National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Environmental risk limits for chlorpropham in water

RIVM letter report 601714017/2011
J.W. Vonk | C.E. Smit

National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Environmental risk limits for chlorpropham in water

RIVM Letter report 601714017/2011

Colofon

J.W. Vonk
C.E. Smit

Contact:
Els Smit
Expertise Centre for Substances
els.smit@rivm.nl

This investigation has been performed by order and for the account of Ministry of Infrastructure and Environment, Sustainable Production Directorate, within the framework of the project "Chemical aspects of WFD"

Abstract

Environmental risk limits for chlorpropham in water

RIVM has derived environmental risk limits (ERLs) for chlorpropham in water. Chlorpropham is used as a herbicide and sprout suppressor. The compound is included in the Dutch decree on water quality objectives in the context of the Water Framework Directive (WFD). The current standard for chlorpropham has to be updated according to the new WFD-methodology. The ERLs in this report are advisory values that serve as a scientific background for the Dutch Steering Committee for Substances, which is responsible for setting those standards.

The maximum permissible concentration in water (MPC_{water}) is the level at which no harmful effects are expected, based on annual average concentrations. This MPC is based on three routes: direct ecotoxicity, secondary poisoning, and consumption of fish by humans. Direct ecotoxicity is the most critical of these three routes and determines the overall MPC_{water} (4 microgram per litre). The $MAC_{eco,\ water}$, which protects ecosystems from effects of short term concentration peaks, is 43 microgram per litre. Monitoring data from 2009 and 2010 do not indicate that these levels will be exceeded.

Keywords:
water quality standard; maximum permissible concentration; WFD

Rapport in het kort

Milieurisicogrenzen voor chloorprofam in water

Het RIVM heeft in opdracht van het ministerie van Infrastructuur en Milieu (I&M), milieurisicogrenzen voor chloorprofam in water bepaald. Chloorprofam is een onkruidbestrijdingsmiddel en wordt ook gebruikt om te voorkomen dat aardappelen voortijdig kiemen. De stof is opgenomen in de Regeling Monitoring Kader Richtlijn Water, waarin staat aan welke eisen oppervlaktewater in Nederland moet voldoen. De huidige norm voor chloorprofam is niet afgeleid volgens de meest recente methodiek, daarom moeten nieuwe waterkwaliteitsnormen worden vastgesteld. De Stuurgroep Stoffen stelt deze nieuwe normen vast op basis van de wetenschappelijke advieswaarden in dit rapport.

Het Maximaal Toelaatbaar Risiconiveau (MTR) is de concentratie in water waarbij geen schadelijke effecten te verwachten zijn, gebaseerd op jaargemiddelde concentraties. Hiervoor zijn drie routes onderzocht: directe effecten op waterorganismen, indirecte effecten op vogels en zoogdieren via het eten van prooidieren en indirecte effecten op mensen via het eten van voedsel. De eerste van deze drie levert de laagste waarde en bepaalt daarmee het MTR_{water} (4 microgram per liter). De Maximaal Aanvaardbare Concentratie ($MAC_{eco, water}$), die het ecosysteem beschermt tegen kortdurende concentratiepieken, is 43 microgram per liter. Op basis van meetgegevens over 2009 en 2010 is er geen aanwijzing dat deze concentraties worden overschreden.

Trefwoorden:
milieurisicogrenzen; MTR; Kaderrichtlijn water

Contents

Summary

In this report, RIVM presents environmental risk limits (ERL) for chlorpropham in water. Chlorpropham is used as a broad spectrum herbicide and sprout suppressor. The compound is listed as a *specific pollutant* in the context of the Water Framework Directive (WFD). The current water quality standard for chronic exposure is 3.3 µg/L. This value dates back to before 2004, and the scientific background is not clear. A maximum acceptable level for peak exposure, which is also required according to the WFD, is not available.
Based on the data from the national and European authorisation dossiers and additional information obtained from the open literature, environmental risk limits for chlorpropham in water have been derived that can be used to set updated water quality standards. The methods used are in accordance with the methodology of WFD and INS (International and National environmental quality standards for Substances in the Netherlands).

Five types of ERL are considered, each representing a different protection aim.

- The Maximum Permissible Concentration (MPC). The MPC represents the concentration that protects man and environment from adverse effects due to chronic exposure. According to the WFD-methodology, three routes have been taken into account for derivation of the MPC: direct exposure of aquatic organisms, secondary poisoning of predatory birds and mammals, and exposure of humans via fish consumption.

