight of mammalian species of concern	[kg]	S/O
Output			
$RCRfood_{bird\text{-}1}$	RCR for single dose toxicity to birds (PED/LD50)	[-]	O[c]
$RCRfood_{bird\text{-}5}$	RCR for acute toxicity to birds (PEC/LC50)	[-]	O[c]
$RCRfood_{mammal\text{-}1}$	RCR for single dose toxicity to mammals (PED/LD50)	[-]	O[c]

7.2 RCR for birds and mammals exposed through uptake of water or dipping fluid.

Besides eating granules, treated seeds, crops or insects, birds and mammals can also be exposed to a pesticide by the uptake of water. This can be either surface water or water on leaves and crops. This route will only be used if the medicinal product is used as sheep dip or foot bath.

$$RCRdip_{bird} = \frac{PECdip \quad DWI_{bird} \quad 1}{LD\,50_{bird} \quad BW_{bird}}$$

$$RCRsurf_{bird} = \frac{PIECsw \quad DWI_{bird} \quad 1}{LD\,50_{bird} \quad BW_{bird}}$$

$$RCRdip_{mammal} = \frac{PECdip \quad DWI_{mammal} \quad 1}{LD\,50_{mammal,oral} \quad BW_{mammal}}$$

$$RCRsurf_{mammal} = \frac{PIECsw \quad DWI_{mammal} \quad 1}{LD\,50_{mammal,oral} \quad BW_{mammal}}$$

Input			
$LD50_{bird}$	LD50 for birds	$[mg_c.kg_{BW}^{-1}]$	S
$LD50_{mammal,oral}$	LD50 for mammals (oral)	$[mg_c.kg_{BW}^{-1}]$	S
DWI_{bird}	daily water intake of bird species of choice	$[l_{water}.d^{-1}]$	O/S
DWI_{mammal}	daily water intake of mammalian species of choice	$[l_{water}.d^{-1}]$	O/S
BW_{bird}	mean bodyweight of bird species of concern	$[kg_{bw}]$	O
BW_{mammal}	mean bodyweight of mammalian species of concern	$[kg_{bw}]$	O
PECdip	concentration in dip or foot bath	$[mg_c.l^{-1}]$	O
PIECsw	initial concentration in surface water	$[mg_c.l^{-1}]$	O
Output			
$RCRdip_{bird}$	RCR for drinking dipping fluid to birds (PEC/LC50)	[-]	O[c]
$RCRsurf_{bird}$	RCR for drinking surface water to birds (PEC/LC50)	[-]	O[c]
$RCRdip_{mammal}$	RCR for drinking dipping fluid to mammals (PEC/LC50)	[-]	O[c]
$RCRsurf_{mammal}$	RCR for drinking surface water to mammals (PEC/LC50)	[-]	O[c]

7.3 RCR for terrestrial organisms.

Earthworms, nitrificating micro-organisms and plants are exposed to concentrations in target soil.

$$RCR_{worm} = \frac{PIECsoil}{PNEC_{earthworm}}$$

$$RCR_{nitr} = \frac{PIECsoil}{PNEC_{nitr}}$$

$$RCR_{plant} = \frac{PIECsoil}{PNEC_{plant}}$$

Input			
PIECsoil	predicted initial concentration in soil	[$mg_c.kg_{wwt}^{-1}$]	O
$PNEC_{worm}$	PNEC for earthworms	[$mg_c.kg_{wwt}^{-1}$]	S
$PNEC_{nitr}$	PNEC for nitrificating bacteria in soil	[$mg_c.kg_{wwt}^{-1}$]	S
$PNEC_{plant}$	PNEC for plants	[$mg_c.kg_{wwt}^{-1}$]	S
Output			
RCR_{worm}	short term RCR for earthworms	[-]	O^c
RCR_{nitr}	short term RCR for nitrifying bacteria	[-]	O^c
RCR_{plant}	short term RCR for plants	[-]	O^c

7.4 RCR for birds and mammals exposed through earthworms.

The uptake of terrestrial organisms by birds and mammals, in other words, the secondary poisoning of birds and mammals, has been described by Romijn *et al.* (1991b). The RCR is in fact the inverse of the MPC.

$$RCRworm_{Tbird} = \frac{C_{worm\text{-}Tbird}}{PNEC_{oral}}$$

$$RCRworm_{Tmammal} = \frac{C_{worm\text{-}Tmammal}}{PNEC_{oral}}$$

Input			
$PNEC_{oral}$	PNEC for secondary poisoning of birds and mammals	[$kg_c.kg_{food}^{-1}$]	O[c]
$C_{worm\text{-}Tbird}$	mean concentration in earthworms over T_{bird} days	[$mg_c.kg_{wet\ worm}^{-1}$]	O
$C_{worm\text{-}Tmammal}$	mean concentration in earthworms over T_{mammal} days	[$mg_c.kg_{wet\ worm}^{-1}$]	O
Output			
$RCRworm_{Tbird}$	RCR for worm-eating birds (PEC/PNEC)	[-]	O[c]
$RCRworm_{Tmammal}$	RCR for worm-eating mammals (PEC/PNEC)	[-]	O[c]

7.5 RCR for aquatic organisms.

For veterinary medicinal products an RCR for the aquatic ecosystem will be calculated. The water organisms fish, crustaceans and algae are supposed to be exposed to water concentrations that are the mean of the concentration over a period of time. For acute exposure the initial value is taken, for chronic exposure a different value is used, depending on the exposure period in the toxicity test. If there is only release through an STP, the concentration in the effluent after dilution and sorption to suspended matter will be used as exposure concentration.

Discharge from fisheries (see § 8.3.3.4): the PEC used will be the exposure concentration calculated for the duration of the test for the most sensitive organisms (i.e. the species with the lowest NOEC).
Indirect exposure: The PEC used will be the initial exposure concentration.

Effects/Exposure	**Exposure**	**Effects**
RCR_{water}	if $NOEC_{algae}$ = lowest: $Cwater_{pest-4}$ if $NOEC_{crus}$ = lowest: $Cwater_{pest-21}$ if $NOEC_{fish}$ = lowest: $Cwater_{pest-28}$	$PNEC_{water}$

$$RCR_{water} = \frac{PECsw_{vmp-T}}{PNEC}$$

Input			
$P(I)ECwater_{vmp-T}$	mean concentration in water over *T* days, T ≥ {0,4,21,28}	$[mg_c.l^{-1}]$	O
$PNEC_{water}$	PNEC for aquatic organisms	$[mg_c.l^{-1}]$	O[c]
Output			
RCR_{water}	RCR for the aquatic ecosystem	[-]	O[c]

7.6 RCR for sediment-dwelling organisms

For veterinary medicinal products an RCR for the sediment ecosystem will be calculated. The sediment are supposed to be exposed to water concentrations in the ditch that are the mean of the concentration over a period of time. The value chosen depends on the exposure period in the toxicity test. If there is only release through an STP, the concentration in the effluent after dilution and sorption to suspended matter will be used as exposure concentration.

$$RCR_{se} = \frac{Csed_{pest\text{-}28}}{PNEC_{se}}$$

Input			
$Csed_{pest\text{-}T}$	mean concentration in sediment over *T* days, T ≥ {7,28}	[$mg_c.kg_{wwt}^{-1}$]	O
$PNEC_{sed}$	PNEC for sediment-dwelling organisms	[$mg.kg_{wwt}^{-1}$]	O
Output			
$RCR_{sed\text{-}7}$	short term RCR for sediment organisms (PEC/LC50)	[-]	O[c]
$RCR_{sed\text{-}28}$	long term RCR for sediment organisms (PEC/NOEC)	[-]	O[c]

7.7 RCR for birds and mammals exposed through fish

The uptake of veterinary medicinal products by water organisms is calculated by means of the bioconcentration factor (BCF). If no experimentally derived BCF is available, the QSAR-calculation given in § 5.3.2 is used.

$$RCRfish_{bird} = \frac{C_{fish\text{-}Tbird}}{PNEC_{oral}}$$

$$RCRfish_{mammal} = \frac{C_{fish\text{-}Tmammal}}{PNEC_{oral}}$$

Input			
$PNEC_{oral}$	PNEC for secondary poisoning of birds and mammals	$[kg_c.kg_{food}^{-1}]$	O[c]
$C_{fish\text{-}Tbird}$	mean concentration in fish over T_{bird} days	$[mg_c.kg_{wet\ fish}^{-1}]$	O
$C_{fish\text{-}Tmammal}$	mean concentration in fish over T_{mammal} days	$[mg_c.kg_{wet\ fish}^{-1}]$	O
Output			
$RCRfish_{bird}$	RCR for fish eating birds (PEC/NOEC)	[-]	O[c]
$RCRfish_{mammal}$	RCR for fish eating mammal (PEC/NOEC)	[-]	O[c]

7.8 RCR for ground water organisms.

For veterinary medicinal products an RCR for the ground water ecosystem will be calculated.

$$RCR_{groun.\ water} = \frac{PIECgw_{vmp}}{PNEC_{groun.\ water}}$$

Input			
$PIECgw_{vmp}$	predicted initial concentration in ground water	$[mg_c.l^{-1}]$	O
$PNEC_{ground\ water}$	PNEC for ground water organisms	$[mg_c.l^{-1}]$	O[c]
Output			
$RCR_{ground\ water}$	RCR for the ground water ecosystem	[-]	O[c]

7.9 RCR for micro-organisms in STP

The concentration of the chemical in the sewage treatment plant aeration tank is compared to the no-effect concentration for micro-organisms. The concentration during an emission episode is used.

$$RCR_{stp} = \frac{PEC_{stp}}{PNEC_{micro\text{-}organisms}}$$

Input			
PEC_{stp}	local PEC in STP during emission episode	[$mg_c.l^{-1}$]	O
$PNEC_{micro\text{-}organisms}$	PNEC for STP micro-organisms	[$mg_c.l^{-1}$]	O^c
Output			
RCR_{stp}	RCR for sewage treatment plant	[-]	O^c

7.10 RCR for dung insects.

The effect of the chemical present in dung at field concentrations to dung fly and dung beetle is compared to the trigger for field testing (50% effect).

Table 46. Default setting for the module to calculate the $RCR_{dung\ insects}$.

parameter	symbol	unit	value
trigger value for field testing dung insects	-	[-]	50

$$RCR_{dung\ insects} = \frac{\%effect}{50}$$

Input			
%effect	effect percentage at field concentration	[-]	O
-	trigger value for field testing	[-]	D[c]
Output			
$RCR_{dung\ insects}$	RCR for dung insects	[-]	O[c]

7.11 RCR for grassland invertebrates (insects).

The effect of the chemical present in dung at field concentrations to grassland invertebrates (insects, mites, collembola, etc.) is compared to the trigger for field testing (79% effect).

Table 47. Default setting for the module to calculate the $RCR_{grassland\ insects}$.

parameter	symbol	unit	value
trigger value for field testing grassland insects	-	[-]	79

$$RCR_{grassland\ insects} = \frac{\%effect}{79}$$

Input			
%effect	effect percentage at field concentration	[-]	O
-	trigger value for field testing	[-]	D[c]
Output			
$RCR_{dung\ insects}$	RCR for grassland insects	[-]	O[c]

8. EVALUATION.

The reviewer performes the assessment with the data provided to the extent suitable for the phase under consideration. The suitable data are first summarised and evaluated according to the instructions in Chapter 10.

Phase I

✔ dossier completeness check: no further evaluation is performed unless all compulsory information is made available (§8.1).

✔ compare the available information to the trigger values in Phase I (§8.2). The evaluation may end here when Phase I trigger values are not exceeded

Phase II-a

✔ dossier completeness check: no further evaluation is performed unless all compulsory information is made available (§ 8.1).

✔ hazard assessment or risk characterisation: in Phase II Tier A the exposure is compared to the effect (§ 8.2 and § 8.3). The evaluation may end here when Phase II Tier A trigger values are not exceeded.

✔ risk estimation: in the event Phase II Tier A trigger values are exceeded, a quantitative estimation of probabilities of effects by including uncertainty analysis is performed, including proposed risk management strategies (§ 8.4);

✔ requests for supplementary information: When certain (necessary or desirable) information is lacking, or when phase II Tier B evaluation is necessary, requests for complemental or supplemental information are drawn up (§ 8.5).

Phase II-b

A phase II-b assessment is performed by the notifier in co-operation with the evaluation institute (e.g. CSR/RIVM) and is made to measure the type of product and the usage. This stage of assessment is subject to expert judgement. As a general rule: all decisions on requests for information should be reported and motivated before the research is carried out.

8.1 Dossier completeness check.

Below the information needed for Phase I assessment is listed. This information should be present in the dossier part for ecotoxicity. If any information is lacking default values are used that will lead to a worst case assessment. Information without brackets in Table 48 is compulsory: without these no assessment is performed.

Table 48. Information needed in Phase I.

Compulsory information Phase I	↖
Substance and product identification	
1. composition of preparation	☐
2. (purities of the components)	☐
3. names (and chemical (IUPAC) names)	☐
4. (empirical formula)	☐
5. (structural formula)	☐
6. (molar mass)	☐
7. (CAS-number)	
Physical-chemical properties (of all substances in a preparation):	
1. (solubility in water)	☐
2. (octanol-water partition coefficient)	☐
3. (vapour pressure)	
4. (pKa)	
Functions and usage	
1 target animals and intended effects	☐
2 dosage in mg/kg bodyweight/day	☐
3 route of application	☐
4 indications for use	☐

For the (preliminary) hazard assessment default values will be used. In Phase I the information on environmental properties (degradation in soil and manure) of the substance are *not compulsory* for performing the assessment, but depending on the worst-case results of this assessment, they may be indispensable for avoiding a complete Phase II.

The supplemental or complemental information needed for phase II follows from the input parameters in the models to be used and from the effect data needed for the hazard assessment. This information may consist of studies on the following issues, depending on the product, the Tier (A or B) and the compartments to be assessed:

Analysis and detection:
-methods for soil and water
Physical-Chemical properties
Environmental behaviour:
-fate and degradation products of active ingredients (a.i.) in soil
-degradation rate in soil (a.i. and metabolites)
-mobility in soil (a.i. and metabolites)
-fate and degradation products of active ingredients (a.i.) in water/sediment systems
-degradation rate in water/sediment systems (a.i. and metabolites)
-degradation in sewage treatment plants (ready and inherent biodegradability)
-sorption to sediment and suspended matter
Ecotoxicology:
-short term/long term toxicity study with daphnids
-short term/long term toxicity study with fish
-short term/long term toxicity study with algae
-short term/long term toxicity study with earthworms
-short term/long term toxicity study with plants
-short term/long term toxicity study with sediment organisms
-study on the influence on the soil nitrification
-study of the influence on the activated sludge respiration and nitrification
-short term/long term toxicity to dung flies and dung beetles
-bioaccumulation (fish, earthworm)
-sub-chronic dietary toxicity to birds and mammals.

In the event these data are not delivered with the dossier, requests for additional information are drawn up (see Appendix IV).

8.2 Phase I.

For all products the following list is checked for exemptions for further testing. The trigger values are relevant to all components of the product. However, if adverse environmental effects are still anticipated from the use of the products, the Phase II assessment must be performed.
One uses the information in Chapter 3 to decide what routes of emission, distribution, and exposure, and what compartments are relevant for the product under consideration. Use Figure 1 for every route and be aware that while one route of emission may lead to Phase II immediately, other routes may end in Phase I.
The Phase I Decision tree presented in Figure 1 contains more information than presented in the Phase I decision tree by EMEA (1997). However, the decision scheme presented here complies fully with the text from EMEA (1997).

I. Product identity and usage.

Exemption for further testing in both phase I and II is in principle acceptable for:

- physiological substances such as vitamins, electrolytes, natural amino acids and herbs.
- products intendended for administration to companion animals (not including horses).
- products intended for individual treatment as opposed to mass medication [10].

This information can be derived from the compulsory dossier. If these exemptions do not apply:

- the route of distribution is determined (Chapters 3 and 4). In Phase I the uses in goats, fur-bearing animals, other poultry than chickens, turkeys, and ducks, are only assessed when no other target animals are specified.

II. Route of distribution.

- the product is used in fisheries:
  - further assessment is needed in a Phase II assessment (§8.3.1).

- product has an external application and will enter the environment directly:
  - decide whether application will be indoors or outdoors;
  - assess the exposure of slurry, soil and ground water (§§ 4.1.1.2, 4.2.4 and 4.3) and assess the insecticidal properties of the substance (§ 6.2);
  - substances without insecticidal activity (see Chapter 6) are exempted from Phase II testing on grassland invertebrates. If insecticidal properties are evident:
  - further assessment is needed in a Phase II assessment for grassland invertebrates(§ 8.3.1).

- the product has an external or internal application and will enter the environment via slurry:

[10] The EMEA (1997) document also gives 'a small number of animals' as a reason for exemption. However, this criterium needs further elaboration before it can be applied in a uniform and objective manner. We see this criterium as a translation of the trigger values for slurry and soil concentrations, and feel that in that event a calculation is more appropriate.

- substances likely to be rapidly degraded in manure (DT50 in manure less than 30 days)[11] are exempted from further assessment. If this does not apply:
- assess the exposure of slurry (§ 4.1.1 and 4.1.2);
- substances that will be present in concentrations lower than 100 µg/kg in slurry are exempted from further assessment. If this does not apply:
- assess the exposure of soil, groundwater, and surface water (§§ 4.2-4.4).

- the product has an internal or external application and will enter the environment via excreta of grazing livestock:
  - assess the exposure of dung from grazing livestock (see §§ 3.1 and 4.1.2.2);
  - substances are present in the fresh dung in concentrations <10 µg/kg: no further assessment for dung insects.
  - substances are present in the fresh dung in concentrations >10 µg/kg: further assessment is needed in a Phase II tier A assessment for dung insects and earthworms (see § 8.3.3).
  - assess the exposure of soil by urine and dung, the exposure of ground water, and assess the insecticidal properties of the substance (see Chapter 6).
  - If the substance is excreted and has insecticidal properties proceed with a Phase II assessment for surface water (see § 8.3.3).

III. Concentrations in soil and ground water

The product reaches the soil compartment. Assess the concentrations in soil and ground water with the appropriate models (§ 4.2; § 4.3).

- substances that will be present in soil in concentrations 10 µg/kg and <0.1 µg/l in groundwater are exempted from further assessment.

In the case these triggers are exceeded a Phase II Tier A assessment is required for soil and ground water (see § 8.3).

IV. Metabolites.

Information on metabolisation and excretion in the animal, transformation in manure, dung, and soil is not compulsory, but will be used when delivered or available. Exemption for further assessment is in principle acceptable for:

- metabolites which represent less than 20% (molar fraction) of the applied dose.

V. Identification of relevant substances and compartments for Phase II assessment.

The compartments and substances that are not exempted from further testing are listed by the reviewer.

[11] The conclusion 'rapidly degradable' can be based on theoretical calculations or experimental studies in relevant compartments. The presence or degradation of relevant residues can also be shown in bioassays involving relevant target organisms. See Chapter 10.

