Environmental risk limits for pirimiphos-methyl

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Rapport in het kort

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Dit rapport geeft milieurisicogrenzen voor het insecticide pirimifos-methyl in water. Milieurisicogrenzen zijn de technisch-wetenschappelijke advieswaarden voor de uiteindelijke milieukwaliteitsnormen in Nederland. De milieurisicogrenzen zijn afgeleid volgens de methodiek die is voorgeschreven in de Europese Kaderrichtlijn Water. Hierbij is gebruikgemaakt van de beoordeling in het kader van de Europese toelating van gewasbeschermingsmiddelen (Richtlijn 91/414/EEG), aangevuld met gegevens uit de openbare literatuur.

Contents

1 Introduction

1.1 Background and scope of the report

In this report, environmental risk limits (ERLs) for surface water are derived for the insecticide pirimiphos-methyl. The derivation is performed within the framework of the project 'Standard setting for other relevant substances within the WFD', which is closely related to the project 'International and national environmental quality standards for substances in the Netherlands' (INS). Pirimiphos-methyl is part of a series of 25 pesticides that appeared to have a high environmental impact in the evaluation of the policy document on sustainable crop protection ('Tussenevaluatie van de nota Duurzame Gewasbescherming'; MNP, 2006) or were selected by the Water Boards ('Unie van Waterschappen'; project 'Schone Bronnen'; http://www.schonebronnen.nl/).

The following ERLs are considered:

- Maximum Permissible Concentration (MPC) – the concentration protecting aquatic ecosystems and humans from effects due to long-term exposure

- Maximum Acceptable Concentration (MAC_{eco}) – the concentration protecting aquatic ecosystems from effects due to short-term exposure or concentration peaks.

- Serious Risk Concentration (SRC_{eco}) – the concentration at which possibly serious ecotoxicological effects are to be expected.

More specific, the following ERLs can be derived depending on the availability of data and characteristics of the compound:

$MPC_{eco, water}$	MPC for freshwater based on ecotoxicological data (direct exposure)
$MPC_{sp, water}$	MPC for freshwater based on secondary poisoning
$MPC_{hh\ food, water}$	MPC for fresh and surface water based on human consumption of fishery products
$MPC_{dw, water}$	MPC for surface waters intended for the abstraction of drinking water
$MAC_{eco, water}$	MAC for freshwater based on ecotoxicological data (direct exposure)
$SRC_{eco, water}$	SRC for freshwater based on ecotoxicological data (direct exposure)
$MPC_{eco, marine}$	MPC for marine water based on ecotoxicological data (direct exposure)
$MPC_{sp, marine}$	MPC for marine water based on secondary poisoning
$MAC_{eco, marine}$	MAC for marine water based on ecotoxicological data (direct exposure)

1.2 Status of the results

The results presented in this report have been discussed by the members of the scientific advisory group for the INS-project (WK-INS). It should be noted that the Environmental Risk Limits (ERLs) in this report are scientifically derived values, based on (eco)toxicological, fate and physico-chemical data. They serve as advisory values for the Dutch Steering Committee for Substances, which is appointed to set the Environmental Quality Standards (EQSs). ERLs should thus be considered as proposed values that do not have any official status.

2   Methods

The methodology for the derivation of ERLs is described in detail by Van Vlaardingen and Verbruggen (2007), further referred to as the 'INS-Guidance'. This guidance is in accordance with the guidance of the Fraunhofer Institute (FHI; Lepper, 2005).

The process of ERL-derivation contains the following steps: data collection, data evaluation and selection, and derivation of the ERLs on the basis of the selected data.

2.1   Data collection

In accordance with the WFD, data of existing evaluations were used as a starting point. For pirimiphos-methyl, the evaluation report prepared within the framework of EU Directive 91/414/EC (Draft Assessment Report) was consulted (EC, 2006; further referred to as DAR). An on-line literature search was performed on TOXLINE (literature from 1985 to 2001) and Current contents (literature from 1997 to 2007). In addition to this, all potentially relevant references in the RIVM e-tox base and EPA's ECOTOX database were checked.

2.2   Data evaluation and selection

For substance identification, physico-chemical properties and environmental behaviour, information from the List of Endpoints of the DAR was used. When needed, additional information was included according to the methods as described in Section 2.1 of the INS-Guidance. Information on human toxicological threshold limits and classification was also primarily taken from the DAR.

Ecotoxicity studies (including bird and mammal studies) were screened for relevant endpoints (i.e. those endpoints that have consequences at the population level of the test species). All ecotoxicity and bioaccumulation tests were then thoroughly evaluated with respect to the validity (scientific reliability) of the study. A detailed description of the evaluation procedure is given in the INS-Guidance (see Section 2.2.2 and 2.3.2). In short, the following reliability indices were assigned:

- Ri 1: Reliable without restriction
  'Studies or data … generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline … or in which all parameters described are closely related/comparable to a guideline method.'

- Ri 2: Reliable with restrictions
  'Studies or data … (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.'

- Ri 3: Not reliable
  'Studies or data … in which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiologic pathways of application) or which were carried out or generated

according to a method which is not acceptable, the documentation of which is not sufficient for an assessment and which is not convincing for an expert judgment.'

- Ri 4: Not assignable
'Studies or data … which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.).'

All available studies were summarised in data-tables, that are included as Annexes to this report. These tables contain information on species characteristics, test conditions and endpoints. Explanatory notes are included with respect to the assignment of the reliability indices.