- The Maximum Acceptable Concentration for ecosystems (MAC_{eco}). The MAC_{eco} is the concentration that protects aquatic ecosystems from adverse effects of short-term concentration peaks. The MPC and MAC_{eco} are equivalent to the long-term and short-term water quality standards that are indicated as AA-EQS and MAC-EQS in the WFD-guidance. They are derived for both the freshwater and saltwater compartment.

- The Negligible Concentration (NC). The NC is calculated by applying an additional factor of 100 to the MPC. The NC represents the concentration at which effects to ecosystems are expected to be negligible and functional properties of ecosystems are fully safeguarded. In the Dutch policy on substances, the NC is used to define a safety margin that takes combination toxicity into account.

- The Serious Risk Concentration for ecosystems (SRC_{eco}). This is the concentration at which serious ecotoxicological risks might occur in aquatic ecosystems.

- The Maximum Permissible Concentration in water for drinking water abstraction ($MPC_{dw, hh}$). The $MPC_{dw, hh}$ represents the concentration at which surface water can be used for production of drinking water without further treatment.

Where applicable, ERLs are derived for freshwater and saltwater. An overview of the newly derived ERLs is presented in Table 1. ERLs that are equivalent to water quality standards required under the WFD are indicated in bold.Based on monitoring data from 2009 and 2010, it is not expected that concentrations in freshwater exceed the newly derived MPC or MAC. Saltwater monitoring data are not available.

Table 1 Environmental risk limits for chlorpropham in water

Environmental risk limit	**Value [µg/L]**
Freshwater	
MPC_{water}	**4.0**
$MAC_{eco, water}$	**43**
NC_{water}	0.04
$SRC_{eco, water}$	480
Surface water for drinking water production	
$MPC_{dw, hh}$	**0.1**
Saltwater	
$MPC_{saltwater}$	**0.8**
$MAC_{eco, saltwater}$	**4.3**
$NC_{saltwater}$	0.008
$SRC_{eco, saltwater}$	480

1 Introduction

1.1 Project framework

In this report, environmental risk limits (ERLs) for surface water are derived for chlorpropham. Chlorpropham is a herbicide that is considered as a specific pollutant for the Netherlands in the context of the Water Framework Directive (WFD). The compound is listed in the Dutch decree on WFD-monitoring (*Regeling monitoring Kaderrichtlijn water*). The aim of this report is to present updated risk limits that can be used to set water quality standards in accordance with the WFD. The derivation of the ERLs is performed in the context of the project Chemical aspects of the Water Framework Directive, which is closely related to the project INS (International and national environmental quality standards for substances in the Netherlands). The following ERLs are considered:

- Maximum Permissible Concentration (MPC) – defined in VROM (1999, 2004) as the standard based on scientific data which indicates the concentration in an environmental compartment for which:
  - 1 no effect to be rated as negative is to be expected for ecosystems;
  - 2a no effect to be rated as negative is to be expected for humans (for non-carcinogenic substances);
  - 2b for humans no more than a probability of 10^{-6} per year of death can be calculated (for carcinogenic substances). Within the scope of the Water Framework Directive (WFD), a probability of 10^{-6} on a life-time basis is used.

  The MPC for water should not result in risks due to secondary poisoning and/or risks for human health aspects. These aspects are therefore also addressed in the MPC derivation. Separate MPC-values are derived for the freshwater and saltwater environment.

- Negligible Concentration (NC) – the concentration in fresh- and saltwater at which effects to ecosystems are expected to be negligible and functional properties of ecosystems are safeguarded fully. It defines a safety margin which should exclude combination toxicity. The NC is derived by dividing the MPC by a factor of 100.

- Maximum Acceptable Concentration (MAC_{eco}) for aquatic ecosystems – the concentration protecting aquatic ecosystems from effects due to short-term exposure or concentration peaks. The MAC_{eco} is derived for freshwater and saltwater ecosystems.

- Serious Risk Concentration for ecosystems (SRC_{eco}) – the concentration in water at which possibly serious ecotoxicological effects are to be expected. The SRC_{eco} is valid for the freshwater and saltwater compartment.

- Maximum Permissible Concentration for surface water that is used for drinking water abstraction ($MPC_{dw, hh}$). This is the concentration in surface water that meets the requirements for use of surface water for drinking water production. The $MPC_{dw, hh}$ specifically refers to locations that are used for drinking water abstraction.

The quality standards in the context of the WFD refer to the absence of any impact on community structure of aquatic ecosystems. Hence, not the potential to recover after transient exposure, but long-term undisturbed function is the protection objective under the WFD. Recovery in a test situation, after a limited exposure time, is therefore not included in the derivation of the MPC and MAC.

1.2 Current standards for chlorpropham

The current MPC_{water} for chlorpropham is 3.3 µg/L. The scientific background of this value is not known, and it is clear that it dates back to 2004 or earlier when the WFD-methodology was not yet adopted.