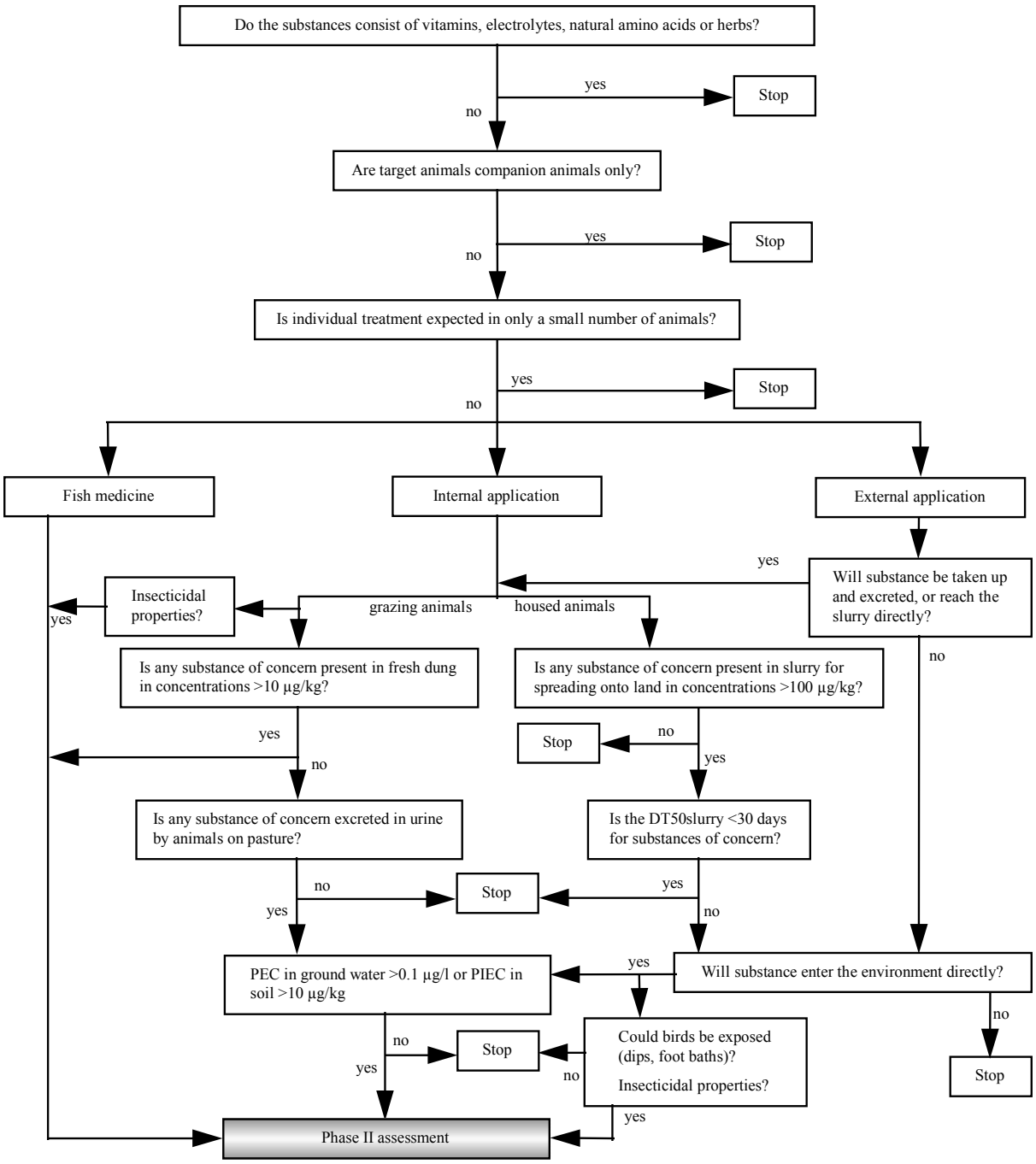

Figure 1. Phase I decision tree.

8.3 Phase II Tier A hazard assessment.

The Phase II Tier A hazard assessment is a complete assessment including emission, distribution, exposure, effects, and hazard identification. At this point, it is important to consider all available documentation relevant to the environmental risk assessment of the product. Follow *all* subsections of § 8.3.

8.3.1 Emission and distribution assessment.

The second phase starts with a more detailed evaluation of the possible fate of the products and/or its relevant metabolites for the relevant compartments identified in Phase I. All default values can be changed due to cogent argumentation for circumstances deviating from the model parameters: e.g. body weights at administration, percentage of the herd treated, incidence of treatment over the year when more cycles are grown.

Proceed with further assessment only for the relevant compartments according to Figure I.

- ⊕ In case of emission to slurry or excretion by grazing animals studies on metabolism in slurry, soil, and manure, and on animal excretion may be required and/or delivered. This elaborated assessment yields environmental concentrations in soil, water and ground water. In Phase II, when at least three $DT50_{soil}$ and three Koc are available, the model Pestla 1.1 (Van der Linden et al., 1989) is used to calculate the concentration in the ground water[12]. The trigger values used in Phase I are still valid.
- ⊕ In case the substance is excreted by grazing animals dung pat degradation may be a point of concern and studies to investigate this aspect may be asked for.
- ⊕ In case the substance is excreted by grazing animals and it has insecticidal properties assess the exposure of the surface water (§ 4.4.1; § 5.3.2; H6). Run-off into surface water is not taken into consideration in case the soil is reached via grazing animals.
- ⊕ In case of external use of high-volume topical applications of insecticidal substances emission to surface dwelling grassland invertebrates and fleece dwelling parasites is direct (§5.2), and so is distribution to birds via the dipping bath (§5.1). Birds are then also exposed through contaminated insects which they use as food source (§5.2).
  The prescribed instructions on how to deal with residual dipping fluid are used for the assessment. When these are not specified, the concentration of the substance in the dipping fluid is divided by the expected surface area the fluid is spread over to give the dosage for the soil (§4.2.4), ground water (§ 4.3) and for the grassland invertebrates. This dosage is also used to make the exposure assessment for birds via invertebrates (§5.2). The concentration in the dipping fluid (§5.1) is the exposure concentration for birds. One should be aware of the possibility that disposal of sheep dips onto land (or even into the ditch) might not be part of recognised good agricultural practice, and as such may not be assessed.
- ⊕ In case of use in fisheries, the concentrations in the STP aeration tank (RIVM, 1994), in the surface water (§ 4.4.3) and in the soil and ground water (§§ 4.2.3 and 4.3) are calculated based on the scenario presented in Chapter 3.11 and the models in Chapter 4. Depending on the use in the fish industry a long term exposure might be expected and in that event the concentration in the sediment is calculated over a longer period. For specific instructions the reader is referred to EMEA (1997), EC (1996), USES (RIVM 1997), and §§ 6.1.2 and 7.6.

[12] The model choice follows the requirements from the Netherlands Pesticide Act.

8.3.2 Exposure assessment.

When a product has an internal or external application and will enter the environment one has assessed the concentration in relevant compartments. See Chapter 4. Gather all calculated concentrations.
For other emission routes and specific distribution routes an exposure assessment needs to be performed. Choose from the possibilities mentioned below.

- ħ the product is used in fisheries:
  - ℘ Substances with a logKow >3 or a BCF_{fish} >1000 (readily degradable substances) or a BCF_{fish} >100 (persistent substances) are assessed on secondary poisoning of vertebrates by fish. See § 5.3.2.

- ħ product has an external application and will enter the environment directly:
  - ℘ Concentrations in feed and 'drinking water' for birds are calculated and presented. See §§ 5.1 and 5.2.

- ħ the product has an external or internal application and will enter the environment via slurry:
  - ℘ assess secondary poisoning via earthworms from soil in case $BCF_{earthworm}$ >20 l/kg (logKow >5). See § 5.3.1.

- ħ the product has an internal or external application and will enter the environment via excreta of grazing livestock:
  - ℘ assess secondary poisoning via earthworms from dung. See §§ 5.3.1 and 5.2.

8.3.3 Effect assessment.

Chapter 6 contains general procedures for effect assessment. The regulatory minumum requirements on toxicity data are different for the various routes of exposure are reported below. Should more information be available, then this can be used.

Effect assessment for residues reaching the soil.

Persistence

Three soil transformation rate studies are required to assess the potential for residues to build up in the soil. This effect is considered relevant at a mean DT90soil >1 year. In case the mean DT50soil >60 days hazard identification for soil micro-organisms is considered necessary, and the trigger for earthworms is lowered (see figure 2).

Mobility and run-off

Three soil adsorption studies are required to assess the potential for residues to run off to the surface water. In case the mean Koc is <500 l/kg and the soil is reached via spreading of slurry the $PECsurface\ water_{run\text{-}off}$ is calculated (§ 4.4.2) and the effect assessment is continued there for surface water.

Phytotoxicity

The most useful EC50 for plants (germination, growth, vigor) is determined. This value is not used for residues on pastures.

Earthworms

The most useful LC50 for earthworms is determined. The result is normalised to 3.5% organic matter for soil and to 30% organic matter for dung. In case the mean DT50soil >60 days the trigger for earthworms is lowered (see figure 2).

Soil micro-organisms

In case the DT50soil >60 days, the data on nitrification are used to derive a PNEC.

Birds

For substances with logKow >5 at least one NOEC from an avian reproduction test is required to calculate the PNEC. Endpoints should be growth, mortality or reproduction (e.g. blood parameters are not relevant). Feeding studies with mammals are acceptable as alternative: see §6.1.6.

Effect assessment for residues reaching the ground water.

Concentration in the ground water.

The standard for ground water of 0.1 µg/l as given in Directive 80/778/EEG is used. Should the standard be exceeded, a Phase II Tier B assessment is required.

Ground water organisms.

In case the PECground water is >0.1 µg/l, one acute Daphnia test is required. Based on the one Daphnia test the PNEC for groundwater organisms is derived.

Effect assessment for residues reaching the surface water indirectly.

Via run-off.

Using at least the results from one acute algae test, one acute Daphnid test, and one acute fish test, a PNEC is derived.

Via direct excretion into surface water.

Only in case the substance has insecticidal properties the result from one acute Daphnia test is required. Based on the one Daphnia test the PNEC is derived.

Via these indirect routes the risk on secondary poisining via fish is considered negligible.

Effect assessment for residues reaching the surface water via discharge from fisheries.

Waterorganisms

Using at least the results from one acute algae test, one acute Daphnid test, and one acute fish test, a PNEC is derived.
When the DT50 hydrolysis/photolysis is >4 days or the Kow >1000 the long-term exposure is calculated with USES 1.0 for both water and sediment (§ 4.4 and 4.5).
NOEC and PNEC values are derived for aquatic and sediment organisms, as are BCF values from fish bioconcentration studies and MPC for sediment. PNEC based on three NOECs are derived.

Birds

For substances with logKow >3 at least one NOEC from an avian reproduction test is required.

Effect assessment for residues from high-volume topical application fluids.

Grassland invertebrates

In a laboratory toxicity test with a susceptible stage of at least two grassland dwelling species a test is performed and the percentage effect is determined. If data from worst-case laboratory tests indicate a more than 79% effect, in any of the test species, then the next stage of testing will be required: a dose-respons laboratory test using natural substrate. This test should be performed with a maximum of four species (1 used in previous test) and a natural substrate (grass). If data from these tests indicate a more than 79% effect, in any of the test species, then the next stage of testing will be required: field studies. For this field study the reader is referred to the EMEA (1997) document, as this stage is part of the Phase II Tier B testing.

Birds

From avian acute toxicity tests LD50 values are derived. From avian short-term dietary toxicity tests LC50 values are derived. The lowest values are used for the assessment of the dietary route.

Effect assessment for residues in dung.

Dung fauna

In case the substance has a DT50 (soil) >60 days, the LC50 for earthworms needs to be determined. The corrected value for 18% o.c. is used.
In case the substance has insecticidal properties, for 1 species dung fly and 1 species dung beetle it is determined whether the effect of the residue is >50% (mortality, reproduction, parasitising capacity). In the event the effect is >50% for dung insects, field studies are required.

8.3.4 Hazard quotients

The hazards quotients are presented and comments are given on the results; e.g. when trigger are exceeded. The hazards quotients are given as RCR values: Risk Characterisation Ratio's (see Chapter 7). The RCR are presented related to the route of exposure:

via spreading of slurry and sludge;
- earthworms, plants, nitrification, ground water, waterorganisms, secondary poisoning via earthworms;

via excretion of dung and urine;
- earthworms, nitrification, ground water, waterorganisms, poisoning of birds and mammals via dung; dung fly and dung beetle.

via discharge to STP/surface water from fisheries;
- activated sludge, waterorganisms, sediment organisms, secondary poisoning via fish;

via external application of (high volume) topical applications:
- earthworms, nitrification, ground water, grassland invertebrates, dietary poisoning birds and mammals, direct uptake fluid by birds.

Below the Phase II Tier A decision schemes are given.

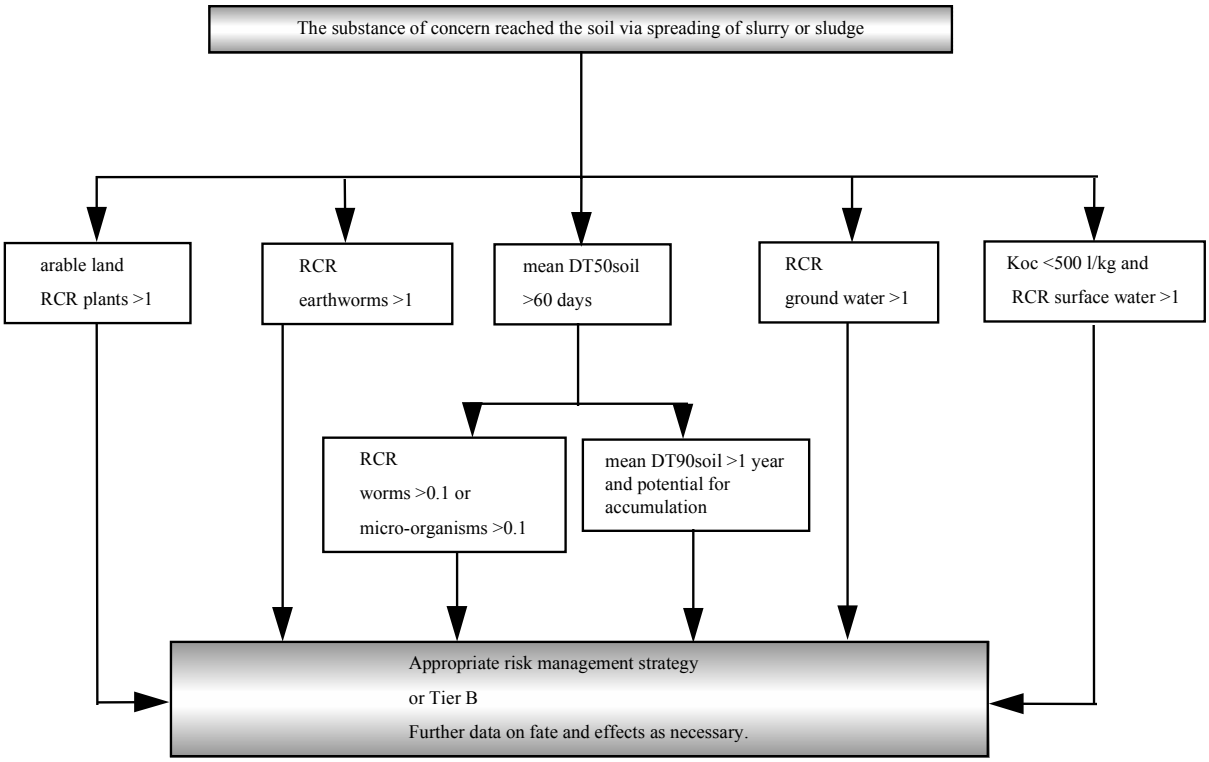

Figure 2. Phase II tier A decision tree for residues spread with slurry.

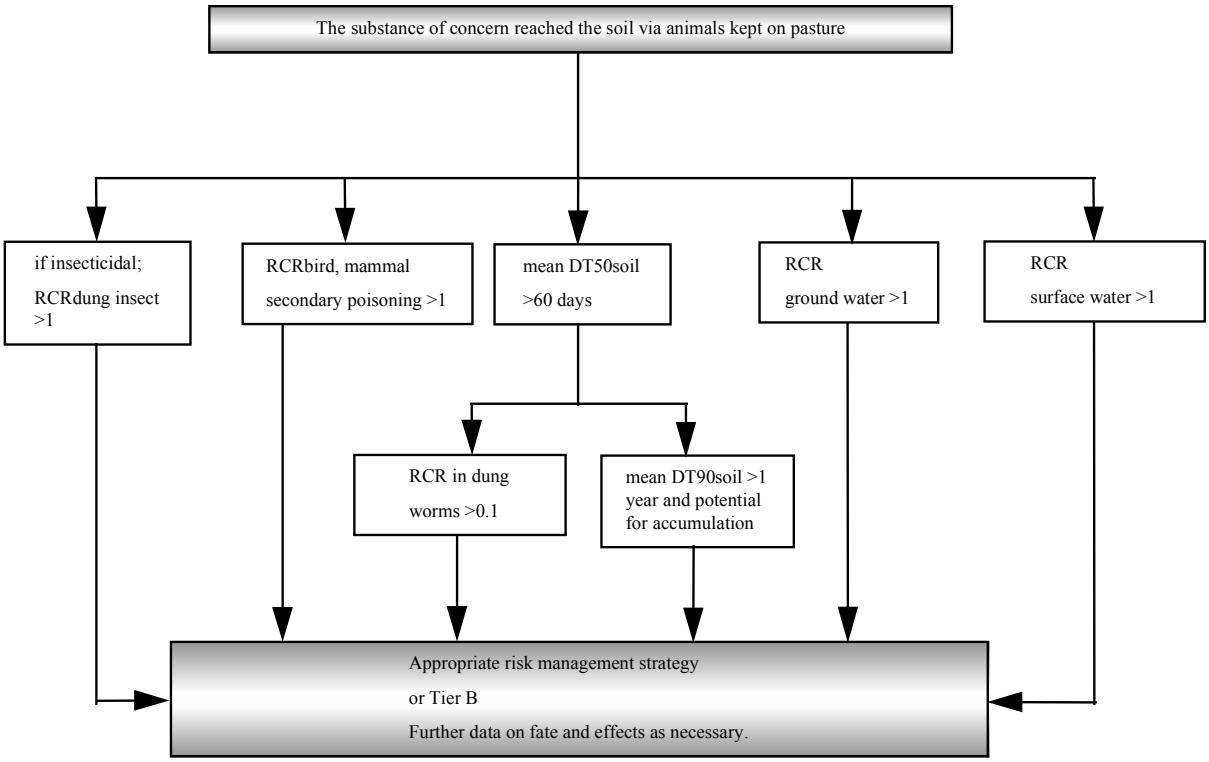

Figure 3. Phase II Tier A decision tree for residues spread by grazing animals.

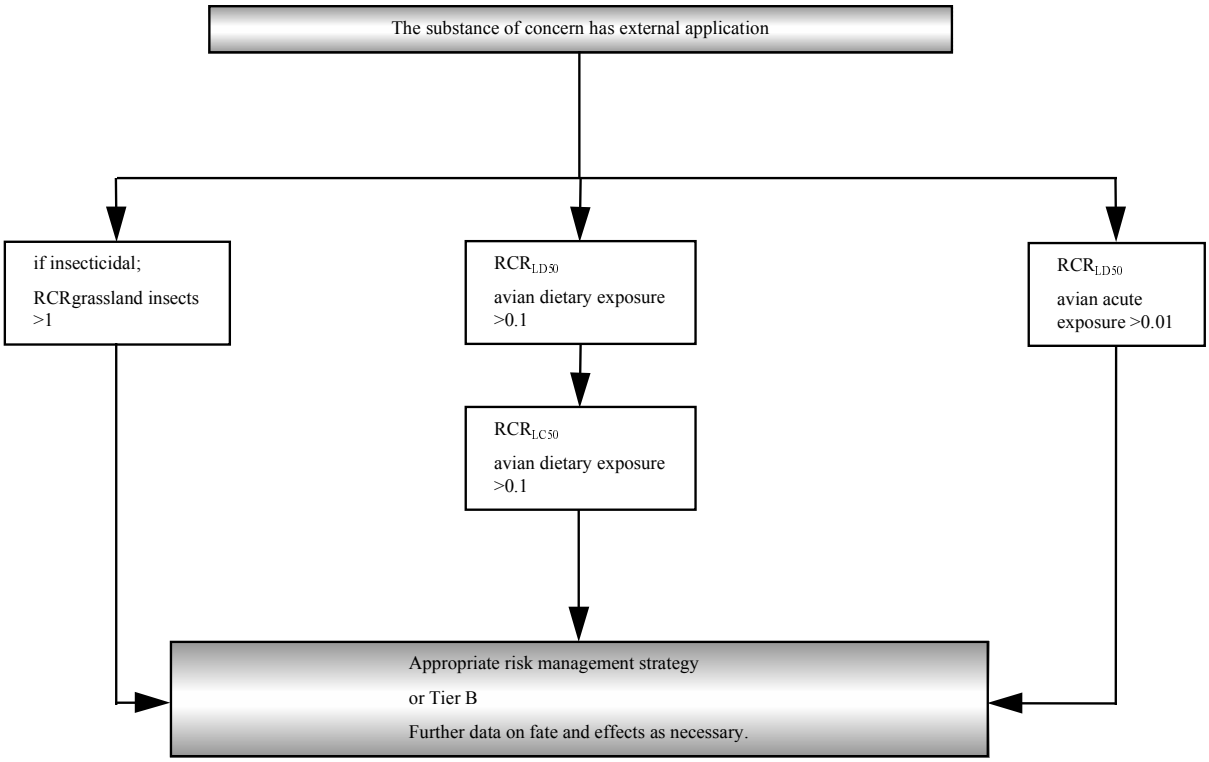

Figure 4. Phase II Tier A decision tree for residues spilled outdoors.