With respect to the DAR, it was chosen not to re-evaluate the underlying studies. In principle, the endpoints that were accepted in the DAR were also accepted for ERL-derivation with Ri 2, except in cases where the reported information was too poor to decide on the reliability or when there was reasonable doubt on the validity of the tests. This applies especially to DARs prepared in the early 1990s, which do not always meet the current standards of evaluation and reporting.

In some cases, the characteristics of a compound (i.e. fast hydrolysis, strong sorption, low water solubility) put special demands on the way toxicity tests are performed. This implies that in some cases endpoints were not considered reliable, although the test was performed and documented according to accepted guidelines. If specific choices were made for assigning reliability indices, these are outlined in Section 3.3 of this report.

Endpoints with Ri 1 or 2 are accepted as valid, but this does not automatically mean that the endpoint is selected for the derivation of ERLs. The validity scores are assigned on the basis of scientific reliability, but valid endpoints may not be relevant for the purpose of ERL-derivation (e.g. due to inappropriate exposure times or test conditions that are not relevant for the Dutch situation). Endpoints from tests with formulated products were not selected if the results (expressed on the basis of the active substance) differed by more than a factor of 3 from the results obtained with the active substance itself.

After data collection and validation, toxicity data were combined into an aggregated data table with one effect value per species according to Section 2.2.6 of the INS-Guidance. When for a species several effect data were available, the geometric mean of multiple values for the same endpoint was calculated where possible. Subsequently, when several endpoints were available for one species, the lowest of these endpoints (per species) is reported in the aggregated data table.

2.3   Derivation of ERLs

For a detailed description of the procedure for derivation of the ERLs, reference is made to the INS-Guidance. With respect to the selection of the final MPC_{water} and the derivation of the $MAC_{eco, \, marine}$, some additional comments should be made:

2.3.1   Drinking water

The INS-Guidance includes the MPC for surface waters intended for the abstraction of drinking water ($MPC_{dw, \, water}$) as one of the MPCs from which the lowest value should be selected as the general MPC_{water} (see INS-Guidance, Section 3.1.6 and 3.1.7). According to the proposal for the daughter directive Priority Substances, however, the derivation of the AA-EQS (= MPC) should be based on direct exposure, secondary poisoning, and human exposure due to the consumption of fish. Drinking water was not included in the proposal and is thus not guiding for the general MPC value. The exact way of implementation of the $MPC_{dw, \, water}$ in the Netherlands is at present under discussion within the

framework of the "AMvB Kwaliteitseisen en Monitoring Water". No policy decision has been taken yet, and the $MPC_{dw,\,water}$ is therefore presented as a separate value in this report. The MPC_{water}, is thus derived considering the individual MPCs based on direct exposure ($MPC_{eco,\,water}$), secondary poisoning ($MPC_{sp,\,water}$) or human consumption of fishery products ($MPC_{hh\,food,\,water}$); derivation of the latter two is dependent on the characteristics of the compound.

Related to this, is the inclusion of water treatment for the derivation of the $MPC_{dw,\,water}$. According to the INS-Guidance (see Section 3.1.7), a substance specific removal efficiency related to simple water treatment should be derived in case the $MPC_{dw,\,water}$ is lower than the other MPCs. For pesticides, there is no agreement as yet on how the removal fraction should be calculated, and water treatment is therefore not taken into account. In case no A1 value is set in Directive 75/440/EEC, the $MPC_{dw,\,water}$ is set to the general Drinking Water Standard of 0.1 µg/L for organic pesticides as specified in Directive 98/83/EC.

3 Derivation of environmental risk limits for pirimiphos-methyl

3.1 Substance identification, physico-chemical properties, fate and human toxicology

3.1.1 Identity
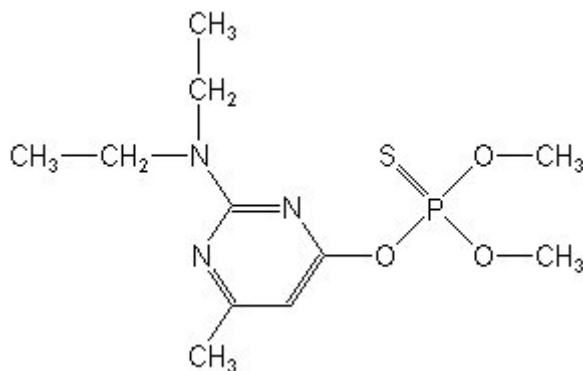
Figure 1. Structural formula of pirimiphos-methyl.

Table 1. Identification of pirimiphos-methyl

Parameter	Name or number	Source
Common/trivial/other name	pirimiphos-methyl	EC, 2006
Chemical name	*O*-2-diethylamino-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphorothioate	EC, 2006
CAS number	29232-93-7	EC, 2006
EC number	249-528-5	EC, 2006
SMILES code	S=P(OC)(OC)Oc1nc(nc(c1)C)N(CC)CC	
Use class	insecticide	EC, 2006
Mode of action	cholinesterase inhibitor with fumigant, contact and stomach action	EC, 2006
Authorised in NL	yes	
Annex 1 listing	yes	

3.1.2 Physico-chemical properties

Table 2. Physico-chemical properties of pirimiphos-methyl.