1.3 Methodology

The methodology for risk limit derivation is described in detail in the INS-guidance document (Van Vlaardingen and Verbruggen, 2007), which is further referred to as the INS-Guidance. The methodology is based on the Technical Guidance Document (TGD), issued by the European Commission and developed in support of the risk assessment of new notified chemical substances, existing substances and biocides (EC, 2003a) and on the Manual for the derivation of Environmental Quality Standards in accordance with the Water Framework Directive (Lepper, 2005). The European guidance under the framework of WFD is currently being revised, the final draft has been approved recently (March, 2011) by the Strategic Coordination Group under the European Water Directors. The risk limits in this report will be used for setting water quality standards that will become effective after the new guidance has come in to force. Therefore, the terminology is harmonised as much as possible and the new guidance is followed in the case it deviates from the INS-guidance. This specifically applies to the treatment of data for freshwater and marine species (see section 4.1.1) and the derivation of the MAC (see section 4.3), for which the new methodology is used (EC, 2011). This also holds for the MPC for surface waters intended for the abstraction of drinking water ($MPC_{dw, hh}$, see section 4.2). In the INS-guidance, this is one of the MPCs from which the lowest value should be selected as the general MPC_{water} (see section 3.1.6 and 3.1.7 of the INS-Guidance). According to the new guidance, the $MPC_{dw, hh}$ is not taken into account for the derivation of the general MPC_{water}, but specifically refers to locations that are used for drinking water abstraction.

1.3.1 Data sources

The derivation of the ERLs for chlorpropham is based on the data available in the EU-dossier. Data from the Draft Assessment Report (DAR; EC, 2003b) were re-assessed for their reliability in view of the specific use for ERL derivation. Data for formulations were collected at the Ctgb (Dutch Board for Authorisation of Plant Protection Products and Biocides) with permission of the product owners. If evaluated summaries were available, the endpoints were taken from these summaries (Van der Veen, 2008; Hooftman, 2004; CTB, 2004). In a few cases the original study reports were consulted. In addition, an on-line literature search was performed via SCOPUS, available via http://www.scopus.com/. For information on coverage, see http://info.scopus.com/detail/what/. For search profile see Annex 3. This search did result in some additional references from which an endpoint could be derived.

1.3.2 Data evaluation

Ecotoxicity studies were screened for relevant endpoints (i.e. those endpoints that have consequences at the population level of the test species) and thoroughly evaluated with respect to the validity (scientific reliability) of the study. A detailed description of the evaluation procedure is given in section 2.2.2 and 2.3.2 of the INS-Guidance and in the Annex to the draft EQS-guidance under the WFD. In short, the following reliability indices were assigned, based on Klimisch et al. (1997):

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.).'

Citations
In case of (self-)citations, the original (or first cited) value is considered for further assessment, and an asterisk is added to the Ri of the endpoint that is cited.

All available studies are 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.

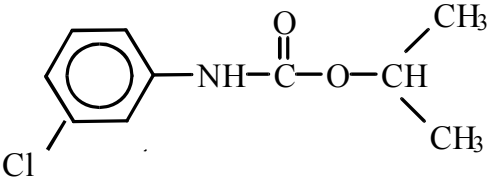
1.4 Status of the results

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 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 advisory values that do not have an official status.

2 Information on the substance

2.1 Identity

Table 2 Substance identification

Name	Chlorpropham
Chemical name	Isopropyl 3-chlorophenylcarbamate
CAS number	101-21-3
Molecular formula	$C_{10}H_{12}ClNO_2$
Molar mass	213.7 g/mol
EC number	EINECS 202-925-7
Structural formula	
SMILES code	Clc1cc(NC(=O)OC(C)C)ccc1
Use class	Herbicide
Mode of action	Mitosis inhibitor, absorbed predominately by roots. Disruption of microtubule organisation in plants. Chlorpropham inhibits root and epicotyl growth, normal cell division, protein and RNA synthesis, suppresses transpiration and respiration, interferes with oxidative phosphorylation and photosynthesis and inhibits the activity of beta-amylase.

2.2 Physico-chemical properties

Table 3 Physico-chemical properties

Parameter	Unit	Value	Remark	Reference
Water solubility	[mg/L]	110	pH 7, 20 °C	EC, 2003b
pK_a		-	No dissociation occurs in water	EC, 2003b
log K_{ow}		3.76	pH 7, 20 °C	EC, 2003b
		3.51	Cited in EPIWIN	Hansch et al., 1995
Vapour pressure	[Pa]	2.4×10^{-2}	20 °C	EC, 2003b
Henry's law constant	[Pa.m^3/mol]	0.047	20 °C	EC, 2003b
Melting point	[°C]	36-49		EC, 2003b
Boiling point	[°C]	256-458		EC, 2003b

2.3 Fate and behaviour

Selected environmental properties of chlorpropham are given in Table 4.