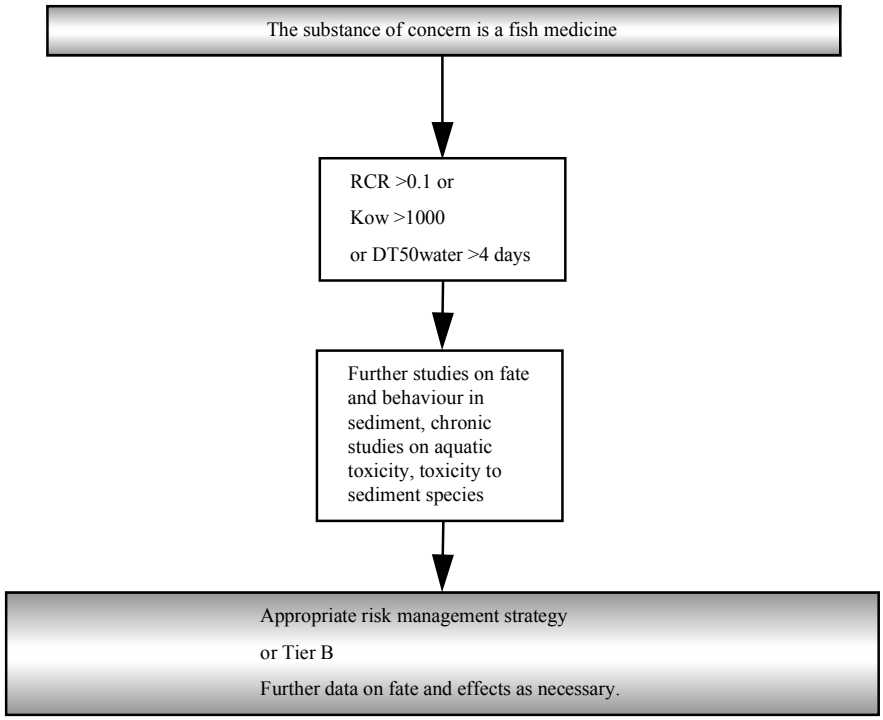

Figure 5. Phase II Tier A decision tree for fish medicines.

8.4 Risk estimation.

The assessment performed has certain limitations that are due to the chosen models and triggers. In this chapter a short comment is given on the alternative results in case different triggers or extreme values from a range were used. This only applies for a Phase II assessment.

An example of a model limitation is the choice of a mixing depth of 5 cm in grassland soil. The slurry is applied by injection. With this method gullies are cut in the turf and the slurry is poured into the gullies. After the injection the soil is closed. With this method a mixing depth of 10 cm is probably more realistic.

8.5 Requests for supplementary information.

In the event the hazard assessment cannot be completed because information is lacking, requests for additional information are made. These requests will be consise and complete, using full sentences. Reference will be made to the paragraph in the assessment the information is needed in, and to the recommended test guidelines and other specific requests.

Supplementary information can also refer to excipients and metabolites. A list of requests for standard information is presented in Appendix V.

Example:

x. No information is available on ..... of (substance). A test performed according to .... Guidelines with (substance) is considered necessary.

9 PREPARATION OF THE ASSESSMENT REPORT.

The assessment report will have a uniform structure to enhance readability.

The report starts with listing the product ingredient and the usage, the chemical identity of the active ingredients, and a comment on the inclusion or exclusion of the other compounds in the risk assessment.
Next the target animals are stated, and the outcome of the first part of the Phase I assessment is determined.
In case the risk assessment is continued, the target animals and subsequent routes of exposure are listed, followed by the environmental compartments that will be assessed. Based on the Phase I trigger values the relevant animals/routes/compartments for the Phase II assessment are listed.

Default values and models are included in the report. All considerations made to change defaults are presented together with the data used from the information on the substance (DT50, Kom etc.). The summarised and evaluated information, from the dossier is compiled after the risk calculation.
All PEC are presented in tables. For the Phase II assessment an overview is presented of the hazard identification (RCR). After each RCR an indication is given whether or not this RCR leads to further assessment.

Finally an overview is given on the results (no further assessment, Phase II-b, or risk reducing measures).

Additional questions are drawn up. To find what questions should be asked, start at chapter 8.3.4, and work backwards towards chapter 8.1. That was you will find what information is lacking.

The expert report is commented upon in a separate section.

On the following pages an example is given. This example is in Dutch. The example is made up of assessments of several products and should be adapted according to ones needs. It should be noted that .

Beoordelend instituut : RIVM/RIKILT-DLO
Aanvraag nr. : 1234
Middelnaam : WONDEROLIE
Aanvrager : fabrikant X

Beoordeelde vragen : III.A.5
Aanvullende informatie gevraagd: ja, t.a.v.

Datum : 14 september 2004

OPMERKINGEN T.A.V. BRD/WRD

(Eind)evaluatie van de gegevens m.b.t. bovengenoemd middel, uitgevoerd in opdracht van het Bureau Registratie Diergeneesmiddelen zoals gevraagd in brief [*kenmerk*] van [*datum opdrachtbrief*], volgens het geldende kwaliteitssysteem CSR.

Project nummer: 613310
Auteur(s) rapport: [*naam beoordelaar (en behandelaar(s))*]
Toetser(s) rapport: [*naam toetser(s)*]
[*(RIKILT-DLO)*]

CSR rapport No.: xxxxxYzz

BEOORDELING VAN GEGEVENS M.B.T. ECOTOXICITEIT, DEEL 3A.5

OMSCHRIJVING VAN HET ONDERZOCHTE PRODUKT

Indicatie :
Farmaceutische vorm :
Samenstelling :
Doeldieren :
Dosering :
Wachttermijnen :
Verwijzing :
Opmerking :

ALGEMEEN

De beoordeling van de ecotoxiciteit is conform de 'Note for guidance: Environmental risk assessment for veterinary medicinal products other than GMO-containing and immunological products' van de 'Committee for veterinary medicinal products' (EMEA/CVMP/055/96), op basis van de aangeleverde gegevens. Voor informatie over de gehanteerde modellen wordt verwezen naar M.H.M.M. Montforts (1997) Environmental risk assessment for veterinary medicinal products. The Dutch appraoch. 1. Non-immunological products. RIVM Rapport nr. 613310001.

BEOORDELING ECOTOXICITEIT (IIIA.5)

De beoordeling ecotoxiciteit is als volgt opgebouwd:

Maak een inhoudsopgave.

1. Inleiding

Het product ..... bevat ..... Volgens het aanvraagformulier is een verdere fase I beoordeling noodzakelijk, omdat het een regulier farmacologisch geneesmiddel betreft, waarbij massamedicatie te verwachten is. Het middel is bedoeld voor runderen die geen melk geven voor humane consumptie. Het middel wordt oraal gedoseerd, waardoor de excreta de meest relevante route vormen voor verspreiding in het milieu. De volgende doeldieren worden onderscheiden.

- Zoogkoeien
- Vleesstieren
- Vleeskalveren

De volgende emissieroutes zijn mogelijk:

- via de gier
- via de mest van de grazers op de weide

De gebruiksaanwijzing sluit geen van beide routes uit. Voor de volgende compartimenten wordt een blootstellingsbeoordeling opgesteld:

- Concentratie in gier (gier)
- Concentratie in mest (grazers)
- Concentratie in de bodem (gier)
- Concentratie in de bodem (grazers)
- Concentratie in grondwater (gier)
- Concentratie in grondwater (grazers)

Voor verspreiding via de gier is de totale uitscheiding van belang, terwijl voor uitscheiding via de faeces op het veld tevens het verloop van de uitscheiding van belang is voor het bepalen van de piekconcentratie.

2. Fase I beoordeling

2.1 Wijze van gebruik en route van verspreiding van residuen

Rund. Afhankelijk van het omweidingsschema en de begrazingsdichtheid dienen de kalveren tot maximaal om de 3-4 weken gedurende de weideperiode ontwormd te worden. Als verspreidingsroute is de verspreiding via grazende vleeskalveren relevant.
Paard. Bij volledige weidegang ontwormen in april, mei, juni, juli en november. Altijd op stal, ‘s zomers op weide: behandelen op moment van weidegang. Als verspreidingsroute is de verspreiding via grazende ponies relevant.
Varken: Mestvarkens: biggen bij opleg en op ongeveer 50 kg lichaamsgewicht ontwormen. Zeugen ontwormen wanneer ze in de kraamafdeling komen. Biggen voor het spenen en beren bij aankoop en nadien tweemaal per jaar ontwormen. Nieuw aangevoerde dieren ontwormen. Bij varkens is verspreiding via de gier van vleesvarkens en van zeugen relevant.
Schaap en geit: Ooien tweemaal per jaar ontwormen: bij het opstallen in de winter of rond de partus en voor het toelaten bij de ram. Lammeren: afhankelijk van de wormsoort, beweidingsplan en bezettingsdichtheid maximaal om de drie weken behandelen.

2.2 Fysisch-chemische eigenschappen.

Bijvoorbeeld in tabelvorm.

2.3 Metabolisme en excretie

Na orale toediening aan varkens (20-22 kg) van 5 mg vmp/kg lichaamsgewicht wordt 40% van de toegediende dosis vmp uitgescheiden in urine en faeces als de werkzame stoffen vmp, metaboliet A en metaboliet B. De metaboliet metaboliet A werd gevonden in gehalten >20% van de toegediende dosis.
Na intra-ruminale toediening aan schapen (10-15 kg) van 5 mg vmp/kg lichaamsgewicht wordt 40% van de toegediende dosis vmp uitgescheiden in urine en faeces als de werkzame stoffen vmp, metaboliet A en metaboliet B. De verdeling over faeces en urine is 35% tegen 5%. Na 3 dagen was c. 67% van de toegediende dosis uitgescheiden via de faeces.
De metaboliet metaboliet A werd door varkens uitgescheiden in gehalten >20% van de toegediende dosis. Voor de fase-I beoordeling worden metaboliet A en metaboliet B als zijnde vmp beschouwd, omdat alle stoffen werkzaam zijn.

2.4 Bodemadsorptie

2.5 Biodegradatie in bodem en mest

2.6 Expert report.

In het expert report worden enkele veronderstellingen gedaan. Deze zijn wel/niet onderbouwd en worden wel/niet bruikbaar geacht voor de beoordeling.

3. Fase I beoordeling.

3.1 Modelberekeningen.

Hieronder worden de concentraties in de verschillende compartimenten berekend. In de invoer-uitvoer tabellen van de modellen komen de volgende afkortingen voor:

S	data Set	een waarde voor deze parameter moet beschikbaar zijn in de aangeleverde gegevens.
D	Default	een vaste waarde, tenzij een betere waarde beschikbaar is in de aangeleverde gegevens.
O	Output	deze waarde is een resultaat van een (vorige) berekening of van een keuzelijst.
c	closed	de waarde mag niet veranderd worden.

Voor de berekeningen zijn diverse specifieke gegevens nodig met betrekking tot de doeldieren en de landbouwpraktijk. De volgende waarden worden gehanteerd (tabellen 1-4).

Tabel 1 Default waarden voor rundvee.

parameter	symbol	unit	value
(averaged) body weight	$m_{beef\ cattle}$	$[kg_{bw}.animal^{-1}]$	218
dung production pasture during grazing period	$Pdung_{beef\ cattle}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	9
stocking density pasture	$Nbeef_{ha\ pasture}$	$[animal.ha^{-1}]$	9.5
number of grazing days	Tgrazing	$[d.yr^{-1}]$	190
number of excretions per day	Nexcretion	$[d^{-1}]$	10.5

Een worst-case benadering is een behandeling om de drie weken: 190:21=9 behandelingen.

Tabel 2 Default waarden voor schapen.

parameter	symbol	unit	value
body weight ewe	m_{sheep}	$[kg_{bw}.animal^{-1}]$	82
body weight lamb	m_{lamb}	$[kg_{bw}.animal^{-1}]$	36
number of cycli per year	$Ncyclus_{sheep}$	$[animal.place^{-1}.yr^{-1}]$	1
number of housing days	$Thousing_{sheep}$	$[d.yr^{-1}]$	0
number of grazing days ewe	$Tgrazing_{sheep}$	$[d.yr^{-1}]$	320
number of grazing days lamb	$Tgrazing_{lamb}$	$[d.yr^{-1}]$	160
dung production pasture during grazing period ewe	$Pdung_{sheep}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	1.025
dung production pasture during grazing period lamb	$Pdung_{lamb}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	1.758
stocking density pasture ewe	$Newe_{ha\ pasture}$	$[animal.ha^{-1}]$	15
stocking density pasture lamb	$Nlamb_{ha\ pasture}$	$[animal.ha^{-1}]$	25
number of excretions per day	Nexcretion	$[d^{-1}]$	10.5

Tabel 3 Default waarden voor paarden.

parameter	symbol	unit	value
body weight	m_{pony}	$[kg_{bw}.animal^{-1}]$	250
number of cycli per year	$Ncyclus_{pony}$	$[animal.place^{-1}.yr^{-1}]$	1
number of housing days pony	$Thousing_{pony}$	$[d.yr^{-1}]$	0
number of grazing days ponies	$Tgrazing_{pony}$	$[d.yr^{-1}]$	365
dung production pasture during grazing period	$Pdung_{pony}$	$[kg_{wwt}.animal^{-1}.d^{-1}]$	7
stocking density pasture	$Npony_{ha\ pasture}$	$[animal.ha^{-1}]$	5
number of excretions per day	Nexcretion	$[d^{-1}]$	10.5

Een worst-case benadering is vijf behandelingen per jaar.

Tabel 4 Default waarden voor varkens.

parameter	symbol	unit	value
(averaged) body weight	m_{sow}	$[kg_{bw}.animal^{-1}]$	240
	$m_{fattening\ pig}$	$[kg_{bw}.animal^{-1}]$	70
number of cycli per year	$Ncyclus_{sow}$	$[animal.place^{-1}.yr^{-1}]$	1
	$Ncyclus_{fattening\ pig}$	$[animal.place^{-1}.yr^{-1}]$	2.8
number of housing days	$Thousing_{pigs}$	$[d.yr^{-1}]$	365
slurry production during housing	$Pslurry_{sow}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	14.8
	$Pslurry_{fattening\ pig}$	$[kg_{wwt}.place^{-1}.d^{-1}]$	3.8
phosphate production during housing	$P_{P2O5\ sow}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.0556
	$P_{P2O5\ fattening\ pig}$	$[kg_{P2O5}.place^{-1}.d^{-1}]$	0.0203

Het lichaamsgewicht van vleesvarkens is gespecificeerd op 50 kg en het gewicht bij opleg (25 kg). Voor de berekening wordt dit vertaald naar een lichaamsgewicht van 25+50/2=37,5 kg in combinatie met twee behandelingen.

3.2 Concentraties in het milieu.

3.2.1 De concentratie in de gier.

Geef de gehanteerde defaults en formules.

Tabel 6 Berekening van de uitgescheiden dosis naar de gier.

	$Q_{product\ x\ C_c}$	m_{animal}	$T_{treatment}$	$F_{excreted}$	Ncyclus	$Q_{excreted}$
	[$mg_c.kg_{bw}^{-1}$]	[$kg_{bw}.animal^{-1}$]	[d]	[-]		[$mg_c.place^{-1}.yr^{-1}$]
vleesvarkens		37,5	2	0,4	2,8	
zeugen		240	1	0,4	1	

Tabel 7 Berekende maximale concentraties in de mest.

	$Q_{excreted}$	$T_{housing}$	$Pslurry_{animal}$	PECslurry
	[$mg_c.place^{-1}.yr^{-1}$]	[$d.yr^{-1}$]	[$kg_{wwt}.animal^{-1}.d^{-1}$]	[$mg_c.kg_{wwt}^{-1}$]
vleesvarkens	420	365	3,8	0,3
zeugen	480	365	14,8	0,09

De concentratie in gier van vleesvarkens is >100 µg/kg en een verdere beoordeling wordt noodzakelijk geacht.

3.2.2 De concentratie in de bodem als gevolg van verspreiding van gier

Geef de gehanteerde defaults en formules.

Tabel 10 Berekende concentraties in de grond.

	$Q_{excreted}$	$T_{housing}$	$P_{P2O5animal}$	PIECsoil bouwland	PIECsoil grasland
	[$mg_c.place^{-1}.yr^{-1}$]	[$d.yr^{-1}$]	[$kg_{P2O5}.place^{-1}.d^{-1}$]	[$mg_c.kg_{soil}^{-1}$]	[$mg_c.kg_{soil}^{-1}$]
vleesvarkens	420	365	0,0203	0,0014	0,008

De concentratie is <10 µg/kg bodem en een verdere beoordeling voor bodem wordt niet noodzakelijk geacht.

3.2.3 De maximale concentratie in de mest van grazers op de weide

Tabel 11 Default waarden voor de berekening van de maximale concentratie in de mest.

parameter	**symbol**	**unit**	**value**
duration of treatment	$T_{treatment}$	[d]	1
highest fraction excreted in dung in one day	$F_{max.\ excreted\ dung}$	[-]	1
number of dung excretion events per day	Nexcretion	[d^{-1}]	10.5

Model voor de berekening van de maximale concentratie in de mest:

$$PECdung = \frac{Q_{product} . C_c . m_{animal} . T_{treatment} . F_{max.excreted.dung} . Nexcretion}{Pdung_{animal}}$$

input

$Q_{product}$	dosage product used	[$kg.kg_{bw}^{-1}.d^{-1}$]	S
C_c	concentration a.i. in product	[$mg_c.kg^{-1}$]	S
m_{animal}	(averaged) body weight	[$kg_{bw}.animal^{-1}$]	S/D

input			
$T_{treatment}$	duration of treatment	[d]	D
$F_{max.\ excreted\ dung}$	highest fraction excreted in dung in one day	[-]	S/D
$Pdung_{animal}$	dung production animal in field	$[kg_{wwt}.animal^{-1}.d^{-1}]$	O
Nexcretion	number of dung excretion events per day	$[d^{-1}]$	D
output			
PECdung	concentration in dung	$[mg_c.kg_{wwt}^{-1}]$	O/S

Uit de gegevens over de excretie van vmp door schapen blijkt dat 67% van de toegediende dosis na 3 dagen uitgescheiden is in de faeces. Wanneer een eerste orde kinetiek in de uitgescheiding mag worden aangenomen, dan blijkt dat de halfwaardetijd voor de uitscheiding ongeveer 1,88 dagen bedraagt. Bij 10,5 ontlastingen per dag vindt de eerste ontlasting na 0,095 dag plaats. Op dat moment wordt 3,4% van de dosis uitgescheiden. Voor de berekening van de maximale concentratie wordt van deze fractie uitgegaan voor zowel schapen als ook paarden en runderen.

Tabel 12 Berekende maximale concentraties in de mest van grazers op de weide.

	$Q_{product\ x}\ C_c$	m_{animal}	$T_{treatment}$	$F_{max.\ excreted\ dung}$ [-]	$Pdung_{animal}$	Nexcretion	PECdung $[mg_c.kg_{wwt}^{-1}]$
	$[mg_c.kg_{bw}^{-1}]$	$[kg_{bw}.animal^{-1}]$	[d]		$[kg_{wwt}.animal^{-1}.d^{-1}]$	$[d^{-1}]$	
schapen	5	82	1	0,034	1,025	10,5	143
vleesstieren	7,5	218	1	0,034	9	10,5	65
ponies	6	250	1	0,034	7	10,5	77

De concentratie is >10 µg/kg en een verdere beoordeling wordt noodzakelijk geacht.

3.2.4 De concentratie in de bodem als gevolg van verspreiding via urine en mest.

Geef de gehanteerde defaults en formules.

Tabel 15 Berekende concentraties in de grond door verspreiding via grazers op de weide.

	$Q_{product\ x}\ C_c$	m_{animal}	$T_{treatment}$	$F_{excreted\ urine}$	$F_{excreted\ dung}$	$Nanimal_{field}$	PIECsoil
	$[mg_c.kg_{bw}^{-1}]$	$[kg_{bw}.animal^{-1}]$	[d]	[-]	[-]	$[animal.ha^{-1}]$	$[mg_c.kg_{soil}^{-1}]$
ooien	5	82	1	0,05	0,35	15	
lammeren schapen	5	36	1	0,05	0,35	25	
vleesstieren	7,5	218	1	0,05	0,35	9,5	
ponies	6	250	1	0,05	0,35	5	

De concentraties zijn <10 µg/kg bodem (behalve voor vleesstieren: 10 µg/kg) en een verdere beoordeling wordt niet noodzakelijk geacht.