Parameter	Unit	Value	Remark	Reference
Molecular weight	[g/mol]	305.4		EC, 2006
Water solubility	[g/L]	0.010	pH 5	EC, 2006
		0.011	pH 7	EC, 2006
		0.097	pH 9	EC, 2006
pK_a	[-]	4.3	at 20 ºC	EC, 2006
$\log K_{OW}$	[-]	**4.2**	20 °C; pH 5 and 7; unionised.	EC, 2006
		3.9	20 °C; pH 4	EC, 2006
		3.4	ClogP	BioByte, 2006
$\log K_{OC}$	[-]	2.14	EpiWin	US EPA, 2007
		2.5	K_{oc} 343 L/kg; soil column experiments; value used for leaching calculations by RIVM	Van de Plassche and Linders, 1990
		3.0	K_{oc} 1100 L/kg; value used in PSD evaluation	FOOTPRINT
		3.0	QSAR for pesticides with Log K_{ow} 4.2	EC, 2003
Vapour pressure	[Pa]	2.0×10^{-3}	at 20 °C	EC, 2006
Melting point	[°C]	21		EC, 2006
Boiling point	[°C]	not applicable		EC, 2006
Henry's law constant	[Pa.m^3/mol]	6.1×10^{-2}	at 20 ºC	EC, 2006

3.1.3 Behaviour in the environment

Table 3. Selected environmental properties of pirimiphos-methyl.

Parameter	Unit	Value	Remark	Reference
Hydrolysis half-life (DT50)	[d]	2	pH 4, 25 °C	EC, 2006
		7	pH 5, 25 °C	
		117	pH 7, 25 °C	
		75	pH 9, 25 °C	
Photolysis half-life (DT50)	[h]	0.46	pH 5, 25 °C	EC, 2006
		0.47	pH 7, 25°C	
Readily biodegradable		not available		EC, 2006
Other DT50/DT90 values		not available		EC, 2006
Relevant metabolites		two degradation compounds (hydrolysis): *O*-2-diethyl amino-6-methylpyrimidin-4-yl *O*-methyl phosphorothioate (<10% at pH 4-7; 13% at pH 9) and 2-diethylamino-6-methylpyrimidin-4-ol (>90% at pH 4-5; 7.7-12% at pH 7-9)		EC, 2006

3.1.4 Bioconcentration and biomagnification

There are no experimental data available for pirimiphos-methyl. Therefore the a BCF (fish) of 741 L/kg has been based on log K_{OW} of 4.2 (see Table 4).

Table 4. Overview of bioaccumulation data for pirimiphos-methyl.

Parameter	Unit	Value	Remark	Reference
BCF (fish)	[L/kg]	741	calculated with log K_{ow} 4.2	Veith et al., 1979
BMF	[kg/kg]	1	Default value for log K_{ow} < 4.5	

3.1.5 Human toxicological threshold limits and carcinogenicity

Pirimiphos-methyl is assigned R22 (EC, 2006; ESIS http://ecb.jrc.it/esis/; date of search 4 April 2008). The ADI is 0.004 mg/kg$_{bw}$/d (EC, 2006), based on 2-year rat and dog studies (overall safety factor 100, supported by human data).

3.2 Trigger values

This section reports on the trigger values for ERLwater derivation (as demanded in WFD framework).

Table **5**. pirimiphos-methyl: collected properties for comparison to MPC triggers.

Parameter	Value	Unit	Method/Source	Derived at section
Log $K_{p, \text{susp-water}}$	2.0	[-]	$K_{OC} \times f_{OC,susp}$ [a]	K_{OC}: 3.1.2
BCF	741	[L/kg]	log $BCF_{fish} = 0.85 \times$ log K_{OW} - 0.70	3.1.4
BMF	1	[kg/kg]		3.1.4
Log K_{OW}	4.2	[-]		3.1.2
R-phrases	R22, R50/53			3.1.5
A1 value	1.0	[µg/L]	Total pesticides	
DW Standard	0.1	[µg/L]	General value for organic pesticides	

[a] $f_{OC,susp}$ = 0.1 kg$_{OC}$/kg$_{solid}$ (EC, 2003).

o pirimiphos-methyl has a log $K_{p, \text{susp-water}}$ < 3; derivation of MPC$_{sediment}$ is not triggered.
o pirimiphos-methyl has a log $K_{p, \text{susp-water}}$ < 3; expression of the MPC$_{water}$ as MPC$_{susp, water}$ is not required.
o pirimiphos-methyl has a log K_{ow} ≥ 3; assessment of secondary poisoning is triggered.
o pirimiphos-methyl has a log K_{ow} ≥ 3 and is assigned R22. Therefore, an MPC$_{water}$ for human health via food (fish) consumption (MPC$_{hh\ food,\ water}$) should be derived.
o for pirimiphos-methyl, no specific A1 value or Drinking Water Standard is available from Council Directives 75/440, EEC and 98/83/EC, respectively. Therefore, the general Drinking Water Standard for organic pesticides applies.

3.3 Toxicity data and derivation of ERLs for water

3.3.1 MPC$_{eco, water}$ and MPC$_{eco, marine}$

An overview of the selected freshwater toxicity data for pirimiphos-methyl is given in Table 6. There are no reliable marine toxicity data. Detailed toxicity data for pirimiphos-methyl are tabulated in Appendix 1.

In view of the rapid photolysis (DT$_{50}$ 0.47 h at pH 7), tests without analytical verification of test concentrations were not considered reliable and assigned Ri 3.

Table 6. Pirimiphos-methyl: selected freshwater toxicity data for ERL derivation

Chronic[a]		Acute[a]	
Taxonomic group	**NOEC/EC10 (µg/L)**	**Taxonomic group**	**L(E)C50 (µg/L)**
crustacea		**crustacea**	
Daphnia magna	0.05	*Daphnia magna*	**0.16**[b]
		Gammarus pulex	1.5
		fish	
		Cyprinus carpio	760
		Oncorhynchus mykiss	354[c]

[a] For detailed information see Appendix 1. Bold values are used for ERL derivation.
[b] Geometric mean of 0.21, 0.05, 0.25, 0.15 and 0.27 µg/L, parameter immobilisation.
[c] Geometric mean of 410, 270, and 400 µg/L.

3.3.1.1 Treatment of fresh- and saltwater toxicity data

ERLs for freshwater and marine waters should be derived separately. For pesticides, data can only be combined if it is possible to determine with high probability that marine organisms are not more sensitive than freshwater organisms (Lepper, 2005). For pirimiphos-methyl, no marine toxicity data are available and ERLs for the marine compartment cannot be derived.

3.3.1.2 Mesocosm and field studies

Mesocosms or field studies useful for ERL derivation are not available. An outdoor experiment with some data on chironomid populations in a pond/sediment system is summarised in Appendix 2. This study indicated no recovery of natural chironomid species until at least 57 days after a single application of 50 µg/L.

3.3.1.3 Derivation of MPC$_{eco, water}$ and MPC$_{eco, marine}$

As reliable data on algae are missing, the base set is not complete. However, in view of pirimiphos-methyl being an insecticide with a specific mode of action (cholinesterase inhibition), it is considered justified to assume that algae will not be the most sensitive species group. Therefore, the data are treated as if the base set is complete.

One NOEC is available for *Daphnia magna*. An assessment factor of 100 applies to the situation where one NOEC is available. Although it can be argued that algae will not be sensitive, lowering the assessment factor to 50 is not considered justified because insects are not present in the dataset. It can thus not be concluded with certainty that the value of *D. magna* represents the most sensitive species group. Applying an assessment factor of 100 to the NOEC of 0.05 µg/L results in an MPC$_{eco, water}$ of 0.0005 µg/L = 0.5 ng/L.

An MPC$_{marine}$ cannot be derived because no marine data are available.

3.3.2 $MPC_{sp, water}$ and $MPC_{sp, marine}$

In view of the BCF $\geq$ 100 L/kg, derivation of the $MPC_{sp, water}$ and $MPC_{sp, marine}$ is triggered. The available toxicity data for mammals and birds are presented in Appendix 3. In Table 7, the MPC_{oral} is derived applying the appropriate assessment factors to the data.

Table 7. Pirimiphos-methyl: derivation of the $MPC_{oral, min}$.

Species	Exposure time	NOAEC $[mg/kg_{diet}]$	AForal	MPC_{oral} $[mg/kg_{diet}]$
bobwhite quail	5 d	304	3000	**0.10**
rat	9 d	300	3000	0.10
rat	91 d	8	90	0.09
rat	2-gen	40	30	1.33
mouse	78 w	50	30	1.67
rabbit	8 d	800	3000	0.267
rabbit	8 d	1600	3000	0.533

The lowest MPC_{oral} for rats is 0.09 mg/kg_{diet}, based on 91-days toxicity study. There are, however, also long-term data available, which according to the INS-Guidance prevail over the shorter study. The MPC_{oral} for rats based on the long-term test is 1.33 mg/kg_{diet}. The NOEACs for rabbit originate from a developmental study and refer to maternal toxicity, teratogenicity and foetotoxicity. Considering all available data, the $MPC_{oral,min}$ is set to 0.10 mg/kg_{diet}.

The $MPC_{sp, water}$ = $MPC_{oral, min}$ / (BCF × BMF) = 0.10 / (741 × 1) = 1.4×10^{-4} mg/L = 0.14 µg/L.

Because toxicity data for marine predators are generally not available, the $MPC_{oral, min}$ as derived above is used as a representative for the marine environment also. To account for the longer food chains in the marine environment, an additional biomagnification step is introduced (BMF_2). This factor is the same as given in Table 4. The $MPC_{sp, marine}$ = $MPC_{oral, min}$ / (BCF × BMF_1 × BMF_2) = .10 / (741 × 1 × 1) = 1.4×10^{-4} mg/L = 0.14 µg/L.

3.3.3 $MPC_{hh food, water}$

Derivation of $MPC_{hh food, water}$ for pirimiphos-methyl is triggered (Table 5). The $MPC_{hh food}$ is calculated from the ADI (0.004 mg/kg_{bw}/d), a body weight of 70 kg and a daily fish consumption of 115 g, as $MPC_{hh food}$ = 0.004 x 0.1 x 70/0.115 = 0.24 mg/kg.
Subsequently the $MPC_{hh food, water}$ is calculated as 0.24 / (BCF_{fish} x BMF_1) = 0.24 / (741 x 1) = 0.32 x 10-3 mg/L = 0.32 µg/L.

3.3.4 $MPC_{dw, water}$

The Drinking Water Standard is 0.1 µg/L, the $MPC_{dw, water}$ is 0.1 µg/L.

3.3.5 Selection of the MPC_{water} and MPC_{marine}

The lowest of the derived MPC values for freshwater is the one for ecotoxicity. Thus, the MPC_{water} is set to the $MPC_{eco, water}$ of 0.0005 µg/L = 0.5 ng/L.

3.3.6   MAC$_{eco}$

3.3.6.1   MAC$_{eco, water}$

The MAC$_{eco}$ is based on the acute toxicity data. The compound has a potential to bioaccumulate (log K$_{ow}$ ≥ 3); the mode of action is specific, and it is likely that the most sensitive species group is included in the dataset. Therefore, an assessment factor of 100 is applied to the lowest short-term EC$_{50}$ of 0.16 µg/L, yielding a MAC$_{eco, water}$ of 0.0016 µg/L.