3.2.5 De concentratie in het grondwater.

Tabel 16 Default waarden voor de module voor grondwater.

parameter	symbol	unit	value
bulk density of soil	RHOsoil	$[kg.m^{-3}]$	1700
density of soil solids	$RHOsolid_{soil}$	$[kg.m^{-3}]$	2500
fraction air in soil	$Fair_{soil}$	$[m^3.m^{-3}]$	0.2
fraction water in soil	$Fwater_{soil}$	$[m^3.m^{-3}]$	0.2
fraction solids in soil	$Fsolid_{soil}$	$[m^3.m^{-3}]$	0.6
weight fraction organic carbon in soil	Foc_{soil}	$[kg.kg^{-1}]$	0.02
temperature at air-water interface	TEMP	[K]	285
gas constant	R	$[Pa.\ m^3.mol^{-1}.K^{-1}]$	8.314

Model voor de berekening van de concentratie in het grondwater.

$$PIECgw = \frac{PIECsoil \,.\, RHOsoil}{K_{soil-water} \,.\, 1000}$$

$$K_{soil-water} = Fair_{soil} \; K_{air-water} \quad Fwater_{soil} \quad Fsolid_{soil} \; \frac{Kp_{soil}}{1000} \,.\, RHOsolid$$

$$Kp_{soil} = Foc_{soil} \,.\, Koc$$

$$K_{air-water} = \frac{VP \,.\, MOLW}{SOL \,.\, R \;\; TEMP}$$

input			
PIECsoil	highest concentration in the soil	[$mg_c.kg_{soil}^{-1}$]	O
RHOsoil	fresh bulk density of soil	[$kg.m^{-3}$]	D
RHOsolid	density of soil solids	[$kg.m^{-3}$]	D
$Fair_{soil}$	fraction air in soil	[$m^3.m^{-3}$]	D
$Fwater_{soil}$	fraction water in soil	[$m^3.m^{-3}$]	D
$Fsolid_{soil}$	fraction solids in soil	[$m^3.m^{-3}$]	D
Foc_{soil}	fraction organic carbon in soil (w/dw)	[$kg.kg^{-1}$]	D
Koc	partition coefficient organic carbon - water	[$dm^3.kg^{-1}$]	650
VP	vapour pressure	[Pa]	S
MOLW	molar mass	[$g.mol^{-1}$]	S
SOL	water solubility	[$mg.l^{-1}$]	S
TEMP	temperature at air-water interface	[K]	D
R	gas constant	[Pa. $m^3.mol^{-1}.K^{-1}$]	D
intermediate results			
$K_{soil-water}$	partition coefficient solids and water in soil (v/v)	[$m^3.m^{-3}$]	O
Kp_{soil}	partition coefficient solids and water in soil (v/w)	[$dm^3.kg^{-1}$]	O
$K_{air-water}$	partition coefficient air and water in soil	[$m^3.m^{-3}$]	O
output			
PIECgw	predicted initial concentration in ground water	[$mg_c.l^{-1}$]	O

Omdat de Koc >500 l/kg is, wordt het risico voor run-off naar het oppervlaktewater verwaarloosbaar geacht.

Tabel 17 Berekende concentraties in het grondwater

	PIECsoil [$mg_c.kg_{soil}^{-1}$]	PECgw [$mg_c.l^{-1}$]
schapen		0,00013
vleesstieren		0,00088
ponies		0,00022
vleesvarkens		0,00069

De concentraties zijn >0,1µg/l en een verdere beoordeling wordt noodzakelijk geacht.

3.2.6 De concentratie in het oppervlaktewater als gevolg van verspreiding via grazers.

Tabel 19 Berekende concentraties in het oppervlaktewater.

	$Q_{product\ x}\ C_c$ [$mg_c.kg_{bw}^{-1}$]	m_{animal} [kg_{bw}.$animal^{-1}$]	$T_{treatment}$ [d]	$Nanimal_{field}$ [$animal.ha^{-1}$]	PIECsw [$mg_c.l^{-1}$]
ooien	5	70	1	15	0,00175
lammeren	5	27,5	5	25	0,00573
schapen					0,0075
vleesstieren	7,5	218	9	9,5	0,0466
ponies	6	250	5	5	0,0125

Het is niet bekend of de stof insecticide eigenschappen heeft. Een verdere beoordeling wordt noodzakelijk geacht.

4 Conclusies Fase I.

De beschikbare gegevens en de rekenmodellen doen besluiten tot de volgende conclusies.

De concentraties in de bodem zijn kleiner dan 10 µg/kg. De concentratie in het poriewater c.q. grondwater zijn maximaal 7 ng/l. Deze gegevens geven geen aanleiding voor een fase II beoordeling van dit produkt. De berekende concentraties in de verse mest op de weide zijn >10 µg/kg versgewicht gedurende de eerste week na toediening. Voor deze verspreidingsroute wordt een fase-II beoordeling noodzakelijk geacht.

5 Fase II.

5.1 Concentraties in het milieu
De concentraties in fase I berekend worden overgenomen met uitzondering van:

5.1a-x (invoegen aanvullende informatie en berekeningen).

5.y Berekening van de PNEC.

compartiment	eindpunt	eindpunt	eindpunt	assessment factor	PNEC
water (run-off, viskweek)	x	y	z	α	....
water (grazers)	q			β	....
grondwater	q			β	....
vogels	a	b	c	α	....
zoogdieren	k	l	m	α	....
regenwormen	p			γ	....
micro-organismen	q			γ	....
planten	r			γ	....
arthropoden	s	t			n.v.t

n.v.t. = niet van toepassing.

5.z Berekening van de RCR.

compartiment	RCR	conclusie
water (run-off, viskweek)	x	
water (grazers)	q	
grondwater	q	
vogels	a	
zoogdieren	k	
regenwormen	p	
micro-organismen	q	
planten	r	
arthropoden	s	

6. Conclusies.

7. Vragen voor aanvullende gegevens.

8. Samenvatting en evaluatie van de gegevens voor de fase I beoordeling.

In deze bijlage worden alle samengevatte studies gepresenteerd, alsmede de literatuur betrokken in de beoordeling.

10. SUMMARISING AND EVALUATING TEST REPORTS.

10.1 General information.

10.1.1 Structure of summaries.

The relevant test conditions and main results form the Header of the summarised test (see Figure 1.1). The Description contains successively:

1. the Methodology (as far as not reported in the Header);
2. the Results (as presented by the author);
3. the Remarks (critical comments on the test, made by the reviewer).

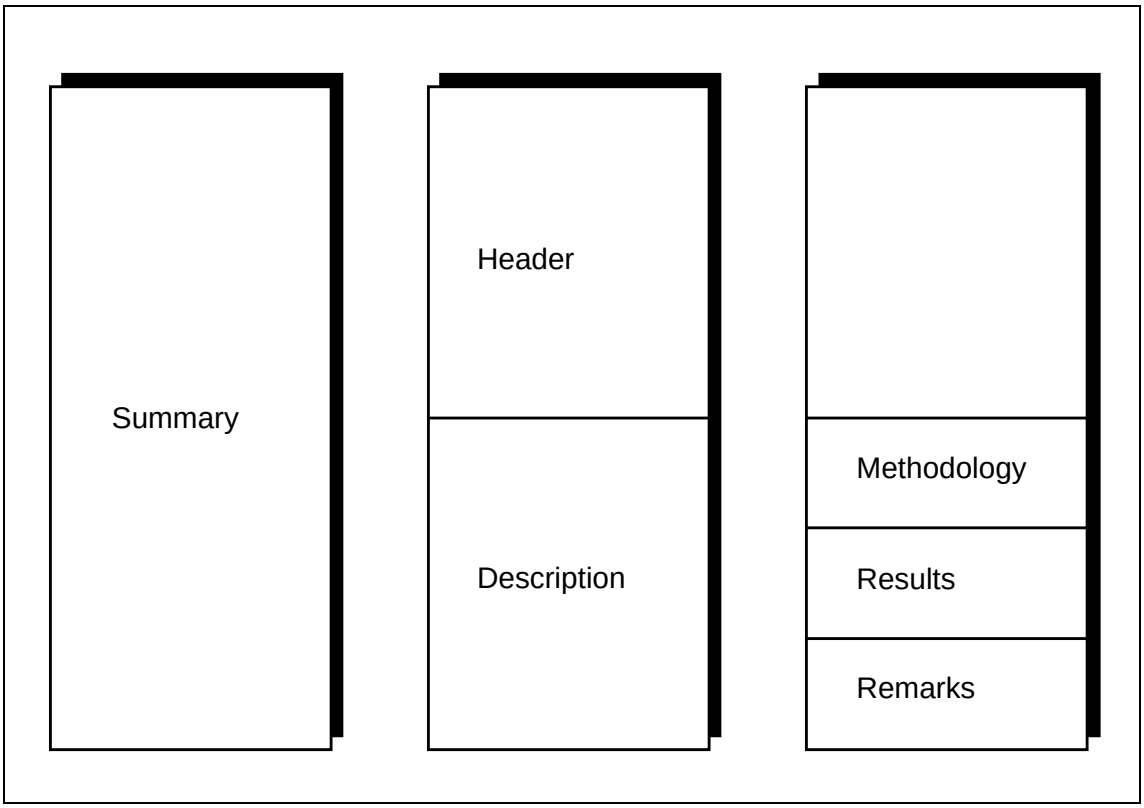

Figure 6. The structure of a Summary.

10.1.2 Instructions.

The instructions given in this chapter comprise both official Guidelines and the CSR directives on summarising and evaluating test reports. The OECD Guidelines and other International Guidelines are the starting points for the instructions. The CSR directives contain decisions on items the official Guidelines do not handle, directives on (re)calculating test results, and directives on the way of reporting various information.
The instructions are of a technical nature: it is stated which information has to be dealt with, and in which way, and how to apply this information in the models and decision schemes without an extensive explanation of all the rationales. The latter can be found in Brouwer et al. (1993); Canton et al. (1991); Linders et al. (1994) and the various (inter)national Guidelines.
In this way the instructions function as a checklist for preparing the Summaries and the RIVM Conclusion. It should also be noted that this document is not a cookery-book (which would result in uniform ARs): expert judgement remains *crucially* important in the process of evaluating the environmental aspects of substances.

10.1.3 Reliability of information.

All delivered test reports are summarised and evaluated on their scientific validity and their usefulness by the reviewer according to this document (parts of these instructions were previously published as Mensink et al. (1995))[13], whether or not they are required for the Phase I or II.
All the studies that are summarised and evaluated in an AR, are given a Reliability Index (RI) as a measure for the *reliability*. The definitions is:
Reliability: the intrinsic reliability of a test with respect to the methodology and the description. Synonym: *betrouwbaarheid (Dutch)* .

reliability index (RI)	definition	description
1	reliable	the methodology and the description are in accordance with the instructions in this Manual
2	less reliable	the methodology and/or the description are less in accordance with the instructions in this Manual
3	not reliable	the methodology and/or the description are not in accordance with the instructions in this Manual

The Reliability Index (RI) is found in the Header of every summarised test in an AR. It is an obligatory record for the reviewer. Although usefulness indicators are not yet developed, there are already instructions on the usefulness of data. From these definitions it follows that reliability + usefulness = quality.

[13] The dossier may contain studies that are not commented upon in CSR/H/007. Expert judgement and sound scientific reasoning are then required.

10.1.4 Instruction tables

The instruction tables (or summary tables) are the core of the instructions. The summary tables structure the abundance of information and help assigning a Reliability Index to the tests. Table 1 is an example. It starts with the 'description' including the relevant test conditions, followed by the 'results' with the relevant test results and it ends by 'pay attention' including those items that should be checked, but need not necessarily be included in the Summary.
In the summary tables you find the requirements which have to be met for a study; the items refer to the *reliability* of a test. Items that refer to the *usefulness* rather than to the reliability are given in the footnotes of the table. It is, however, felt by the authors that one may dispute whether certain test items fall within reliability or usefulness. One may e.g. argue whether the item on the λ of the light source in a photolysis test in water (see Table 8), implies that a test with λ <290 nm is less reliable or that such a test is less useful as the λ does not reflect natural conditions. In this way the summary tables keep on fostering discussions. The tables should therefore not be seen as too compelling.

If items reported are not in accordance with the summary tables, the reliability of a study decreaseS. In the column with the heading 'Reliability lower?' this is indicated by a Y(es) or an E(xpert judgement):

Y. Y(es) indicates that solely based on not fulfilling this requirement for this item, the reliability of the entire study is expected to decrease. This can be reflected in assigning an RI of 2 to a test, or even an RI of 3. It is up to expert judgement in the latter case, to decide how many "Y"-items are required for assigning an RI of 3 to a particular test.
E. E(xpert judgement), indicates that no clear guidance can be given. The reviewer can consult a specialist.

It should always be stated clearly in a Summary under Remarks why a certain RI has been assigned, so that this can be verified.

Table 10.1: Example of a summary table

	Items	Notes	Reliability lower?
Description	**These items should always be included in the test description in a Summary.**	These notes explain the requirements which have to be met for a reliable test (i.e. with an adequate methodology and description). If items in a study deviate from these requirements, check in the next column ("reliability lower?") whether the reliability with respect to that particular item may decrease. Y(es) This note indicates that the reliability can be considered to decrease. E(xpert judgement) This note indicates that the assignment of an RI is up to the reviewer.	Y E
	These items should only be included, if a test is not performed according to a Guideline.		
Results	**These results should always be included, under Results.**		
Pay attention	The items here should not necessarily be included into a Summary, but should be checked. These items —if deviating from the requirements— can be included under Remarks.		

10.2 Degradation in manure.

The EMEA (1997) document comments on the degradation in manure as follows:

Substances likely to be rapidly degraded in manure (DT50 in manure less than 30 days) are exempted from further testing. The conclusion 'rapidly degradable' can be based on theoretical calculations or experimental studies in relevant compartments. The presence or degradation of relevant residues can also be shown in bioassays involving relevant target organisms.

This environmental property is important for the further assessment. The delivered information is closely evaluated, keeping the following directives (☞) in mind:

☞ *... rapidly degraded in manure (DT50 in manure less than 30 days)...*
The relevant temperature is 20°C for pigs, 10°C for cattle and 25°C for chickens and horses. We accept tests at other temperatures within a range of c. 10°C, and recalculate the result with the Arrhenius-equation. Manure from pigs and cattle should be incubated wet/anaerobic; manure from chickens should be incubated dry/aerobic.

☞ *... on theoretical calculations...:.*
With theoretical calculations mainly the Arrhenius-equation is intended.

☞ *... or experimental studies in relevant compartments...*
readily biodegradability tests when the substance proved readily or inherently biodegradable are relevant and are equivalent to DT50 <30 days;
Soil enriched with manure, but only aerobic studies for chicken and horse manure, and only anaerobic studies for pigs or cattle manure, are relevant and results will be recalculated to the appropriate temperature;
anaerobe soil studies in case the soils were inundated for pigs and cattle manure are relevant and results will be recalculated to the appropriate temperature;
anaerobe water sediment studies for pigs and cattle manure are relevant and results will be recalculated to the appropriate temperature;
hydrolysis studies with broad pH-ranges tested indicating rapid hydrolysis;
degradation derived from in-vivo metabolism studies are not relevant.

☞ *... be shown in bioassays involving relevant target organisms...*
According to CSR/H/007 results obtained with bioassays are less reliable. For the Phase I assessment however they are considered useful, provided the bioassays are performed in the most adequate way. The test organisms should be able to respond to changes in concentration at the relevant fortification level, until 90% degradation is reached.

For further reading on degradation of medicines in manure see Bouwman and Reus (1994).

Table 10.2: Manure transformation studies

	Items	Notes	Reliability lower ?
Description	**1. test type** **a. laboratory/stable** **b. aerobic/anaerobic** **c. sterile/non-sterile** **2. test substance and position of label** **3. vehicle** **4. manure** **4.1 type** **4.2 pH** **4.3 water content** **4.4 % o.m.** **4.5 storage conditions** **5. weight of sample** **6. temperature** **7. application method and rate** **8. light condition** **9. test system** **10 incubation time** **11 sampling frequency** **12 extraction/analysis method**	b. aerobic: chickens and horses; anaerobic: cattle and pigs c. method of sterilisation should be given 4. give type (slurry, stable manure); fresh, unaltered manure should be used 4.5 storage before testing should be appropriate 5. weight sample should be X g. [X= 10] 6 . temperature should be constant (±2°C) 8. incubation in the dark[14] 9. closed with volatile traps? 10 preferred until 90% transformation or up to 100 days 11 5 time points are needed for adequate regression analysis 12 This should be appropriate for the substance and the metabolites, and the recovery of the substance should be >X% [X= 70] and <Y% [Y= 110]	1b. E 4. Y 5. E 10. E 11. Y 13. E
Results	**1. DT_{50} and %a.i. at end** **2. total recovery** **3. kinetic order** **4. bound residue** **5. produced CO_2** **6. metabolites:** **6.1 ≥ 20%:** **6.2 < 20%:** **6.3 ≥ 20%:**	2. (if applicable): >80% at every time-point 3. check 1st order kinetics with Hockey-stick model 4. (if applicable):maximum and time and amount at end 5. (if applicable): maximum and time and amount at end 6. identified and quantified separately 6.1 chemical name, maximum and time, and amount at end 6.2 number of metabolites <5% 6.3 if reliable DT_{50} can be calculated, these can be used.	2. E
Pay attention	1. the dissipation type 2. the manure 3. the concentration tested. 4. the weight of the analysis samples in relation to the distribution within the manure 5. lag-phase	1. transformation or dissipation 2. the manure structure and components might influence the transformation rate. The manure structure depends a.o. onthe feed type. 3. the substance might inhibit microbial activity. Concentrations that differ a factor X [X= 5] from the calculated are considered less reliable unless it has been proven that the substance does not inhibit microbial degradation at either the expected concentration or the highest concentration tested. 4. it is possible the substance is not homogeneously distributed; corse material should be removed from analysis samples. 5. a lag-phase should be identified with at least three time-points.	

[14] Unless it has been shown that phototransformation is of no importance.

10.3 Transformation in the top soil.

DT_{50} values should be based on transformation.

Transformation means the compound is converted to smaller or larger molecules by biological, microbiological, and/or chemical action.

Degradation means the compound is converted to smaller molecules by biological, microbiological, and/or chemical action.

Dissipation means that the compound "disappears": by transformation, volatilisation, leaching, plant uptake, or run-off.

Mineralisation means the compound degrades to inorganic compounds (e.g. H_2O, CO_2).

If raw data are available, the DT_{50} values always have to be recalculated. The calculation of a reliable DT_{50} value has to meet the following conditions.

In general at least five time points including the value at t = 0 (to enable adequate regression analysis) within the first 100 days of the study (because after 100 days the biological activity of the soil may have declined substantially (Anderson, 1987)) are needed.

1. At least three time points are needed to ensure that there is a lag phase. The lag phase is not included in the calculation of the DT_{50}.

2. Only data showing mole fractions of 10% are taken into account; at lower fractions e.g. diffusion may influence the transformation rate.

3. To check whether the curve shows first-order kinetics, or consists of two successive first-order processes, the 'hockey stick' model is applied using all timepoints selected in step 1 and 2 (See Appendix III Mensink et al 1995). In the case of a 'hockey stick' curve, a period with a higher transformation rate is followed by a period with a lower transformation rate, resulting in a hinge point in the transformation curve. With the 'hockey-stick' model a calculation is performed to estimate whether this model gives a better fit compared to the single log-linear model. In case of a significant hinge point (p 0.05) within 50 - 100 days after application of the substance only the time points up to the hinge point will be used for the calculation of the DT_{50}. In case of a significant hinge point before 50 days, or in case the hinge point is after 100 days and the % residues are high (molar fraction >50%) after 100 days, both periods should be mentioned (hinge point and slopes), and expert judgement is required to establish the DT_{50}.

4. The DT_{50} value is calculated with a log-linear regression model using all selected time points, provided that first-order kinetics appear to be valid. If not, the DT_{50} is determined graphically (Linders et al., 1994). If r^2 <0.7, the regression is not valid.

The recalculated DT_{50} value is recorded in the Header. The DT_{50} value calculated by the authors is mentioned in the Results. In the Remarks is stated

DT_{50} in Header derived from data given by the author.