3.3.6.2   MAC$_{eco, marine}$

As there are no marine toxicity data an MAC$_{eco, marine}$ cannot be derived.

3.3.7   SRC$_{eco}$

The geometric mean of all acute L(E)C$_{50}$s is 16 µg/L. There is one NOEC available (0.05 µg/L) which is lower than 1/10 of the geometric mean L(E)C$_{50}$ (1.6 µg/L). Therefore, the SRC$_{eco}$ is based on the NOEC with an assessment factor of 1. The SRC$_{eco}$ is 0.05 µg/L.

3.4   Toxicity data and derivation of ERLs for sediment

Since log $K_{p, susp-water}$ < 3, derivation of ERLs for sediment is not triggered.

4   Conclusions

In this report, the risk limits Maximum Permissible Concentration (MPC), Maximum Acceptable Concentration for ecosystems (MAC_{eco}), and Serious Risk Concentration for ecosystems (SRC_{eco}) are derived for pirimiphos-methyl in water. No risk limits were derived for the marine compartment because data were not available. Derivation of ERLs for sediment is not triggered.

The ERLs that were obtained are summarised in the table below. The MPC value that was set for this compound until now, is also presented in this table for comparison reasons. It should be noted that this is an indicative MPC ('ad-hoc MTR'), derived using a different methodology and based on limited data.

Table 8. Derived MPC, MAC_{eco}, and SRC values for pirimiphos-methyl.

ERL	Unit	MPC	MAC_{eco}	SRC_{eco}
Water, old[a]	µg/L	0.002	-	-
Water, new[b]	µg/L	0.0005	0.0016	0.05
Drinking water[b]	µg/L	0.1[c]	-	-
Marine	µg/L	n.d.[d]	n.d.[d]	-

[a]   indicative MPC ('ad-hoc MTR'), source: Helpdesk Water
http://www.helpdeskwater.nl/emissiebeheer/normen_voor_het/zoeksysteem_normen/

[b]   The $MPC_{dw, water}$ is reported as a separate value from the other MPC_{water} values ($MPC_{eco, water}$, $MPC_{sp, water}$ or $MPC_{hh food, water}$). From these other MPC_{water} values (thus excluding the $MPC_{dw, water}$) the lowest one is selected as the 'overall' MPC_{water}.

[c]   provisional value pending the decision on implementation of the $MPC_{dw, water}$ (see Section 2.3.1)

[d]   n.d. = not derived due to lack of data

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Appendix 1. Detailed aquatic toxicity data

Table A1.1. Acute toxicity of pirimiphos-methyl (freshwater)

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Hardness CaCO$_3$ [mg/L]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference
Protozoa																
Paramecium caudatum				a.s. in acetone	t.g.	Chalkley's solution				0.17 h	LC100	mortality	8.0	3	12	Rajini et al. 1989
Paramecium caudatum				a.s. in DMSO	t.g.	Chalkley's solution				0.17 h	LC100	mortality	15	3	12	Rajini et al. 1989
Algae																
Pseudokirchneriella subcapitata		N	S		91					96 h	EC50	growth rate	4.90	3	1	EC, 2006
Pseudokirchneriella subcapitata		N	S		91					96 h	EC50	biomass	1.00	3	1	EC, 2006
Pseudokirchneriella subcapitata		N	S	EC	50					96 h	EC50	growth rate	2.45	3	2	EC, 2006,
Pseudokirchneriella subcapitata		N	S	EC	50					96 h	EC50	biomass	1.20	3	2	EC, 2006
Crustacea																
Daphnia magna	<24h	N	S		t.g.		7.5	20	200	24 h	EC50	immobilisation	0.00027	3	3	Vighi et al. 1991
Daphnia magna		Y	S		99.5					48 h	EC50	immobilisation	0.00021	2	3	EC, 2006
Daphnia magna		Y	S	Actellic 50EC	50					48 h	EC50	immobilisation	0.00005	2	3,13	EC, 2006,
Daphnia magna		Y	S	Actellic 50EC	50	rw	7.8-8.1	20		48 h	EC50	immobilisation	0.00025	1	3	Van de Plassche and Linders, 1990
Daphnia magna		Y	S	Actellic 50EC	50	rw	7.8-8.1	20		48 h	NOEC	immobilisation	0.000125	1	3	EC, 2006
Daphnia magna		Y	S	Actellic 8EC	8	rw	7.8-8.1	20		48 h	EC50	immobilisation	0.00015	1	3	EC, 2006
Daphnia magna		Y	S	Actellic 8EC	8	rw	7.8-8.1	20		48 h	NOEC	immobilisation	0.0000625	1	3	Van de Plassche and Linders, 1990
Daphnia magna		Y	S	Actellic Dust	2	rw	7.8-8.1	20		48 h	EC50	immobilisation	0.00027	1	3	EC, 2006
Daphnia magna		Y	S	Actellic Dust	2	rw	7.8-8.1	20		48 h	NOEC	immobilisation	0.0000625	1	3	Van de Plassche and Linders, 1990
Gammarus pulex	adult ♂, > 5mm	Y	SS		t.g.	art. pond water	7.3	15		144 h	EC10	feeding rate	0.00049	2	4	McLoughlin et al. 2000
Gammarus pulex	adult ♂, > 5mm	Y	SS		t.g.	art. pond water	7.3	15		144 h	LC50	mortality	0.0015	2	4	McLoughlin et al. 2000
Insecta																
Chironomus riparius	4th instar larvae	N	S			dechlorinated tw		20		24 h	LC50	mortality	0.064	3	5	Ibrahim et al. 1998
Chironomus riparius	4th instar larvae	N	S		t.g.		7	3		96 h	LC50	mortality		3	5	Callaghan et al. 2002
Chironomus riparius	4th instar larvae	N	S		t.g.		7	12		96 h	LC50	mortality	> 0.010	3	5	Callaghan et al. 2002
Chironomus riparius	4th instar larvae	N	S		t.g.		7	22		96 h	LC50	mortality	> 0.010	3	5	Callaghan et al. 2002
Pisces																
Cyprinus carpio		N	S	Actellic 25C	95.3					48 h	LC50	mortality	1.40	3	11	EC, 2006
Cyprinus carpio		Y	FT	Actellic 25C	25					96 h	LC50	mortality	0.76	2	6	EC, 2006
Cyprinus carpio		Y	FT	Actellic	25					48 h	NOEC	mortality	< 0.05	2	6	EC, 2006
Melanotaenia duboulayi	adult ♂; 78±4.3 mm adult ♀; 70±3.2 mm	N	S	Actellic	90	nw		25		1 h	LC50	mortality	> 0.33	3	7	Brown et al. 2002
Melanotaenia duboulayi	juveniles < 72h 3.7±0.37 mm	N	S	Actellic	90	nw	7.1	25	n.r.	1 h	LC50	mortality	0.015	3	7	Brown et al. 2002
Oncorhynchus mykiss		Y	FT		88.9					96 h	LC50	mortality	0.41	2	3	EC, 2006
Oncorhynchus mykiss		N	S		95.3					96 h	LC50	mortality	0.20	3	10	EC, 2006
Oncorhynchus mykiss		Y	FT	Actellic 25EC	25					96 h	LC50	mortality	0.27	2	6	EC, 2006
Oncorhynchus mykiss	7.49g; 86 mm	Y	CF		88.9		7.5-7.7	12	30-53	96 h	LC50	mortality	0.4	1	3	Van de Plassche and Linders, 1990
Oreochromis mossambicus	fingerlings, 24-45 mm	N	S	Actellic 50	50	aged tw		28-29		48 h	LC50	mortality	1.10	3	8	Shafiei and Costa 1990
Oreochromis mossambicus	fry, length 10-15 mm	N	S	Actellic 50	50	aged tw		28-29		48 h	LC50	mortality	0.69	3	9	Shafiei and Costa 1990

NOTES

1. Unreliable endpoint because the actual concentration was not determined, whereas a.i. is photolytically very unstable.
2. Unreliable endpoint because the actual concentration was not determined, whereas a.i. is photolytically very unstable.
3. Based on nominal concentrations.
4. Based on actual concentrations. Photoperiod of 12 h.
5. Test without sediment. Tests are unreliable as it the light conditions were not reported. This is of particular importance in view of the photolytic instability of the a.i..
6. Based on mean measured concentrations.
7. 1-h Pulse exposure followed by 24 h exposure in untreated freshwater.
8. At concentrations ≥ 0.75 mg.L^{-1} spinal bending to the right and to the left were observed (LOEC = 0.75 mg.L^{-1}). Test value unreliable because of possible degradation under light conditions due to photolytic instability of a.i..
9. At concentrations ≥ 0.20 and ≥ 0.40 mg.L^{-1} spinal bending to the right and to the left respectively were observed (LOEC = 0.20 mg.L^{-1}). Test value unreliable because of possible degradation under light conditions due to photolytic instability of a.i..
10. Test value is unreliable because of possible degradation under light conditions due to photolytic instability of a.i..
11. Test value is unreliable because of possible degradation under light conditions due to photolytic instability of a.i..
12. Test value is unreliable because of possible degradation under light conditions due to photolytic instability of a.i..
13. EC50 of formulation is > factor of 3 lower than that of technical substance, but other tests with same product do not show consistent differences; therefore, value is kept

Table A1.2. Acute toxicity of pirimiphos-methyl (marine)

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Salinity [‰]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference
Pisces																
Pseudomugil signifer	late juvenile to adult, 27±2.1 mm	N	S	Actellic	90	filtered nw (salt marsh pools)	7.3	25	27	96 h	LC50	mortality	0.091	3	1	Brown et al. 1998

NOTES
1   Test value is unreliable because of possible degradation under light conditions due to photolytic instability of a.i..

Table A1.3 Chronic toxicity of pirimiphos-methyl (freshwater)

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Hardness CaCO$_3$ [mg/L]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference
Algae																
Pseudokirchneriella subcapitata		N	S		91					96 h	NOEC	growth rate	0.56	3	5	EC, 2006
Pseudokirchneriella subcapitata		N	S		91					96 h	NOEC	biomass	0.14	3	5	EC, 2006
Pseudokirchneriella subcapitata		N	S	EC	50					96 h	NOEC	growth rate	0.41	3	5	EC, 2006
Pseudokirchneriella subcapitata		N	S	EC	50					96 h	NOEC	biomass	0.22	3	5	EC, 2006
Crustacea																
Daphnia magna	first instar	Y	SS		89.3			19-22		21 d	NOEC	reproduction	0.00005	2	1	EC, 2006
Daphnia magna	first instar	Y	SS		89.3			19-22		21 d	EC50	immobilisation	0.00008	2	1	EC, 2006
Pisces																
Oncorhynchus mykiss		Y	FT		90			15 ± 2.0		28 d	LC50	mortality	0.61	2	2	EC, 2006, Sankey 1990
Oncorhynchus mykiss		Y	FT		90			15 ± 2.0		28 d	NOEC	fish weight	< 0.023	2	2	EC, 2006, Sankey 1990
Poecilia reticulata		Y	SS		t.g.					14 d	LC50	mortality	1.9	2	1	De Bruijn and Hermens 1993
Oreochromis niloticus niloticus		n.r.	n.r.	Actellic 25	25						LC50	mortality	0.00087	3	3	Ufodike and Omoregie 1991
Oreochromis niloticus niloticus	fingerling, 10.6 g	N	CF	Actellic 25	25		6.7	23		10 w	EC10	growth rate	0.000029	3	4	Ufodike and Omoregie 1991
Oreochromis niloticus niloticus	fingerling, 10.6 g	N	CF	Actellic 25	25		6.7	23		10 w	EC50	growth rate	0.000038	3	4	Ufodike and Omoregie 1991