In the Remarks should always be stated, if the transformation followed first-order kinetics or not, and if the DT_{50} was calculated or determined graphically. In case DT_{50} values are based

on CO_2-production or dissipation, this is stated in the Header (Header field 'remarks') and in the Remarks. In case the DT_{50} was extrapolated, this should also be mentioned in the Remarks. The 90% transformation point can be used to check whether the transformation followed first-order kinetics (as a rule of thumb): DT_{90} is c. three times the DT_{50}).

In the Remarks all deviations from the instructions (in this section and in Table 2) are stated. If DT_{50} values are used in the RIVM Conclusion, in the Remarks is stated:

DT_{50} value(s) used for the RIVM Conclusion is (are).. .
Converted DT_{50} value(s) (20 C) is (are) .. .

Storage conditions of sampled soil, that is not immediately used for transformation studies, should be as follows: in the laboratory at 4±2 C for at most three months (to avoid anaerobic conditions)(also in accordance with the ISO 10381-6 Guideline); in the open or in a glasshouse under well-drained conditions (to avoid desiccation). The maximum allowable storage time can be estimated as follows:

$$T_{storage} = 90 \quad e^{-0.1(t-4)}$$

input			
storage temperature	t	[°C]	S
output			
storage time	$T_{storage}$	[d]	S

The pF of the soil can be represented as a function of the soil water content. The soil water content can be expressed as volume water per volume soil (v/v) or as weight water per weight soil (w/w).

$$Fwater_{soil} \ (v/v) = Fwater_{soil} \ (w/w) \,.\, RHOsoil$$

The application rate in the test should preferably be in the range of a factor two from the PEC. A test performed at higher concentrations might underestimate the transformation rate because of inhibition of the micro-organisms, but it is also possible that adaptation mechanisms come into play, leading to inaccurate results. Tests performed at lower concentrations might underestimate the inhibition of micro-organisms.

With respect to the moisture contents of the soils in aerobic studies the following can be remarked. At pF 2 - 3 the soils are at field capacity, and these moisture tensions are preferred. Soils with pF 4.2 are not used for the risk evaluations because the wilting point is reached. Soils should not become too wet or too dry also during pretreatment.

With respect to enrichment of the test soils the following can be remarked. For pesticide evaluation enrichment with e.g. alfalfa is not allowed. For veterinary medicinal products, that will be spread in slurry, we accept test performed in soil/slurry mixtures. The expected concentration slurry in the soil after spreading is c. 6 g/kg soil. In the event higher ratio's are used (e.g. soil:manure 1:1), one should be careful in evaluating the usefulness of the results.

The classification of the soil type, given by the authors, should be checked with the American Soil Classification System (see Appendix 2) (USDA, 1951), and this US-classification is reported in the Header. If verification is not possible, the classification given by the authors is used (if necessary a literal translation from Dutch, French or German). It should clearly be stated in the Description, which classification was used.
The sizes of soil particles are fastened down in the different classification systems. The sizes are however not identical in the different systems. Pay attention to this when classifying a soil according to the American Soil Classification system.
If it concerns soil types not representative for the Dutch situation, like paddy soil and volcanic soil, this should be clearly stated.

The pH of the soil can be measured in the water phase (pH-H_2O) of the soil, or after a solution of KCl or $CaCl_2$ was added (pH-KCl and pH-$CaCl_2$, respectively). pH-KCl and pH-$CaCl_2$ are always lower than pH-H_2O as more protons in the soil solution can be measured. It is assumed that the pH-$CaCl_2$ (0.01 N) gives the best estimate for the soil solution, and is therefore the most convenient value with respect to bioavailability for plants. It is assumed that the pH-KCl (1.0 N) gives the best estimate for the sorption of pesticides to soil particles. Record in the TOXIS Header the pH-KCl, if available. If not, record the pH-$CaCl_2$ or the pH-H_2O (in this order of preference). It should always be indicated in the Description, which pH is used.

In the Header always the substance code is given, even if it was applied as a preparation. In the Description this should then clearly be stated: e.g. Sub1 was applied as preparation X (Y % a.i.).

Useful formulas

1) % organic matter (o.m.) = 1.7 % organic carbon (o.c.)
2) 1 kg a.i./ha = 1.33 mg a.i./kg dw soil (assuming the compound is homogeneously mixed over a soil depth of 5 cm, and a dry bulk density of 1500 $kg.m^{-3}$).

Table 10.3 Soil aerobic transformation studies (top soil)

	Items	Notes	Relia-bility lower ?
Description	**1. test type** **a. laboratory/field** **b. aerobic/anaerobic** **c. sterile/non-sterile**	b. method of sterilisation should be given	1b. E
	2. test substance and position of label		
	3. vehicle		
	4. soil	4. top soil (0-20 cm) should be used	4. Y
	4.1 soil type	4.1 US-class. and other relevant data (paddy, etc.)	
	4.2 pH		
	4.3 CEC		
	4.4 % o.m.		
	4.5 storage conditions	4.5 storage before testing should be appropriate (see text)	
	5. weight of soil sample	5. weight soil sample should be X g. [X= 25]	5. E
	6. temperature		
	7. application method and rate		
	8. moisture content		
	9. light condition	9. incubation in the dark[15]	9. Y
	10. test system	10. should be closed with volatile traps	10. E
	11. incubation time	11. preferred until 90% transformation or up to 100 days	11. E
	12. sampling frequency	12. 5 time points are needed for adequate regression analysis	12. Y
	13. extraction/analysis method	13. This should be appropriate for the substance and the metabolites, and the recovery of the substance should be >X% [X= 70] and <Y% [Y= 110]	13. E
Results	**1. DT_{50} and %a.i. at the end of incubation**		
	2. total recovery	2. the recovery at every time point should be >X% [X= 80] (recovery of radiolabel or the sum of compounds)	2. E
	3. kinetic order	3. check 1st order kinetics with Hockey-stick model	
	4. bound residue	4. maximum and time, amount after 100 days, and amount at end	
	5. produced CO_2	5. maximum and time, amount after 100 days, and amount at end	
	6. metabolites:	6. identified and quantified separately	
	6.1 ≥ 5%:	6.1 chemical name, maximum and time, amount after 100 days, and amount at end	
	6.2 < 5%: number	6.2 number of metabolites <5%	
	6.3 ≥X [X=10% for pesticides; X=20% for medicines]: DT_{50}	6.3 if no reliable DT_{50} can be calculated, separate transformation studies are required.	
Pay attention	1. the dissipation type	1. this should be transformation	1. E
	2. the agricultural history soil	2. no prior use of compounds that may have lead to adapted microorganisms in the previous two years	2. E
	3. storage	3. BBA/Speyer soils before 1982 were probably stored too dry	3.2 Y

[15] Unless it has been shown that soil phototransformation is of no importance.

10.4 Adsorption studies.

In the adsorption/desorption studies the distribution constant is indicated as K_F as they are derived from the Freundlich equation:

$$S = K_F \quad C^{1/n}$$

input		
amount of chemical sorbed	S	[$mg_c.kg^{-1}$]
equilibrium concentration in water	C	[$mg_c.l^{-1}$]
Freundlich exponent	1/n	[-]
output		
Freundlich constant	K_F	[$dm^3.kg^{-1}$]

The $K_{s/l}$ is derived from the partitioning between the concentrations in the solid and liquid phase. Because the adsorption is generally not irrespective of the amount of substance present, a correction factor is introduced: the Freundlich exponent 1/n. The correction results in a 'different' $K_{s/l}$: the K_F.
The concentration dependent sorption behaviour cannot be used in standard equations. For matters of convenience, we accept the K_F as a $K_{s/l}$ for further model calculations, provided that the Freundlich exponent is within the range 0.7 - 1.1. K_F values with 1/n outside the range 0.7 - 1.1 are not selected for K_{om} calculations (Boesten and Van der Linden, 1991).

In case transformation was too high in the adsorption experiment, a reliable $K_{s/l}$ can only be calculated if besides the concentration in the liquid phase, also the amount of the substance adsorbed to the soil is determined.

The Kom value is derived from the $K_{s/l}$ value with:

$$Kom = \frac{K_{s/l}}{Fom_{soil}}$$

input		
sorption constant soil-liquid	$K_{s/l}$	[$dm^3.kg^{-1}$]
weight fraction organic matter in soil	Fom_{soil}	[-]
output		
sorption constant normalised on organic matter content	Kom	[$dm^3.kg^{-1}$]

In case the $K_{s/l}$ is not reliable because [$K_{s/l}$ * (ratio soil/water)] <0.1, the result is not used for RIVM Conclusions, unless the substance is measured in both the water fraction and the soil fraction (Boesten, 1990) or better data are not available.

Table 10.4: adsorption studies

	Items	Notes	Reliability lower?
Description	**1. test substance + position of label** **vehicle** soil[16] **soil type (USDA-class.)** **pH** **CEC and %clay** **% o.m.** **weight of soil sample** **soil/water ratio (kg/dm^3)** **temperature** **number of concentrations** **number of replicas** **shaking time** **extraction/analysis method**	3. soil must be relevant for the Dutch situation 7. min. X concentrations [X= 4] should be used 8 . t est should be performed in duplo 9 . shaking time (in hours) should be shorter than the DT_{50} (in days)[17]; no longer than 48 hours 10. recovery should be >X% [X= 70]	7 Y 8. Y 9. E 10. E
Results	**1. distribution constants** **2. Freundlich exponent** **3. the relative decrease should be ≥0.1** **4. total recovery (maximum, and time)**	1. 2. only $K_{s/l}$ with 1/n of X [X= 0.7 - 1.1] are used for the calculation of K_{om}[18] 3. $K_{s/l}$ is not accurate if $K_{s/l}$ • (soil/water ratio) <0.1][19] 4. recovery should be >X% [X= 80]	2. Y 3. Y 4. E
Payattention	1. water solubility 2. transformation 3. pK_a of the substance 4. soil handling	1. initial and equilibrium concentrations should not exceed water solubility 2. there should be no major loss due to transformation (max. 3%), unless both the amount sorbed and the decline in concentration of the substance in the liquid phase has been determined 3. if 2<pK_a<6: $K_{s/l}$ should be determined at pH 7-8 4. no manipulation, with exception of sieving (2 mm) allowed. Sterilisation is not allowed	1. Y 2. E 4. Y

[16] For some substances (e.g. those containing a phosphate moiety) the amounts of sesqui-oxides/hydroxides in soil might explain the amounts sorbed. For some pesticides (e.g. those with a positive charge) the amounts of clay might explain the amounts sorbed.

[17] This requirement has to be met if only the decline in concentration of the substance in water is analysed and not the amount sorbed to the soil: if the shaking time (in hours) is longer than the DT_{50} (in days), the concentrations in both soil and water must be measured.

[18] 1/n not within this range indicates poor accuracy or strange sorption behaviour.

[19] This requirement need not be met if the amount sorbed is also measured.

10.5 Birds.

In acute study birds may vomit due to the high dose that is applied. This results in underestimation of the toxicity. In case no mortalities are observed and the birds have vomited, the LD_{50} is assumed to be higher than the highest concentration at which no vomiting occurs. The concentrations at which vomiting is observed are not used for calculations with the Spearman-Karber model. If the birds vomit, this should be reported under Results.

In chronic tests (according to OECD 206) the exposure time is at least 20 weeks, and the following effects are studied: mortality of the adults, egg production, cracked eggs, egg shell thickness, viability, hatchability and effects on young birds.

Table 10.5: Birds acute and subacute toxicity studies

	Items	Notes	Reliability lower
Description	**1. test substance** **2. test species** **3. applied concentration(s) of toxicant (in feed or vehicle)** **4. use of vehicle** **5. type of application**	3. min. X concentrations [X= 5][20] 5. oral (by e.g. gavage), or dietary	3. E
	6. sex, weight and age of the birds ***7. feed type (LC_{50} study)*** ***8. exposure time (LC_{50} study)*** ***9. observation time*** ***10. number of animals per group*** ***11. availability of feed and water*** [21] ***12. housing conditions*** ***13. vehicle control***	8. preferably X days [X= 5] 9. LD_{50}: c. X days [X= 14] LC_{50}: after five days exposure X days of observation [X= 3] 10. min. X animals per concentration [X= 10]	8. E 9. E 10. E 11. Y
Results	**1. LC_{50} or LD_{50}, and 95% confidence limits** **2. mortality data in all groups** **3. sublethal effects (overt signs of toxicity and macroscopic effects)** **4. feed consumption** **5. body weight change** **6. measured concentrations (LC_{50} study)** **7. repellency**[22]	1. raw data should be available for recalculation 2. the mortality in the controls should not exceed X% [X= 10] at the end of a test 6. actual test concentrations should be at least 80% of nominal concentrations	1. Y 2. Y 6. E
Pay attention	1. vomiting 2. repellency 3. LC_{50} test: stability/homogeneity of the substance in the diet 4. LC_{50}: mortality at the lowest concentration	1. if vomiting occurs the actual feed intake is unknown (lowered) 2. if a substance is repellent actual feed intake is not known, and cause of death could be starvation rather than a toxic effect 3. stability/homogeneity should be maintained throughout the test 4. at the lowest concentration no toxic effects should appear	1. E 3. Y 4. E

[20] Unless the range finding test shows that LD_{50} >2000 mg/kg, or 8-day LC_{50} >5000 mg/kg feed.

[21] If applicable the following standard sentence is used: "Feed and water were provided ad libitum".

[22] If repellency is claimed, or if feed consumption decreases with increasing test concentrations, see Luttik (1993).

10.6 Aquatic organisms, acute.

There are important differences between short-term and long-term tests. Naturally, the exposure time is longer in the latter (*Daphnia*, 14-21 days; fish, depending on species, e.g. 28 days). Further, the test system has to be either semi-static or flow through, never static. Also feeding is allowed or even required, in contrast with short-term tests. The studied effects are:

Daphnia: effects on mortality, time of first production of young, number of young born, signs of intoxication;

fish: effects on the stage of embryonic development, hatching and survival, abnormal appearance, abnormal behaviour, weight, and length (darkened skin is not considered relevant).

For more detailed information, the reader is referred to OECD 202 II (*Daphnia*, reproduction), and OECD 210 (fish, Early-Life Stage).

The actual averaged concentrations have to be used (and mentioned in the Results), if possible.

The Spearman-Karber model cannot be applied on algae because the measured effect is not from a binomial distribution. Use a log-logistic model. For calculation of the NOEC see the instructions in the OECD201 Guideline.

In the Remarks it has to be reported whether the incipient $L(E)C_{50}$ was reached or not. The incipient $L(E)C_{50}$ is the $L(E)C_{50}$ value that does not decrease in time any more. If an incipient $L(E)C_{50}$ has not been reached, this indicates that the organisms tested may be more sensitive to the pesticide after a longer period of exposure.
If the $L(E)C_{50}$ values of the last two (three) time points are the same, it is assumed that the incipient value is reached. If not, all the $L(E)C_{50}$ values are put into a graph, and it is estimated whether the curve reaches a plateau; a minimum of three points is necessary to reach a conclusion, so for 48 hours tests (often with only two time points), the incipient value cannot be determined.

Dissipation of the substance
There should be no major loss due to photolysis, volatilisation, hydrolysis, adsorption to glass, etc. The test design should be adequate as to maintain >80% of the nominal concentration. In case photolysis occurs, tests with *Daphnia* and fish may be performed in the dark. In case of photolysis, volatilisation, hydrolysis, or adsorption to glass, a flow-through system might be adequate.
For tests with slightly soluble substances or rapidly hydrolysing substances some additional instructions are mentioned below.

Table 10.6: Waterorganisms, short-term toxicity tests

	Items	Notes		Reliability lower?	
Description	**1. test species**				
	2. test substance				
	3. concentrations (nominal)				
	3.1 number		3.1 X concentrations [X= 5][23];	3.1	E
	3.2 range		3.2 test concentrations should not exceed water solubility >X times [X= 10]	3.2	Y
	4. use of vehicle	4.	concentration vehicle <100 mg/l	4.	E
	5. analysis method				
	6. age (crust.+fish); length+weight (fish)	6.	*Daphnia*: maximum age 24h	6.	Y
	7. number of animals	7	*Daphnia*: min. 20/conc.: preferably 4 replicas of 5; fish: min. 7/conc.	7.	E
	8. test vessels	8.	suitable for tested compound		
	9. loading				
	9.1 algae		9.1 algae: initial cell conc.= c. 10^4/ml	9.1	E
	9.2 Daphnia		9.2 *Daphnia*: max. 1 *Daphnia* per 2 ml	9.2	E
	9.3 fish		9.3 fish: max. 1 g/l (flow-through: loading can be higher)	9.3	E
	10. control	10.	vehicle: also solvent control should be tested	10.	Y
	11. test system: static, renewal, flow through				
	12. exposure time	12.	algae: 72-96h; *Daphnia*: 24-48h; fish: 96h	12.	E
	13. test water/medium: temperature, pH, diss. O_2 (DO), hardness, salinity (seawater)	13.	good quality natural water or reconstituted water; hardness 10-250 mg $CaCO_3$/l; pH 6.0-8.5; temperature: see OECD 201-203	13.	Y
	14. feeding	14.	no feeding	14.	Y
	15. light conditions				
	15.1 algae		15.1 algae: source, continuous 120 mE/m^2s ≥8000 lx	15.1	Y
	15.2 Daphnia		15.2 *Daphnia*: optional	15.2	E
	15.3 fish		15.3 fish: 12-16 h light per day	15.3	E
	16. effects studied	16.	algae: biomass (b) or growth (r), *Daphnia*: immobility; fish: mortality and sublethal effects	16.	E
	17. sampling frequency test concentrations	17.	at least at the start and at the end of test	17.	E
Results	**1. algae NOEC and EC_{50}, Daphnia EC_{50}, fish LC_{50}; 95% confidence limits**	1.	preferably based on measured concentrations	1.	E
	2. raw data	2.	raw data should be available	2.	Y
	3. mortality/effect	3.	mortality/effect in the control should be <10% (or <1 fish if 7, 8, or 9 fish are used)	3.	Y
	4. measured concentrations	4.	measured test concentrations should be at least 80% of the nominal concentrations	4.	Y
	5. pH, DO, temperature	5.	pH and T should be constant; DO should be 60% of air saturation value.	5.	E
	6. incipient LC50	6.	incipient value should preferably be reached	6.	E
Pay attention.	1. the dissipation type	1.	there should be no major loss due to hydrolysis, photolysis, volatilisation, or adsorption to glass. Is the test design adequate?	1.	E
	2. log K_{ow}	2.	bioconcentration, adsorption to glass and particle in solution may occur for lipophilic compounds	2.	E
	3. effects at lowest and highest test concentration	3.	lowest: no toxic effect should appear; highest: algae: at least 50% inhibition; *Daphnia*: 100% immobilisation is preferred; fish: no percentage mortality is mentioned.	3.	E

[23] The minimum number of test concentrations can be smaller if the range finding test shows that $L(E)C_{50}$ will probably be >100 mg/l (no mortalities at this concentration, else a full test should be performed), or if it is very likely that no mortalities will occur below the water solubility.

Tests with slightly soluble substances[24]
In case very slightly soluble compounds (water solubility S <0.1 mg/l) are tested at concentrations up to the water solubility, and e.g. no effects are observed, the test in principle is reliable. However, the compound cannot be classified; only the 'bare' toxicity result is mentioned then (e.g. NOEC >0.05 mg/l). Toxicity values from a test in which the slightlysoluble compound was tested at nominal concentrations that are larger than 10 times the solubility, should be regarded as unreliable (RI is 3). The reader is referred to Vaal et al. (1992) for more information on the evaluation of slightly soluble substances.

Tests with rapidly hydrolysing pesticides [31]
The EC and OECD Test Guidelines have been devised for stable compounds. However, one can be confronted with an unstable pesticide.
According to the official Guidelines, the loss of test substance in an ecotoxicological test should be less than 20% to consider the compound stable enough for the purposes of toxicity testing. If this is not the case there is serious doubt if the test has been performed adequately, technically speaking. However, the high loss may be caused by fast hydrolysis of the compound; in this case the test has been performed in a technically adequate way, in other words, the high hydrolysis rate is an intrinsic property of the compound and could not not have been avoided.[25]
If the loss of test substance is higher than 20%, first it should be checked if the loss is caused by bad performance of the test (in which case the RI is lowered), or by fast hydrolysis. The latter is done by inspecting the results of the hydrolysis test, and if these are not available (or in case of doubt), by consulting the specialist.
Once it is established that hydrolysis is the (main) cause for the high loss, the second question is if the metabolite(s) should have been tested instead of the parent compound (of course it can also be concluded that testing of both parent compound and metabolite(s) is necessary). The following limits[26] are used:

DT_{50} 24 h : the test is started with the parent substance
DT_{50} <4 h : (n) tests are started with (n) metabolites
DT_{50} 4-24 h : expert judgement

In case the DT_{50} (hydrolysis) <4 h, and the toxicity test has been started with the parent compound, the result is considered as unreliable (RI is 3) because the (major) metabolite(s) should have been tested.