NOTES
1 Based on nominal concentrations.
2 Based on mean measured concentrations.
3 This LC50 value was cited in Ufodike and Omoregie (1991) without additional information.
4 Calculated by RIVM method. The high toxicity may have been due to other components than the a.i..
5 Unreliable endpoint because the actual concentration was not determined, whereas a.i. is photolytically very unstable.

Appendix 2. Detailed sediment toxicity data

Table A2.1. Toxicity of pirimiphos-methyl to sediment organisms.

Species	Species properties (age, sex)	Sediment type	A	Test compound	Purity [%]	pH	o.m. [%]	Clay [%]	T [°C]	Exp. time	Criterion	Test endpoint	Result sediment [mg/kg$_{dw}$]	Result std. sediment [mg/kg$_{dw}$]	Ri	Notes	Reference
Chironomus riparius	4th instar larvae	Y	S	Actellic D	25			26-47	5.7-28.5	48h	LC50	mortality	0.061		3	1,2,3	Maycock et al. 2003

NOTES

1 outdoor in-situ bioassay; study is summarised in Appendix 4
2 organic matter content not given; not possible to recalculate endpoint into standard sediment
3 LC50 estimated by linear regression of a logistic concentration response curve, using mortality data from graph and mean measured concentrations in sediment

Appendix 3. Detailed bird and mammal toxicity data

Species	Species properties	Purity [%]	Application route	Exp. time	Criterion	Test endpoint	Value [mg/kg$_{bw}$d]	Value [mg/kg$_{diet}$]	Ri	Notes	Reference
mallard duck		90.8	diet	5 d	LC50	mortality		633	3	1,5	EC, 2006
bobwhite quail		90.8	diet	5 d	LC50	mortality		207	3	1,5	EC, 2006
bobwhite quail	juveniles	89.3	diet	5 d	LC50	mortality		304	2	5	EC, 2006
chicken	laying hens and cockerels	97	diet	28 d	NOAEL	mortality, food consumption, body weight, reproduction		≥ 40	2	5	EC, 2006
chicken	14 m old hens	93.5	by gavage	90 d	NOAEL	neuropathy	≥ 10	≥ 80	2	5	EC, 2006
rat	AP Wistar rats	88.5	gavage	9 d	NOAEL	foetotoxicity, maternal toxicity	15	300	2	6	EC, 2006
rat	AP Wistar rats	88.5	gavage	9 d	NOAEL	teratogenicity	≥ 150	≥ 3000	2	6	EC, 2006
rat	Wistar(6 w old) rats	97	diet	28 d	NOAEC	mortality, body weight gain, clinical effects		≥ 50	2	2,5	EC, 2006
rat	Sprague Dawley rats	86.7	diet	2-gen	NOAEC	female body weight		40	2	5	EC, 2006
rat	Sprague Dawley rats	86.7	diet	2-gen	NOAEC	reproduction		≥ 160	2	5	EC, 2006
rat	Alderley Park SPF rats	93.1	diet	91 d	NOAEC	mortality, body weight, food consumption		8	2	5	EC, 2006
rat	Sprague Dawley rats	89.8	diet	92 d	NOAEL	neuropathy		≥ 300	2		EC, 2006
rat	Wistar rats	86.8	diet	104 w	NOAEC	mortality; body weight		≥ 300	2	5	EC, 2006
mouse	CD-1 mice	86.7	diet	91 d	NOAEC	mortality		≥ 270	2	3,5	EC, 2006
mouse	CD-1 mice	89.8	diet	78 w	NOAEC	mortality, nephropathy, urinary bladder destruction		50	2	5	EC, 2006
dog	beagles	see note 4	diet	2 y	NOAEL	body weight (males), clinical signs (males)	2	80	3	4,6	EC, 2006
rabbit	NZ white rabbits	86.7	by gavage	8 d	NOAEL	foetotoxicity	24	800	2	6	EC, 2006
rabbit	NZ white rabbits	86.7	by gavage	8 d	NOAEL	teratogenicity	48	1600	2	6	EC, 2006

NOTES
1   Study unreliable due to insufficient reporting of test details.
2   No histopathological investigations were performed.
3   This study was performed as a range-finding investigation prior to a carcinogenicity study and was reported within the report of that carcinogenicity study (Martin, 1996).
4   The test material was supplied in 6 batches, 4 of unspecified purity with the remainder of 97% and 99% purity. The clinical signs and transient body weight effects may be secondary to capsule dosing in a small volume (0.1 mL) to which the animals adapted for the latter 80% of the study.
5   endpoint based on dietary concentrations in test
6   endpoint calculated with default conversion factor

Appendix 4. Description of mesocosm studies

Species; Population; Community	plants, invertebrates, *Chironomus riparius* in bioassay
Test Method	outdoor pond microcosm
System properties	5 x 5 m; natural sediment and river water
Formulation	ActellicD (25% as)
Exposure regime	50 µg as/L; injection with 5 L
Analysed	Y
Temperature [°C]	max. 12.5-28.5 °C at start in August; 10.7-19.3 °C end September; 5.7-13.8 °C end of study (October)
pH range	not reported
Hardness [mg CaCO$_3$/L]	not reported
Exposure time	results reported up to 59 days
Criterion	48-h LC50
Test endpoint	Chironomid survival (bioassay)
Value [µg/kg dwt sediment]	61
GLP	N
Guideline	
Notes	no emergence of natural populations until day 57
Ri	2
Reference	Maycock et al., 2003

Test system. Two outdoor ponds of butyl rubber, 5 x 5 m, 5-10 cm natural sediment (C.S. Lewis Nature Reserve, Oxford) and river water (River Thames at Medmenham).

Natural populations of plants and invertebrates; dense growth of pond weed (mostly Elodea Canadensis) was removed but recolonised rapidly. Three individual test chambers (68 mm Ø PVC pipes) were driven into the sediment of each microcosm to a depth of 5-10 cm. Aeration was supplied. Application took place in August. Nominal initial concentration 50 µg as/L by injection of 5 L of a solution of ActellicD (25% as).

Analytical sampling. Samples of water and sediment (top 2 cm) were taken on days 1, 3, 7, 14, 20, 27 and 57. Analysis by GC, after liquid-liquid extraction with DCM/hexane (water) or after 6-hours extraction with hexane/acetone (sediment) and clean-up by SPE (C18).

Biological observations.

In-situ bioassays.

Fourth instar larvae of laboratory cultured *Chironomus riparius* were introduced in the test chambers and surviving organisms were collected after 48 hours. Bioassays took place 13 and 8 days before application, and 1, 3, 7, 14, 20, 27 and 57 days after application.

Monitoring of natural Chironomid populations

Floating boxes (20 x 20 x 20 cm; mesh sides; perspex top) were placed at random locations; traps were removed on the same days as the larvae were removed from the bioassays chambers. Individuals were counted, sexed and males were identified to the species level.

Statistical analysis.

The results were analysed using ANOVA with Tukey's test when requirements for normality and homogeneity of variances were met; otherwise non-parametric Kruskall-Wallis was used..

RESULTS

Chemical analysis. Concentrations in water and sediment are given in the table below:

		Day 1	Day 3	Day 7	Day 14	Day 20	Day 27	Day 57
water	Pond 1	16	42	18	-	-	-	-
[µg/L]	Pond 2	35	29	6	-	-	-	-
	average	25.5	35.5	12	-	-	-	-
sediment	Pond 1	85	139	39	20	61	20	19
[µg/kg]	Pond 2	615	962	88	13	61	24	n.d.
	average	350	550.5	63.5	16.5	61	22	19

In-situ bioassays.
Pre-application survival was confounded by the presence of indigenous chironomid larvae. On days 3, 5 and 9 after pesticide application (assays started 1, 3 and 7 days after application), 100% mortality occurred. Recovery in the treated ponds was first observed on day 16 (bioassay started on day 14), with 53.3% survival. Survival was 33.3% and 80% in the bioassays run from day 20-22, and 57-59, respectively.

Monitoring of natural Chironomid populations
Einfelda longipes (51.2%) and *Chironomus pseudothummi* (15.7%) dominated emergence from all ponds prior to treatment. Emergence continued from the control ponds throughout the study, but there was a change in dominance to *Psectrotanypus varius* (31.2%), and *Tanypus punctipennis* (14.9%), *C. pseudothummi* (24.1%) and *Psectrocladius edwarsi* (17.2%). Some other species were recorded in low numbers. Emergence from the treated ponds was not observed until at least 57 days after treatment. Dominant species was *P. edwarsi*, *C. sylvestris* and *Parachironomus parilis* were present to a much lower extent.

Evaluation of the scientific reliability of the field study
Criteria for a suitable (semi)field study
1. Does the test system represent a realistic freshwater community? No. Study was focussed on Chironomids, other invertebrates were not included.
2. Is the description of the experimental set-up adequate and unambiguous? Yes
3. Is the exposure regime adequately described? Yes. Sediment analyses, however, show that there is a large variation between the two replicate ponds until 7 days after application.
4. Are the investigated endpoints sensitive and in accordance with the working mechanism of the compound? Yes. Pirimiphos-methyl is an insecticide, but Daphnids may be more sensitive.
5. Is it possible to evaluate the observed effects statistically? No, significant differences in survival are not indicated.

These criteria result in an overall assessment of the study reliability. The study is considered to be less reliable mainly due to the variability in exposure (Ri 2).

Using the survival data given by the author, and reading the value for the bioassay run from day 27 to 29 and the control performance from a graph, the control corrected mortality was calculated for each bioassay. The 48-h LC_{50} was estimated by fitting the control corrected mortality to the mean measured concentrations in sediment, assuming a log-logistic concentration-response relationship. The resulting 48-hours LC_{50} value is 61 µg/kg dwt sediment. Because the organic matter content of the sediment is not given, the result cannot be used for ERL-derivation.
It should further be noted that emergence of natural populations was inhibited until 57 days after treatment, while Chironomids in the bioassays survived as from day 14. This may indicate that exposure in the bioassays was lower than in the whole microcosms. Probably, the larvae in the bioassays spent more time in the water column and were thus less exposed to sediment.

Appendix 5. References used in the appendices

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