In all other cases (i.e. loss of test substance >20%, metabolites neither qualified nor quantified, DT_{50} (hydrolysis) 4 h), the test results are considered as less reliable (RI is 2), as it remains unclear which compound causes the observed effect(s) and at what concentration. The toxicity is expressed in terms of the nominal (initial) concentration (Whitehouse and Mallet (1993) use the term loading rate). Therefore the following standard sentences should be used in the Remarks:

> The toxicity is determined by a mixture of the parent compound and one or more transformation products because of rapid hydrolysis of the parent compound. Because these transformation products are not identified and quantified, the $L(E)C_{50}$ value in the

[24] Other difficult substances (e.g. volatile, strongly to glassware sorbing substances) are not dealt with in this Manual
[25] In some cases a different test system can avoid a high loss of the parent compound, for example applying a flow-through system instead of a (semi) static system.
[26] The limits are derived from Whitehouse and Mallet (1993). The 12 hours limit is changed to 24 hours, because of the compatibility with the water/sediment transformation test.

Header is expressed in terms of the nominal concentration. The test is considered less reliable / unreliable.

In the RIVM Conclusion (see FEF, Appendix 8):

A mixture of ...(parent compound) and unidentified and unquantified metabolite(s) is acute ...(classification) toxic for...(aquatic organism). This mixture was the result from rapid hydrolysis of the parent compound.

In the RIVM Conclusion —the subsection with the title **Aquatic organisms:**— the following should be stated (see FEF, Appendix 8):

The L(E)C_{50} values are expressed as nominal concentrations, due to rapid hydrolysis.

Long-term exposure

For instructions on summarising and evaluating long-term toxicity tests the reviewer is referred to the OECD 202, the EC Directive XI/681/86, and the OECD 210 Guidelines.

Male daphnids may indicate bad culture conditions, and influence the number of offspring as well as the statistical analysis. Check the effect of the number of males on the calculated NOEC, as the latter should be based on females.

10.7 Insects and other beneficial arthropods.

In case of laboratory tests with other insects, mites, spiders, always check with the EPPO Guidelines (142, 151, 180) or EPPO Bulletin 15, for species-specific instructions on testing and evaluating. For instructions on semi-field and field tests with bees or other insects, mites, and spiders, see EPPO Bulletin 170 or 15.

Table 10.7: Insects (bees excluded), mites and spiders, L(E)C_{50}/NOEC studies

	Items	Notes	Reliability lower?
Description	**1. test substance**		
	2. test species	2. species must be relevant for the crop; preferably laboratory-reared, uniform in age[27]	2. Y
			3. Y
	3. route of exposure	3. expose to fresh dry pesticide film; depending on behaviour of species use as exposure target: glass plates, plant leaves, or soil	
	4. test concentration(s)		
	4.1 nominal dose	4.1 recommended (field) concentrations	4.1 E
	4.2 actual dose	4.2 dose measured by weighing the target	4.2 E
	4.3 control dose	4.3 control groups with water application	4.3 Y
	5. vehicle	5. standard amount of fluid: 1-2 mg/cm^2 (glass and leaf), 6 mg/cm^2 (soil)	5. Y
	6. duration of test	6. adequate exposure period	6. E
	7. feed type		
	8. number of animals	8. number per test and per vessel depends on species; see Guideline	8. Y
	9. ventilation	9. adequate ventilation	9. Y
	10. housing conditions	10. see EPPO Guidelines	
	11. test conditions	11. see EPPO Guidelines	
Results	**1. reduction in beneficial capacity/mortality compared to controls**	1. see EPPO Guidelines (e.g. mortality, egg laying, feeding)	
	2. beneficial capacity/mortality controls		
	3. overt signs of toxicity		
Pay att.			

[27] *Pardosa* species (wolf spiders): a breeding method has not been developed yet. Spiders collected in the field are allowed for testing.

10.8 Soil micro-organisms.

A specific feature of tests with micro-organisms is that the uptake of substances is in general very quick. Therefore the effect can be apparent after half an hour up to two hours after application. Also the adaptation can be very quick.

Four types of tests can be distinguished:
1. single species test (e.g. Microtox);
2. test on the activity of enzyms (e.g. dehydrogenase, phosphatase, arylsulphatase);
3. test on soil processes (e.g. respiration, nitrification);
4. test on microbial diversity.

In Beelen et al (1996) more information is given on the usefulness of these test types.

Nitrification tests have to be performed with at least two soil types, relevant for the Dutch situation. Nitrification is a process in which several species of micro-organisms are involved. The process consists of the oxidation of ammonium to nitrite and the subsequent oxidation of nitrite to nitrate. The proces of nitrification is relatively susceptible to disturbance.
Sometimes tests have been carried out in which the effects on ammonification (organic-N to NH_4^+) or on denitrification (NO_3^- to N_2) were measured.
The Microtox test is carried out with e.g. *Photobacterium phosphoreum*, a salt water bacteria. The inhibition of light production is measured.

Storage conditions of sampled soil, that is not immediately used, are preferably as follows: in the laboratory at 4 °C for at most three months (to avoid anaerobic conditions); in the open or in a glasshouse under well-drained conditions (to avoid desiccation)

Table 10.8: Micro-organisms and enzymes in soil and manure

	Items	Notes	Reliability lower?
Description	**1. test substance** **2. vehicle** **3. applied concentrations** **4. soil**[28] 4.1 soil type (US-class.) 4.2 pH 4.3 CEC 4.4 % o.m. 5. analysis method 6. sampling frequency 7. **additives (lucerne meal, ammonia)**	3. min. X concentrations [X= 2]: the recommended dose, and ten times the recommended dose 6. min. X samples [X= 2]: after 7 or 14 days, and after 21 days 7. micro-organisms can be influenced negatively by too high concentrations of some additives (e.g. ammonium sulphate)	3. E 6. E
	8. light condition ***9. temperature*** ***10. moisture content*** ***11. vehicle control (if applicable)***	8. dark conditions are preferred 9. temperature should be X °C [X= 15 - 25] 10. pF 2 - 3	8. E 9. Y 10. Y
Results	**1. % reduction of level of enzymatic or other biochemical processes (with/without additives)** **2. time of recovery of activity**	1. relative to control	1. Y
Pay atten.	1. the agricultural history soil 2. storage	1. no manipulation with fertiliser, no (prior) use of pesticides that may have lead to adapted micro-organisms (in the previous five years). Special attention should be paid to compounds interfering with the N-cycle in the soil. 2. if there is no immediate use, storage in the lab or in the open should be appropriate (see text)	1. E 2. Y

[28] Nitrification tests should be performed with two soil types.

10.9 Earthworms

The risk assessment for earthworms is based on an acute test in soil. The soil can be a natural soil, or an artificial (laboratory composed) soil. An example of artificial soil test substrate (OECD 207): 10% sphagnum peat, 20% kaolin clay; 70% industrial sand; calcium carbonate is added to adjust the pH to 6.0 ± 0.5.

An LC_{50} value from a test with filter paper, or from an Artisol test (a medium of silica gel) is less useful for risk assessment. A description of an Artisol test is found in Reinecke (1992).

In TOXIS the scientific name of worms can only consist of two words:
Eisenia foetida andrei becomes *Eisenia andrei*;
Eisenia foetida foetida becomes *Eisenia foetida*.

Tests performed according to the ISO 11268-2 (draft) Guideline on reproduction of earthworms are not yet accepted officially for pesticide registration.

Table 10.9: Earthworms, LD_{50}/LC_{50} studies

	Items	Notes	Reliability lower?
Description	**1. test substance** **2. test species** **3. applied concentration(s)** **4. vehicle** **5. analysis method** **6. way of exposure (filter paper contact test or artificial soil test)** **7. medium:** **7.1 artificial soil** **7.2 natural soil: soil type (US-class.); pH, CEC, % o.m.** **8. duration of exposure and observation period** **8.1 artificial soil test**	3. X treatment levels (geometric series) [X= 5], unless range finding test shows that LC50 >1000 mg/kg soil 6. filter paper contact test or Artisol test are considered less relevant 7. 7.1 pH 6.0 ± 0.5 and moisture content should be c. 35% of dry weight 8. 8.1 mortality is assessed 7 and 14 days after application	3. 6. 7.1 8.1
	9. number of worms per concentration ***9.1 artificial soil test*** ***9.2 natural soil test*** ***10. age and weight*** ***10.1 age*** ***10.2 weight*** ***11. temperature*** ***12. light condition*** ***12.1 artificial soil test*** ***12.2 natural soil test*** ***13. vehicle control (if applicable)***	9. 9.1 Four replicas/treatment level and 10 worms/replicate 10. 10.1 worms should be adult (min. 2 months old with clitellum) 10.2 individual wet weight should be 300-600 mg 11. 20 ± 2°C 12. 12.1 test should be performed under continuous light: illuminated cabinet or chamber controllable to 20 ± 2°C with a light intensity of 400-800 lx	9.1 10.1 10.2 11. 12.1
Results	**1. LC_{50} or LD_{50} value, and 95% confidence limits** **2. mortality in control groups** **3. overt signs of toxicity** **4. bodyweight change**	2. the mortality in the controls should not exceed X% at the end of either test [X= 10]	2.
Pay att.	1. moisture content	1. pay attention: e.g. 35% of dry weight is not the same as 35% of WHC	

10.10 Activated sludge

Table 10.10: Influence on activated sludge (respiration)

	Items	Notes	Reliability lower?
Description	**1. test substance** **2. applied concentration(s)**	2. at least X concentrations [X= 5] should be tested; difference between concentrations should not exceed factor 3.2	2.
	3. test system (e.g. BOD-flask) **4. duration test**	4. 30 minutes or 3 hours 'contact'	4.
	5. type of microbial inoculum	5. usually activated sludge from a sewage treatment plant (STP)	
	6. source of sludge	6. e.g. a municipal or an industrial STP	
	7. temperature *8. air supply*	8. aeration should take place	8.
	9. nutrient solution *10. controls*	10. the two control respiration rates are within 15% of each other	10.
	11. reference substances	11. at least three concentrations of 3,5-dichlorophenol: the EC_{50} (3 hours) of 3,5-dichlorophenol must be in the range 5 - 30 mg/l	11.
Results.	**1. EC_{50} and 95% confidence limits**		
Pay attent.	1. water solubility	1. test concentrations should not exceed water solubility	1.
	2. the dissipation type	2. there should be no major loss due to hydrolysis, photolysis, or volatilisation: is the test design adequate?	2.

10.11 Bioconcentration in waterorganisms

For compounds with a water solubility >1000 mg/l, or a $\log K_{ow}$ <4.3, it may be sufficient to calculate the BCF from the $\log K_{ow}$.
The BCF should be based on fat weight (BCF_{fw}) (for organics with the exception of organo-metals), or on total wet weight (BCF_{wo}) (for e.g. dissociating compounds).
Studies based on OECD 305 A - E Guidelines should be checked with these Guidelines for evaluation. These Guidelines differ from each other with respect to the test system and the mathematical interpretation of the results.
The OECD Guidelines 305 B-E use the model mentioned below. Guideline 305 A uses a different model, therefore the equations mentioned below cannot be used for 305 A. The Guidelines 305 B-D consider only the calculation of the bioconcentration factor. When in these tests no steady state is reached, no bioconcentration factor can be determined, which means that the result is quite useless for conclusions. This does not apply for the 305 E Guideline, because the rate constants that are determined in this test give insight in the behaviour of the chemical in the environment.

The OECD 305 B - E Guidelines are based on the next model. The mass balance in the system consisting of water, organism (fish, or other) and test compound is:

$dC_f / dt = k_1 * C_w - k_2 * C_f$ [equation 1]

in which C_f is the concentration of test compound in the organism [mg/kg], C_w is the concentration in water [mg/l], t is time [d], k_1 is the uptake rate constant [$l.kg^{-1}.d^{-1}$], and k_2 is the elimination rate constant [d^{-1}]. The elimination rate constant k_2 describes every elimination process of the test compound from the organism, hence it includes physico-chemical elimination and biotransformation.

Integration of equation 1 is only possible when C_w is constant. When C_w declines it must be checked if the authors included this in their calculations of the rate constants. If not, the rate constants can be recalculated using BIOFIT (Gobas & Zhang, 1992). BIOFIT can also be used if the C_w is constant.

Assuming C_w is constant, the next calculations should be performed. Consider equation 1 during the phase of initial uptake, C_f will be then negligible:

$dC_f/dt = k_1 * C_w$, or $C_f = k_1 * C_w * t$

However, it is difficult to determine when C_f ceases to be negligible, so it is hard to use this formula in a good way. Another way to determine the uptake rate constant is described in OECD 305 E. For this method the k_2 is nessecary.

Consider then equation 1 during period of elimination instead of uptake, C_w is then negligible:

$dC_f/dt = -k_2 * C_f$ or $C_f = e^{(-k2 * t)}$

Table 10.11: Bioconcentration in waterorganisms, studies with organisms

	Items	Notes	Reliability lower?
Description	**1. test substance**		
	2. test species		
	3. applied concentration(s)	3.1 min. X concentrations [X= 2]	3.1 Y
		3.2 highest concentration <(0.1 ´ LC_{50}); lowest concentration >(10 ´ detection limit)	3.2 E
	4. vehicle	4. should not exceed 0.1 ml/l	4. E
	5. analysis method		
	6. test system		
	7. exposure time and depuration time	7. uptake phase: 3 hours - 30 days; depuration phase: 6 hours - 60 days, or 3 ´ DT_{50}	7. E
	8 age, length, weight of the organisms		
	9. number of animals per group		
	10. loading		
	11. (solvent) control		
	12. type of water (pH, DO, etc.)	12. DO should not vary more than ± 3 mg/l	12. E
	13. temperature	13. should not vary more than ± 1°C	13. E
	14. feeding		
	15. light condition		
	16. sampling frequency		
	16.1 samples of test water		
	16.2 samples of organisms	16.2 uptake phase: min. X [X= 4]; depuration phase: min. X [X= 5]	16.2 E
Results	**1. BCF**	1.1 preferably based on whole body wet weight or lipid content	1.1 E
		1.2 based on a.i., not on r.a.; give C_{water} and C_{fish}	1.2 Y
	2. steady state	2. steady state reached: yes/no, time point	2. E
	3. rate constants	3. k_1 (uptake) and k_2 (depuration); duration of phases should be sufficient	3. E
	4. k_2 and steady state	4. the time to reach 50% of the equilibrium concentration (steady state C_f) should equal the half-life for depuration[29]	4. E
	5. measured concentrations in water	5. should be (in water) at least 80% of the nominal concentrations	5. E
	6. signs of toxicity	6. no toxic effects should occur	6. Y
Pay attn.	1. test concentrations	1. test concentrations should not exceed water solubility, and should be <1 mg/l	1. E
	2. loss of test substance	2. there should be no major loss due to hydrolysis, photolysis, biotransformation in water, volatilisation, and adsorption to vessel or particles: is the test design adequate?	2. E

[29] A difference of a factor X [X= 2] is acceptable.

When $\ln C_f$ is plotted against time, the slope of the straight line is k_2; k_2 can then be used to determine k_1. Integration of equation 1 gives:

$C_f = k_1/k_2 * C_w * [1 - e^{(-k2 * t)}]$

k_1 is then calculated as (t means time point at which the C_w and C_f are determined):

$k_1 = C_f * k_2 / C_w * [1 - e^{(-k2 * t)}]$

Finally, for the bioconcentration factor, consider equation 1 at equilibrium:

$k_1 * C_w = k_2 * C_f$

From this equation it is clear that the bioconcentration factor (K_c or BCF (l/kg)) is defined by:

$BCF = k_1 / k_2 = C_f / C_w$

The first part of this equation ($BCF = k_1 / k_2$) can be used to determine the BCF also when no equilibrium in the test has been reached. The second part ($BCF = C_f / C_w$) can never be used to calculate BCF when equilibrium has not been reached.

The k_2 or half-life (DT_{50}) determines when equilibrium will be reached. The time required to reach 50% of equilibrium concentration in the organism equals the half-life in the depuration part of the experiment. Whether the time to reach 50% equilibrium and the halflife are comparable or not, should be checked in the original uptake curve. If this is not the case, the RI of the test is lowered.

Equation 1 considers first-order, one-fish compartment kinetics. However, more-fish compartments are possible. When more compartments are present, more rate constants are needed to describe the kinetic behaviour of the compound.

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APPENDIX I GLOSSARY.

Definitions on risk assessment.

Hazard	the inherent potential of a substance to cause adverse effects.
Risk	the probability of a substance to cause adverse effects.
Hazard identification	the identification of the adverse effects which a substance has an inherent capacity to cause.
Dose-response assessment	the estimation of the relationship between a dose or concentration and the incidence and severity of an effect.
Assessment of environmental aspects	determination of the physical-chemical properties and properties of (bio)transformation and sorption.
Effect assessment	concerns the hazard identification and dose-reponse assessment.
Exposure assessment	the determinations of the emissions, pathways and rates of movement of a substance and its transformation or degradation products in order to estimate the concentrations/doses to which ecological systems and populations are or may be exposed.
Hazard assessment	the process designed to estimate the incidence and severity of the adverse effects likely to occur in an environmental compartment due to actual or predicted exposure.
Risk estimation	the quantitative estimation of probabilities of clearly described effects by including uncertainty analysis. The risk assessment is complete when the hazard assessment includes risk estimation.

Terminology and abbreviations.

acute toxicity test	toxicity test serving to study the effects occurring in a short time following the administration of a single dose or multiple doses given within this short time period.
Additional Questions	a list with the questions that should be answered by a company that claims admission of a medicine on the Dutch market. This list reflects the uncompleteness of the data supplied by a company.
adsorption	enrichment of one or more components in an interfacial layer.

advection	intercompartmental transfer of a chemical by a carrier that physically flows from one compartment to the other; examples are atmospheric deposition, sedimentation, and resuspension.
adverse effect	change in morphology, physiology, growth, development or lifespan of an organism
Advisory Report	a report on a substance that consists of the Summaries of the supplied tests and the RIVM Conclusion with the concluding remarks on the physico-chemical properties, the fate in the environment, the effects, and the hazards.
AR	see Advisory Report.
AQ	see Additional Question(s).
BCF	BioConcentration Factor: the ratio of the test substance concentration in (part of) an organism (e.g. fish, plant) to the concentration in a medium (e.g. water, soil) at steady state.
bioaccumulation	the net result of the uptake, distribution, and elimination of a substance due to all routes of exposure.
bioconcentration	the net result of the uptake, distribution and elimination of a substance due to water-borne exposure.
biodegradation	see degradation.
biotransformation	see transformation.
BOD	Biological Oxygen Demand.
bound residue	residu that cannot be extracted from soil or sediment after several subsequent extractions, applying methods that do not alter the chemical structure of these residues substantially.
BRD	Agency for the Registration of Veterinary Medicinal Products
CEC	Cation Exchange Capacity.
Chemical Identity	menu in TOXIS to registrate identifying data of a substance (e.g. CAS number).
Chemobiokinetics	menu in TOXIS to registrate the metabolism routes of a substance.
chronic toxicity test	toxicity test in which organisms are observed during the whole life-span and in which exposure to a substance takes place over the whole observation time or a substantial part thereof.

CTB	College voor de Toelating van Bestrijdingsmiddelen (Dutch), Board for the Authorisation of Pesticides (English).
degradation	conversion of a molecule to smaller molecules by (micro)biological or chemical action.
degradation rate	the rate at which a pesticide can be degraded. This is often expressed as a DT_{50}.
degradation route	route along which a substance is degraded to metabolites.
Description	unstructured part of a Summary consisting of the Methodology, the Results, and the Remarks (see Summary, Results, and Remarks). A Description and a Header form a Summary. One Description per test.
DLV	Agricultural Information Service, Houten.
dirty water	Washings from stables, generally containing <3% dry matter, and made up of water contamintaed by manure, urine, crop seepage, milk, other dairy products and cleaning materials.
dissipation	disappearance of the parent compound from a compartment (such as soil or water) in which various processes such as conversion, evaporation, leaching, etc. can play a role.
DO	Dissolved Oxygen.
DOC	Dissolved Organic Carbon
dose-response assessment	the estimation of the relationship between dose or concentration and the incidence and severity of an effect.
DT_{50}	time in which 50% of the parent compound has disappeared from soil or water by transformation or degradation (under standard conditions). See degradation and transformation.
$DT_{50,sys}$	DT_{50} in the whole system (water + sediment). This DT_{50} pertains to a biodegradation test in water with the accompanying sediment.
$DT_{50,wat}$	DT_{50} in the water column. This DT_{50} pertains to a biodegradation test in water with the accompanying sediment. This DT_{50} is often considered as relevant for the actual exposure of algae, waterfleas and fish (rather than the $DT_{50,sys.}$
dung	feces from grazing animals.
EC_{50}	median Effective Concentration: 1. the concentration resulting in a 50% change in a parameter (e.g. algal growth) relative to the control 2. the concentration at which a particular effect (e.g. daphnia immobilization) is observed in 50% of the organism population relative to the control.

ECO	Laboratorium voor Ecotoxicologie (Dutch), Laboratory of Ecotoxicology (English).
effect	the extent of biological changes.
FC	field capacity.
field capacity	the moisture content of the soil at pF= 2 - 3.
Fixed Field	see Header.
formulation	synonym for preparation.
Formulations	menu in TOXIS to registrate preparations.
Free Text	unstructured part of a Summary to be stored in TOXIS in which any kind of information can be included.
GLP	Good Laboratory Practice: a set of rules describing how a laboratory should work, how it should be organised and how it can produce valid data; GLP principles are described by e.g. OECD.
Guideline	an official Guideline (i.e. authorized by national or international institutions, e.g. EPA, NEN, BBA, OECD) for the protocol and the report of a test.
H	see Henry's Law Constant.
hardness (of water)	property of water indicating the total amount of calcium, magnesium and barium.
Header	structured part of a Summary to be stored in TOXIS. A Header contains the most relevant items of a test and forms in this way the "head" of a summarised test. The Header contains Fixed Fields (i.e. specifically meant for including a particular item, e.g. one for the pH and one for the DT_{50} in a soil degradation test).
Henry's law constant	air-water partition coefficient; the ratio between the partial pressure in the gas phase of a compound and its concentration of a substance in water. Henry's law constant can be with (Pa m^3 mol^{-1}, synonym is H') or without dimension (synonym is H)
hydrolysis	a chemical reaction of a substance with water in which a part of the molecule of the reacting substance is replaced by an OH group.
IC_{50}	median Inhibitory Concentration: the concentration resulting in a 50% inhibition of growth relative to the control.

index	value used as a measure for e.g. reliability (see Reliability Index). The plural, for reasons of convenience, is indicators.
indicator	plural of index (see index).
ID-DLO	Institute for Animal Science and Health of the Agricultural Research Department at Lelystad.
Instructions	the instructions comprise both the official Guidelines on testing and reporting and the CSR-directives on summarising and evaluating test reports. Instructions refer to all guidance giving statements in this report: standards, cut-off values, useful formulas, standard sentences, selection criteria, etc; they point out what items should be included in the summary and how to handle the abundant information.
IUPAC	International Union of Pure and Applied Chemistry.
K_{aw}	air-water partition coefficient. See Henry's law constant.
K_F	Freundlich coefficient: a soil-water partition coefficient —or sorption coefficient— *dependent* on the ratio 1/n (n is an empirical entity which describes the non-linearity of an adsorption isotherm).
K_{om}	sorption coefficient normalised to the fraction of organic matter in soil.
K_{ow}	octanol-water partition coefficient.
$K_{s/l}$	a soil-water partition coefficient —or sorption coefficient— *independent* on the ratio 1/n (n is an empirical entity which describes the non-linearity of an adsorption isotherm).
LAC	Laboratorium voor Anorganische Chemie (Dutch), Laboratory of Inorganic Analytical Chemistry (English).
LBG	Laboratorium voor Bodem en Grondwater Onderzoek (Dutch), Laboratory for Soil and Groundwater Research (English).
leachate	water leached out from a soil (column).
leaching	transfer of a chemical from the top layer of soil to the subsoil (and subsequently to the groundwater).
LC_{50}	median Lethal Concentration: a statistically derived concentration that can be expected to cause death in 50% of animals exposed for a specified time.
LD_{50}	median Lethal Dose: statistically derived single dose that can be expected to cause death in 50% of dosed animals.

LNV	Ministerie van Landbouw, Natuurbeheer en Visserij (Dutch), Ministry of Agriculture, Nature Management and Fisheries.
LOC	Laboratorium voor Organische Chemie (Dutch), Laboratory of Organic Analytical Chemistry (English).
long term	duration of exposure 96 hours (aquatic organisms); duration of exposure 5 days feeding (birds).
manure	mixture of feces and urine produced by housed animals. When mixed with dirty water, the mixture is denoted by slurry.
metabolite	substance formed from the parent compound by transformation, synonym for transformation product.
maximum water holding capacity	the moisture content at pF = 0 (saturation).
mineralisation	degradation of a substance into inorganic end products; it is usually estimated in terms of CO_2 production.
MWHC	see maximum water holding capacity.
NOEC	No-Observed-Effect-Concentration: the highest concentration without adverse effects.
o.c.	organic carbon.
o.m.	organic matter.
partition coefficient	ratio of the distribution of a substance between two phases when the heterogeneous system (of two phases) is in equilibrium; the ratio of concentrations (or, strictly speaking, activities) of the same molecular species in the two phases is constant at constant temperature.
PEC	Predicted Environmental Concentration; the expected concentration in an environmental compartment.
persistence	residence time of a substance in a compartment; the disappearance rate being dependent on one or more dissipation processes.
PESTLA	PESTicides Leaching and Accumulation model: calculates concentrations in soil and groundwater.
photochemical transformation	the breakdown of a compound as a result of irradiation by light.
photolysis	see photochemical transformation.
phototrans-	the reaction of a compound with (hydroxyl, ozone, nitrate) radicals

formation	produced by the action of light.
PIEC	Predicted Initial Environmental Concentration.
pK_a	-log K_a. K_a is the dissociation constant of an acid or base at equilibrium, in other words, the pH at which 50% of the molecules of is dissociated—an acid—or protonated—a base.
PP	Research Station for Poultry Husbandry, Beekbergen.
PR	Research Station for Cattle, Sheep, and Horse Husbandry, te Lelystad.
PV	Research Station for Pig Husbandry, Rosmalen.
preparation	form and composition in which a medicine is; beside the active ingredient the preparation contains ingredients which make it more manageable, or improve its application potential, efficacy or safety.
quality	the degree of excellence of a test as determined by both its reliability and usefulness (see reliability and usefulness).
Quality Assurance	internal laboratory control system to ascertain that tests are in compliance with GLP principles.
reliability	the intrinsic reliability of a test with respect to methodology and description.
Reliability Index	value —1,2,3,or 4— indicating the reliability of a test.
Reliability Indicators	plural of Reliability Index.
Remark(s)	unstructured part of a Summary to enter critical statements on e.g. the reliability of a test, and on the usefulness of the test for the hazard assessment.
Result(s)	unstructured part of a Summary to enter the results of a test and the comments of the reviewer.
Rf	retardation factor: the distance moved by a substance relative to the distance moved by the water front.
RI	see Reliability Index.
RIVM Conclusion	the RIVM Conclusion contains the concluding remarks on classification of the physico-chemical data, the environmental fate data, and the (eco)toxicological data (i.e. the effect and the exposure assessment) and on the hazard assessment. Together with the Summaries, the RIVM Conclusion forms an Advisory Report

RIZA	Rijksinstituut voor Integraal Zoetwaterbeheer en Afvalwaterbehandeling (Dutch), Institute for Inland Water Management and Waste Water Treatment (English).
short-term	duration of exposure 96 hours (aquatic organisms); duration of exposure 5 days feeding (birds).
SLOOT.BOX	a model which calculates the concentration in a fictitious ditch.
slurry	the mixture of manure and dirty water in the feedlot basin used for spreading on land.
SOL	water solubility.
STP	Sewage Treatment Plant (synonym for WWTP).
Substances	mmenu in TOXIS to registrate substances.
Summary	a Summary is a concise text, consisting of a Header and a Description (see Header and Description) including the most relevant aspects of a test.
summary table	a table in this report with a concise overview of the items in a particular test that can influence the reliability.
TAG	see Toxicology Advisory Group
TLC	Soil Thin or Thick Layer Chromatography.
TOC	Total Organic Carbon.
Toxicology Advisory Group	a panel of specialists from both ACT and other laboratories of RIVM. Each Advisory Report has to be accorded by such a panel (synonym for beoordelingsgroep, Dutch).
transformation	conversion of a molecule to larger or smaller molecules by (micro)biological or chemical action.
transformation rate	the rate at which a pesticide can be transformed. This is often expressed as a DT_{50}.
transformation route	route along which a substance is transformed to metabolites.
Uniform Principles	EU guidance on the evaluation of plant protection products.
usefulness	the extent to which a test is appropriate for a particular purpose (e.g. standard setting procedures, hazard or risk assessment) Synonyms: relevance, bruikbaarheid (Dutch).

USES	Uniform System for the Evaluation of Substances, a decision-support system, including models for calculation of exposure and hazard in environmental compartments.
VP	vapour pressure.
water holding capacity	the moisture content at field capacity (pF = 2 - 3).
wo	whole organism.
WWTP	Waste Water Treatment Plant (synonym for STP).

APPENDIX II DUNG PRODUCTION.

II.1 Dung production in relation to animals and habitat.

Many medicine residues will be excreted with the urine and faeces. These two excreta are therefore important emission routes. The excreta consist of faeces and urine. In the field these two components are dispersed separately, whereas in the stable they are mixed.

The excreta obtained indoors, referred to as manure, are collected and stored for some time. Slurry is the mixture of manure and materials from the housing of animals (e.g. spilled feed, straw, litter, sand, water, down).

The faeces of grazing animals in the field is referred to as dung. As the dung is not collected and stored over time, for the hazard assessment the peak concentrations and the drug excretion pattern in time are important. We need to know how much faeces and urine the grazing animals produce and how many times they defaecate. The figures used for the mass balance of dry matter and water are drawn up in association with Mr. van Vuren of ID-DLO Lelystad and Dr. G. Bruin of PR Lelystad (see II.2.3). They are based on indicative values for a 600 kg dairy cow. For a Phase II Tier B assessment more detailed information should be gathered.

Faeces production is related to feed intake. Grazing animals feed on grass, that contains 80-85% water (Jongbloed et al. 1994b). When grazing they ingest 0.4-14% of the daily DM intake as soil (McDowell, 1985). We assume the soil intake amounts to 2.5% of the daily dry feed intake (USES 1.0). This soil contains c. 33% w/w water. About 75% of the ingested feed is digested for growth, metabolism and milk production. The milk contains c. 12.5% dry matter. The big animals lose c. 10 kg water/day from transpiration and breathing. Depending on the mineral intake (Na, K, Mg) dairy cow produce 20-60 litre urine a day. The density of cow dung is c. 1.04 kg/l; of horses 0.9 kg/l (KWIN 1996).

In some investigations in the period 1945-1966 (Marsh, 1970) cows were observed to defaecate 10.5 times a day. The fresh cow dung contains up to 89% water. The dry matter consists of 10-20% dead and living bacteria, 20-40% ashes, and mostly undigested plant material. Beef cattle was reported to void c. 1-3 kg organic matter (o.m.) per day, and dairy cows 2.8-3.5 kg o.m. per day: mean 3.22 kg o.m. (sd. 0.3, n=5). With 20% ash on dry weight this means 4 kg dry matter. Marsh assumes that the faeces contain 14% dry matter: the production corresponds with 28.6 (sd. 2.7) kg faeces per day for dairy cows. Four data points are obtained from grazed dairy cows, and one from housed dairy cows. Housed dairy cows produced 3.5 kg o.m.; 31 kg faeces. The bodyweight of these cattle was however not reported.

In an investigation into the nutritional limitations of free-ranging cattle, Wallis de Vries (1996) measured the Daily Feed Intake (DFI) of the steers. In April on the riverine grassland the cattle (319 kg) had a high DFI of 40 g dw/kg bw: 12.76 kg dw per day. After six months, in November the cows weighed 528 kg and the DFI was 20 g dw/kg bw: 10.56 kg dw per cow per day. Apparently grazing cattle eat more in spring than in autumn, the difference can be as much as 170%. Season, habitat, and body weight influence the amount of dry matter eaten.

II.2 Partitioning of dung.

II.2.1 Dung dry matter.

Table 49 Default settings for the calculations on dung dry matter.

parameter	symbol	unit	value
density of solids	RHOsolid	[kg.m^{-3}]	2500
density of o.m.	RHOom	[kg.m^{-3}]	1400
weight fraction solids (not o.m.) in dung solids	$Fsolid_{dung}$	[kg.kg^{-1}]	0.25
weight fraction organic matter in dung solids	Fom_{dung}	[kg.kg^{-1}]	0.75

Model calculation

$$RHOsolid_{dung} = Fsolid_{dung} \,.\, RHOsolid + Fom_{dung} \,.\, RHOom$$

$$Foc_{dung} = 0.59 \,.\, Fom_{dung}$$

input			
RHOsolid	density of solids in soil	[kg.m^{-3}]	D
RHOom	density of organic matter	[kg.m^{-3}]	D
$Fsolid_{dung}$	weight fraction solids (not o.m.) in dry dung	[kg.kg^{-1}]	D
Fom_{dung}	weight fraction organic matter in dry dung	[kg.kg^{-1}]	D
output			
Foc_{dung}	weight fraction of organic carbon in dry dung	[kg.kg^{-1}]	O
$RHOsolid_{dung}$	density of dung solids	[kg_{dwt}.m^{-3}]	O

For calculations of partitioning of organic substances between organic matter and water in dung a value of 18% organic carbon is used, because at high organic matter levels (>30%) the relationship between sorption and Foc is different from the one at lower level (2-30% o.m.). This approach is a standard operating procedure in the Centre for Substances and Risk Assessment of the RIVM, Bilthoven (Kalf et al, 1995).

II.2.2 Partitioning in fresh dung.

Table 50 Pick-list for the partitioning of dung.

animal	**$Fair_{dung}$ [$m^3.m^{-3}$]**	**$Fsolid_{dung}$ [$m^3.m^{-3}$]**	**$Fwater_{dung}$ [$m^3.m^{-3}$]**
dairy cow	0.025	0.075	0.90
beef cattle	0.03	0.09	0.88
horse	0.21	0.17	0.62
sheep	0.07	0.26	0.67

input			
-	livestock main category	[-]	P
output			
$Fcomp_{dung}$	volume fractions in dung	[$m^3.m^{-3}$]	O

Table 51 Default settings for the partitioning of dung.

parameter	**symbol**	**unit**	**value**
density of dung solids	$RHOsolid_{dung}$	[$kg_{dwt}.m^{-3}$]	1675
density of water	RHOwater	[$kg.m^{-3}$]	1000
density of air	RHOair	[$kg.m^{-3}$]	1.3

Model calculation

$$RHO_{dung} = Fair_{dung} \,.\, RHO_{air} + Fwater_{dung} \,.\, RHO_{water} + Fsolid_{dung} \,.\, RHOsolid_{dung}$$

input			
RHOair	density of air	[$kg.m^{-3}$]	D
RHOwater	density of water	[$kg.m^{-3}$]	D
$RHOsolid_{dung}$	density of dung solids	[$kg_{dwt}.m^{-3}$]	O
$Fair_{dung}$	fraction air in dung	[$m^3.m^{-3}$]	O
$Fwater_{dung}$	fraction water in dung	[$m^3.m^{-3}$]	O
$Fsolid_{dung}$	fraction solids in dung	[$m^3.m^{-3}$]	O
output			
RHOdung	density of fresh dung	[$kg_{wwt}.m^{-3}$]	O

II.2.3 Calculation of dung production.

The values in the mass balance are derived from Berende (1998a+b). The data for the dairy cow are based on cows with a milk production of 40 kg milk/day, for cattle on data of 28 cattle with body weight of 212-479 kg. The data on sheep are averages based on two-and-a-half year old and four year old ewes, year-round. The body weight and dung production of the lambs is chosen at 32 calender weeks (end of May) as the average for ewes and rams, single and twins (Berende, 1998a).
For the calculations of the amounts of dung produced in the meadow we suggest to use the figures in table 54. As there were no data available for horses these were manufactured using the data for beef cattle (as this animal is not lactating; the average dung production (dwt) per kg bw is 0.005 kg/kg).

Table 52. Dietary mass balance for grazing livestock.

	intake in [kg dwt]		metabolism and excretion in [kg dwt]	
body weight [kg]	feed	soil	metabolism	excreted
600 dairy cow	25	0.625	19.3	6.29
330 beef cattle	5.6	0.14	4.04	1.65
82 sheep	1.413	0.035	1.04	0.41

The different animal grazing categories (cattle, sheep, horses) produce different dung, which has consequences for partitioning calculations in dung. Weight fractions are derived from Berende (1998a+b) for cattle and sheep and from KWIN (1996) for horses.

Table 53. Pick list for calculation of the wet weight and wet volume of dung.

animal	**dry weight production dung $Pdung_{dwt}$ [$kg_{dwt}.d^{-1}$]**	**weight fraction water in dung $Fwater_{dung}$ [$kg.kg^{-1}$]**	**weight fraction solids in dung $Fdwt_{dung}$ [$kg.kg^{-1}$]**	**density of fresh dung RHOdung [$kg_{wwt}.m^{-3}$]**
cattle 600 kg	6.29	0.88	0.12	1030
cattle 330 kg	1.65	0.85	0.15	1030
horse 600 kg	3.00	0.69	0.31	900
pony 250 kg	1.25	0.69	0.31	900
sheep 82 kg	0.41	0.6	0.4	1090

model calculation

$$Pdung = \frac{Pdung_{dwt}}{Fdwt_{dung}}$$

input			
$Pdung_{dwt}$	livestock dung production dry matter	[$kg_{dwt}.d^{-1}$]	O
$Fdwt_{dung}$	weight fraction dry matter in dung	[$kg.kg^{-1}$]	P
output			
Pdung	fresh dung production	[$kg_{wwt}.d^{-1}$]	O

Table 54. Pick list dung production in the meadow.

animal	body weight m_{animal} [$kg_{bw}.animal^{-1}$]	production dung P_{dung} [$kg_{wwt}.d^{-1}$]
dairy cows	600	52
beef cattle	330	11
horses	600	9.7
ponies	250	4.0
sheep	82	1.025

Table 55. Pick list excretion events and stocking densities.

animal	body weight [$kg_{bw}.animal^{-1}$]	number of excretion events [d^{-1}]	stocking density [$animals.ha^{-1}$]
dairy cows	600	10.5	3.5[30]
beef cattle	330	10.5	9.5
horses	600	10.5	3
ponies	250	10.5	5
sheep	82	10.5	15

[30] The range 1.5-3.5 cows/ha applies to 81.5% of all cattle. The density 2-2.5 is the median value and applies to 30% of all animals (CBS 1996).

APPENDIX III USEFUL FORMULAS, UNITS, AND MISCELLANEOUS INFORMATION.

Units

All quantities should be expressed in units of the S.I. system (Système International d'Unités). Some exceptions are the dosage in [kg/ha] instead of [g/m^2], and the matric suction (or moisture tension) of the soil (pF) in [log(cm)] instead of [Pa].

Table 56. Recalculation of English/American units.

Length	Volume
1 inch = 2.54 cm 1 foot= 12 inches = 30.48 cm 1 yard = 3 feet = 0.9144 m 1 mile = 1.60934 km	1 cubic inch = 16.3871 cm^3 1 cubic foot = 28.3168 dm^3 1 cubic yard = 0.76455 m^3 1 pint = 1/8 engl. gallon = 0.568261 dm^3 1 quart = 1/4 engl. gallon = 1.13652 dm^3 1 engl. gallon = 4.54609 dm^3 1 amer. gallon = 3.785 dm^3 1 fluid pint = 1/8 amer. gallon 1 fluid quart = 1/4 amer. gallon
Area	**Weight**
1 sq. inch = 6.4516 cm^2 1 sq. foot = 9.290304 dm^2 1 sq. yard = 0.8361 m^2 1 sq. mile = 2.59 km^2 1 acre = 4047 m^2	1 grain = 64.7989 mg 1 ounce (oz) = 28.35 g 1 pound (lb) = 0.453592 kg

Soil

CEC: 1 meq/100 g = 10 mmol/kg.

The pF is expressed in [log $cm_{water\ column}$]. Alternative units are [bar] and [Pa]. When reading the pF scale in [bar] be aware that the bar scale is logarithmic.

Table 57. Recalculation of moisture tension units.

pF	**cmH_2O**	**bar**	**kPa**
1	10	0.01	1
2	100	0.1	10
3	1000	1	100
4	10000	10	1000

Pressure
The vapour pressure is calculated with:

$$\log P = \frac{0.05233 \,.\, a}{TEMP} + b$$

input		
TEMP	temperature in Kelvin	[K]
a	constant	[-]
b	constant	[-]
output		
P	vapour pressure at temperature TEMP	[mmHg]

The constants a and b can be calculated if the vapour pressure is known for two or more temperatures. In table 58 the relation between pressure units is presented. For example: 133.3 mmHg are equivalent to 1 Pa.

Table 58. Recalculation from pressure units (rows to columns).

	Pa	mmHg	atm	bar	Torr	psi
Pa	1	0.0075	9.9e-6	1-e5	0.0075	1.46e-4
mmHg	133.3	1			1	
atm[31]	101300		1	1		
bar	100000		1	1		
Torr	133.3	1			1	
psi[32]	6860					1

example: 1 mmHg equals 133.3 Pa.

Temperature
Conversion of degrees Fahrenheit to Celcius.

$$t[\ C] = \frac{t[\ F] - 32}{1.8}$$

input			
t [°F]	temperature in degrees Fahrenheit	[°F]	S
output			
t [°C]	temperature in degrees Celcius	[°C]	O

[31] One [atm] is 98100 [Pa] technical and 101300 [Pa] physical, according to OECD104.
[32] psi = pounds per square inch.

Water hardness

Table 59. Recalculation from water hardness units.

1° hardness	**[mg.l^{-1}] as $CaCO_3$**	**[mg.l^{-1}] as CaO**	**grain per gallon as $CaCO_3$**
German (dH)	17	10	
French	10		
American	1		
English	10		1

Water oxygen saturation

Table 60. O_2 saturation in water.

temperature C	Solubility of oxygen in mg/l (100% saturation at 1 atm)				
	fresh water	seawater 5 g Cl/l	seawater 10 g Cl/l	seawater 15 g Cl/l	seawater 20 g Cl/l
10	11.3	10.7	10.1	9.6	9.0
11	11.1	10.5	9.9	9.4	8.8
12	10.8	10.3	9.7	9.2	8.6
13	10.6	10.1	9.5	9.0	8.5
14	10.4	9.9	9.3	8.8	8.3
15	10.2	9.7	9.1	8.6	8.1
16	10.0	9.5	9.0	8.5	8.0
17	9.7	9.3	8.8	8.3	7.8
18	9.5	9.1	8.6	8.2	7.7
19	9.4	8.9	8.5	8.0	7.6
20	9.2	8.7	8.3	7.9	7.4
21	9.0	8.6	8.1	7.7	7.3
22	8.8	8.4	8.0	7.6	7.1
23	8.7	8.3	7.9	7.4	7.0
24	8.5	8.1	7.7	7.3	6.9
25	8.4	8.0	7.6	7.2	6.7
26	8.2	7.8	7.4	7.0	6.6
27	8.1	7.7	7.3	6.9	6.5
28	7.9	7.5	7.1	6.8	6.4
29	7.8	7.4	7.0	6.6	6.3
30	7.6	7.3	6.9	6.5	6.1

Light intensity

One footcandle [ft-c] equals 0.0929 lux.

Temperature correction for reaction rates.
Transformation half-lives are recalculated with the Arrhenius-equation:

$$DT50 = DT50_{test} \quad e^{(0.08(t_{test} - t_{comp}))}$$

input			
default temperature of compartment	t_{comp}	[°C]	D
temperature under test conditions	t_{test}	[°C]	S
half-life time for transformation (first order kinetics) under test conditions	$DT50_{test}$	[d]	S
output			
half-life time for transformation under default conditions	DT50	[d]	O

Rounding off
Results have to be rounded off correctly; only after the last calculation the result is rounded off. Numbers of 9999 are written as two-digit figures (= 1 - 9), and numbers >10000 as three-digit figures. Examples: 0.0347 becomes 0.035; 1.645E-8 becomes 1.6E-8; 288 becomes 290; 11253 becomes 11300.

Statistics
The standard deviation of an arithmetic mean must be based on the standard deviation of the sample (σ_{n-1}). Lotus123 calculates a standard deviation of the population (σ_n). To recalculate σ_n to σ_{n-1} use:

$$\sigma_{n-1} = \sigma_n \quad \frac{\sqrt{n}}{\sqrt{n-1}}$$

Linear regression analysis needs to be performed with at least five data points. The next requirement for validity is: r^2 0.7. When r^2 <0.7, the result is less reliable.

Mean and median.
Reliable and useful data on transformation and sorption in an environmental compartment are averaged to give one mean value and a range based on the standard deviation. The minimum value is the mean minus the standard deviation, the maximum is the mean plus the standard deviation. The range cannot exceed the experimentally determined range. In case of > or < values, a median value and a range, based on the lowest and highest value, are determined.

Table 61. Examples for the calculation of mean and median values, and ranges.

example	values	mean	median	s.d.	range
1	32, 30, 33, 23	29.5		4.5	25-33
2	32, 30, 33, <23		(30+32)/2=31		<23-33
3	32, 30, 33, <23, 35		32		<23-35

Toxicity
TLm (median tolerance limit) is comparable to the LC_{50}.
MATC is the mean of the NOEC and LOEC.

APPENDIX IV ADDITIONAL QUESTIONS.

The additional questions are in Dutch. The reviewer is not restricted to the use of the questions listed below. However, it is advised to copy the structure of the questions.

Gegevens omtrent de excretie van vmp en van metaboliet A in de faeces en urine van runderen en paarden worden wenselijk geacht.

Gegevens omtrent de omzetting van vmp en van metaboliet A in gier worden wenselijk geacht.

Gegevens omtrent de dampspanning van vmp en van metaboliet A worden noodzakelijk geacht.

Gegevens omtrent de pKa van vmp en van metaboliet A worden noodzakelijk geacht.

Stofidentificerende gegevens (molmassa, chemische naam, CAS-nummer) van metaboliet A worden noodzakelijk geacht.

Gegevens omtrent de wateroplosbaarheid van metaboliet A wordt noodzakelijk geacht.

Gegevens omtrent de logKow van metaboliet A worden noodzakelijk geacht.

Er zijn geen gegevens beschikbaar omtrent de insecticide eigenschappen van vmp en van metaboliet A. Uitvoering van bioassays met 1 soort mestvlieg en 1 soort mestkever wordt noodzakelijk geacht.

Er zijn geen gegevens beschikbaar omtrent de omzetting van vmp en van metaboliet A in grond. Uitvoering van omzettingssnelheidstudies in tenminste 3 grondsoorten wordt noodzakelijk geacht. Voor criteria t.a.v. de laboratoriumstudie wordt verwezen naar de Bijlagen Regeling Uitvoering Milieutoelatingseisen Bestrijdingsmiddelen, Staatscourant 3 februari 1995. Een uitzondering wordt gemaakt voor criterium 1.11: de grond mag voor aanvang van het experiment verrijkt worden met mest, tot een concentratie van 6 g/kg grond.

Er zijn geen gegevens beschikbaar omtrent de sorptie van vmp en van metaboliet A in grond. Uitvoering van schudproeven of kolomproeven met tenminste 3 grondsoorten ter bepaling van $K_{s/l}$ wordt noodzakelijk geacht. Voor criteria t.a.v. de laboratoriumstudie wordt verwezen naar de Bijlagen Regeling Uitvoering Milieutoelatingseisen Bestrijdingsmiddelen, Staatscourant 3 februari 1995.

Uitvoering van proeven ter bepaling van de omzettingsroute van vmp en/of metaboliet A in 1 grondsoort wordt noodzakelijk geacht. Voor criteria t.a.v. de laboratoriumstudie wordt verwezen naar de Bijlagen Regeling Uitvoering Milieutoelatingseisen Bestrijdingsmiddelen, Staatscourant 3 februari 1995. Een uitzondering wordt gemaakt voor criterium 1.11: de grond mag voor aanvang van het experiment verrijkt worden met mest, tot een concentratie van 6 g/kg grond. Indien een metaboliet in een omzettingsstudie in de bodem wordt gevormd in een gehalte van meer dan 20% van de hoeveelheid toegevoegd vmp/metaboliet A, dient met die metaboliet een omzettingssnelheidstudie in tenminste 1 grondsoort en een schudproef of een kolomproef met tenminste 1 grondsoort ter bepaling van K_{om} uitgevoerd te worden. Voor criteria t.a.v. de laboratoriumstudies wordt verwezen naar de Bijlagen Regeling Uitvoering Milieutoelatingseisen Bestrijdingsmiddelen, Staatscourant 3 februari 1995.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de omzetting van ..... in een water/slib systeem. Uitvoering van een studie met tenminste 2 / 1 extra slootbodem-materia(a)l(en) wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de adsorptie aan slibdeeltjes van ..... Uitvoering van een studie met 2 (kleine ondiepe wateren) / 1 (grote oppervlaktewateren) slootbodem-materia(a)l(en) wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de fotochemische afbraak van ..... Uitvoering van een studiewordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de hydrolyse van ..... Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de acute orale toxiciteit van ..... voor vogels. Uitvoering van een studie met tenminste 2 / 1 extra vogelsoort(en) wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de subacute orale toxiciteit van ..... voor vogels. Uitvoering van een studie met tenminste 2 / 1 extra vogelsoort(en) wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de semi-chronische orale toxiciteit voor vogels. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de acute toxiciteit van ..... voor algen. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de acute toxiciteit van ..... voor kreeftachtigen. Een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de acute toxiciteit van ..... voor vissen. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de chronische toxiciteit van ..... voor kreeftachtigen. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de chronische toxiciteit van ..... voor vissen. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de toxiciteit van ..... voor nuttige insekten en mijten. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent de toxiciteit van ..... voor regenwormen. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent het effekt van .....op de bodemademhaling. Uitvoering van een studie wordt noodzakelijk geacht.

Er zijn geen / onvoldoende / onvoldoende betrouwbare gegevens beschikbaar omtrent het effekt van ..... op de nitrificatie. Uitvoering van een studie wordt noodzakelijk geacht.

Op grond van de Kow wordt voor ..... een BCF van > 1000 berekend. Uitvoering van een bioconcentratiestudie met organismen (bij voorkeur met vis) ter bepaling van de BCF wordt noodzakelijk geacht.

Lozing van ..... op het riool is te verwachten. Uitvoering van een studie naar het effect van ..... op de respiratie of de TOC-verwijdering (OECD 305A-E) en op de nitrificatie door geadapteerd slib volgens H.5 (OECD 209 en OECD 305A-E) wordt noodzakelijk geacht.

Een volledige beschrijving van een methode voor de kwalitatieve en kwantitatieve bepaling van residuen van ..... in water dient geleverd te worden.

APPENDIX V LIST OF GUIDELINES

OECD Guidelines

Guideline Code	Guideline Description
OECD101	UV-VIS absorption spectra
OECD102	Melting Point/Melting Range
OECD103	Boiling Point/Boiling Range
OECD104	Vapour Pressure Curve
OECD105	Water Solubility
OECD106	Absorption/Desorption
OECD107	Partition Coefficient (n-octanol/water)
OECD108	Complex Formation Ability in Water
OECD109	Density of Liquids and Solids
OECD110	Particle size Distribution/Fibre Length and Diameter Distributions
OECD111	Hydrolysis as a Function of pH
OECD112	Dissociation Constants in Water
OECD113	Screening Test for Thermal Stability and Stability in Air
OECD114	Viscosity of Liquids
OECD115	Surface tension of Aqueous Solutions
OECD116	Fat Solubility of Solid and Liquid Substances
OECD117	Partition Coefficient (n-octanol/water), HPLC Method
OECD201	Algae, Growth Inhibition Test
OECD202	*Daphnia* spp. Acute Immobilisation test and Reproduction Test
OECD203	Fish, Acute Toxicity Test
OECD204	Fish, Prolonged Toxicity Test: 14-day Study
OECD205	Avian Dietary Toxicity Test
OECD206	Avian Reproduction Test
OECD207	Earthworm, Acute Toxicity Tests
OECD208	Terrestrial Plants, Growth Test
OECD209	Activated Sludge, Respiration Inhibition Test
OECD210	Fish, Early-Life Stage Toxicity Test
OECD301	Ready biodegradability:
OECD301A	DOC Die-away Test
OECD301B	CO2 Evolution Test
OECD301C	Modified MITI Test (I)
OECD301D	Closed Bottle Test
OECD301E	Modified OECD Screening Test
OECD301F	Manometric Respirometry Test
OECD302	Inherent biodegradation:
OECD302A	Modified SCAS Test
OECD302B	Modified Zahn-Wellens Test
OECD302C	Modified MITI Test (II)
OECD303A	Aerobic Sewage Treatment: Coupled Units Test
OECD304A	Inherent Biodegradability in Soil
OECD305	Bioconcentration:
OECD305A	Sequential Static Fish Test
OECD305B	Semi-Static Fish Test
OECD305C	Degree of Bioconcentration in Fish
OECD305D	Static Fish Test
OECD305E	Flow-Through Fish Test
OECD306	Biodegradability in Seawater
OECD401	Acute Oral Toxicity

EPPO Guidelines

Guideline Code (EPPO Bulletin)	Guideline Description
(15)	Standard methods to test the side-effects of pesticides on natural enemies of insects and mites developed by the IOBC/WPRS Working Group 'Pesticides and Beneficial Organisms'. Eppo Bulletin 15 (1985) 214-255.
(22)	Method for honeybee brood feeding test with insect growth-regulating insecticides. Oomen, P.A., A. de Ruijter & J. van der Steen. Eppo Bulletin 22 (1992), p. 613-616.
142	Guidelines for the evaluation of side-effects of plant protection products. No 142. *Encarsia formosa*. Eppo Bulletin 19 (1989), 355-372.
151	Guidelines for the evaluation of side-effects of plant protection products. No 151. *Phytoseiulus persimilis*. Eppo Bulletin 20 (1990), 531-550.
170	Guideline on test methods for evaluating the side-effects of plant protection products on honeybees. Eppo Bulletin 22 (1992) p. 203-215.
180	Guidelines for the evaluation of side-effects of plant protection products. No 180. *Trichogramma cacoeciae*. Eppo Bulletin 23 (1994), 329-352.

EPA Guidelines

Guideline Code	Guideline Description
EPA-540/9-85-002	Honey bee - acute contact LD_{50} test
EPA-540/9-85-003	Honey bee - toxicity of residues on foliage
EPA-540/9-85-005	Acute toxicity test for freshwater invertebrates
EPA-540/9-85-006	Acute toxicity test for freshwater fish
EPA-540/9-85-007	Avian single-dose LD_{50}
EPA-540/9-85-008	Avian dietary LC_{50} test
EPA-540/9-85-009	Acute toxicity test for estuarine and marine organisms (estuarine fish 96-hour acute toxicity test)
EPA-540/9-85-010	Acute toxicity test for estuarine and marine organisms (shrimp 96-hours acute toxicity test)
EPA-540/9-85-011	Acute toxicity test for estuarine and marine organisms (mollusc 96-hour flow-through shell deposition study)
EPA-540/9-85-012	Acute toxicity test for estuarine and marine organisms (mollusc 48-hour embryo larvae study)
EPA-540/9-85-013	Hydrolysis studies
EPA-540/9-85-014	Aqueous photolysis studies
EPA-540/9-85-015	Aerobic soil metabolism study
EPA-540/9-85-016	Soil photolysis study
EPA-540/9-85-017	Soil column leaching study
EPA-540/9-85-130	Non-target plants: target area testing
EPA-540/9-85-130	Growth and reproduction of aquatic plants
EPA-540/9-85-135	Non-target plants: terrestrial field testing
EPA-540/9-85-136	Aquatic field testing
EPA-540/9-85-137	Fish life-cycle toxicity tests
EPA-540/9-86-138	Fish early life-stage
EPA-540/9-86-139	Avian reproduction test
EPA-540/9-86-141	*Daphnia magna* life-cycle (21 day renewal) chronic toxicity test
EPA-540/9-86-152	Acute dietary LC_{50} test for waterfowl and upland gamebirds (addendum)
EPA-540/9-87-198	Aquatic testing for marine/estuarine and freshwater fish and invertebrates
EPA-540/9/88-006	Wild mammal toxicity test (addendum)

ISO Guidelines

Guideline Code	Guideline Description
ISO 11268-1	Soil quality — Effects of pollutants on earthworms (*Eisenia fetida*) — Part 1: Determination of acute toxicity using artificial soil substrate
ISO 11268-2 (draft)	Soil quality — Effects of pollutants on earthworms (*Eisenia fetida*) — Part 2: Method for the determination of effects on reproduction

EU Guidelines

Guideline Code	Guideline Description
Annex V.A1[33]	Melting/Freezing temperature
Annex V.A2	Boiling temperature
Annex V.A3	Relative density
Annex V.A4	Vapour pressure
Annex V.A5	Surface tension
Annex V.A6	Water solubility
Annex V.A7	Fat solubility
Annex V.A8	Partition coefficient
Annex V.A9	Flash point
Annex V.A10	Flammability (solids)
Annex V.A11	Flammability (gases)
Annex V.A12	Flammability (substances and preparations which, in contact with water or damp air, evolve highly flammable gases in dangerous quantities)
Annex V.A13	Flammability (solids and liquids)
Annex V.A14	Explosive properties
Annex V.A15	Auto-flammability (determination of the temperature of self-ignition of volatile liquids and of gases)
Annex V.A16	Auto-flammability (solids - determination of relative self-ignition temperature)
Annex V.A17	Oxidising properties (solids)
Annex V.C1	Acute toxicity for fish
Annex V.C2	Acute toxicity for *Daphnia*
Annex V.C3	Growth inhibition test with algae
Annex V.C4A	DOC - die away test
Annex V.C4B	Modified OECD screening test
Annex V.C4C	Carbon dioxide CO2-development test
Annex V.C4D	Manometric respiration test
Annex V.C4E	Closed Bottle test
Annex V.C4F	MITI test
Annex V.C5	Degradation - biochemical oxygen demand
Annex V.C6	Degradation - chemical oxygen demand
Annex V.C7	Degradation - abiotic degradation: hydrolysis as a function of pH

[33] This Annex V is implemented in the EC Council Directive of 25 April 1984 containing technical adaptations of Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging, and labelling of dangerous substances (84/449/EEC)

BBA Guidelines

Guideline Code	Guideline Description
BBA IV/4-1	Persistence of plant protection products in the soil; degradation, transformation, and metabolism
BBA IV/4-2	Seepage behaviour of plant protection products
BBA VI/1-1	Auswirkungen auf die Aktivität der Bodenmikroflora
BBA 23-1	Richtlinien für die Prüfung von Pflanzenbehandlungsmitteln auf Bienengefährlichkeit
BBA 23-2.1.-8	Richtlinien zur Prüfung der Wirkung von Pflanzenbehandlungsmitteln auf Nutzarthropoden.
BBA 23-2.3.3	Richtlinie zur Prüfung der Wirkung von Pflanzenbehandlungsmitteln auf Nutzarthropoden der Baumschicht im Freiland
BBA 23-2.3.4	Richtlinie für die Prüfung der Auswirkung von Pflanzenbehandlungsmitteln auf Raubmilben im Weinbau
BBA 25-1	Richtlinie zur Prüfung von Pflanzenbehandlungsmitteln auf Vogelgefährdung
BBA 36	Unterlagen zum Verhalten von Pflanzenbehandlungsmitteln im Boden im Rahmen des Zulassungsverfahrens.
BBA 37	Seepage behaviour of plant protection products
BBA 55	Prüfung des Verhaltens von Pflanzenbehandlungsmitteln im Wasser

NEN Guidelines

Guideline Code	Guideline Description
NEN 6501	Determination of acute toxicity with *Daphnia magna*
NEN 6502	Determination of chronic toxicity with *Daphnia magna*
NEN 6504	Determination of acute toxicity with *Poecilia reticulata*
NEN 6506	Determination of toxicity with algae
NEN 6511	Water - Determination of acute toxicity in nitrificating active sludge by measurement of ammonia degradation.
NEN 6512	Water - Determination of acute toxicity in aerobic active sludge by measurement of the respiration rate.
NEN 5794	Determination of the acute toxicity of chemical substances to earthworms
NEN 5795	Determination of the influence of chemical substances on the nitrification in soil
NEN 5797	Determination of the effect of chemical substances to reproduction of earthworms