Table 4 Selected environmental properties of chlorpropham

Parameter	Name/Unit	Value	Remark	Reference
log K_{oc}	log [L/kg]	2.53	Average of three values	EC, 2003b
Hydrolysis half-life	DT_{50} [d]	> 365 > 365 > 365	pH 4, 20 °C pH 7, 20 °C pH 9, 20 °C	EC, 2003b
Photolysis half-life	DT_{50} [d]	47-83	DT_{50} field	EC, 2003b
Biodegradation in water/sediment systems	DT_{50} [d]	44	Whole system; average of 5 systems	EC, 2003b

2.4 Bioconcentration and biomagnification

Based on experimental data, the BCF for fish is 144 L/kg (see Annex 1, Table A1.1). Since the trigger for bioconcentration and biomagnification is exceeded (BCF ≥ 100 L/kg), an MPC for secondary poisoning has to be derived. The $MPC_{sp, water}$ and $MPC_{sp, saltwater}$ for secondary poisoning are derived in Section 4.1.3.

3 Human toxicology and ecotoxicological effect data

3.1 Human toxicology

3.1.1 Human toxicological threshold limits and carcinogenicity

Chlorpropham is assigned: R40 (carcinogen category 3), R48/R22 (ESIS, date of search January 2011). According to the triggers as given in Table 17 of the INS-Guidance, the $MPC_{hh\ food,\ water}$ should be derived. The ADI is 0.05 mg/kg bw/d, based on the NOAEL of 5 mg/kg bw/d from a 60-week study with dogs and an assessment factor of 100. (List of Endpoints, DAR; EC, 2003b).

3.2 Ecotoxicological effect data

3.2.1 Laboratory data

Detailed aquatic toxicity data for chlorpropham are tabulated in Annex 2. Unbound values are not used in ERL derivation, unless they indicate that the derived value is not protective and consequently the assessment factor should be adapted. The selected valid acute and chronic ecotoxicity data for freshwater organisms are summarised in Tables 5 and 6, data for marine species are presented in Table 7. Organisms are considered marine species if they are representative for marine and brackish water environments and are tested in water with salinity > 0.5 ‰.
It should be noted that in some studies, analytical verification of test concentration was not performed. At the time the DAR was prepared, this aspect was generally paid less attention to than nowadays. Chlorpropham has a log K_{ow} of > 3, and Henry's constant is relatively high. This means that problems in maintenance of test concentrations due to sorption and/or volatilisation could be an issue. In some cases where concentrations were measured, there was a decline in concentrations during the test, in other studies concentrations remained constant. The lowest endpoints all refer to nominal concentrations since for those studies no measured concentrations were available, and for that reason they are considered less reliable. Considering all data there was no clear indication that actual concentrations deviate strongly from nominal and it was decided to take these values into account for derivation of risk limits. Furthermore, it can be argued that when actual concentrations had been measured, the endpoints might have even been lower. Leaving these studies out of consideration might lead to risk limits that are under-protective.

3.2.2 Field data

There are no field data available.

Table 5 Selected acute ecotoxicity data of chlorpropham for freshwater organisms. The bold value is used for derivation of the $MAC_{eco,\ water}$.

Endpoints	$L(E)C_{50}$ [mg/L]	Remark	Reference
Algae[a]			
Chlamydomonas eugametos	**0.43**	Cell density	Hess, 1980
Desmodesmus subspicatus	3.04	Growth rate	Vryenhoef and Mullee, 2009
Navicula pelliculosa	1.65	Growth rate	EC, 2003b
Pseudokirchneriella subcapitata	1.65	Geometric mean of 3.3, 1.9, 2.14, 0.90, 1.8, 1.36, 1.13 mg/L (growth rate)	EC, 2003b; Van der Veen, 2008; Hooftman, 2004; CTB, 2004; L'haridon, 2003c; Kuhl and Wydra, 2009b
Macrophyta[a]			
Lemna minor	3.46	Geometric mean of 3.82 and 3.14 mg/L (growth rate)	EC, 2003b
Crustacea			
Daphnia magna	2.25	Geometric mean of 4.0, 3.7, 8.4, 2.6, 2.3, 4.3, 3.59, 0.47, 2.5, 0.98, 3.51, 0.37 (immobilisation)	EC, 2003b; Van der Veen, 2008; Hooftman, 2004; CTB, 2004; L'Haridon, 2003a; Priestly and Mullee, 2010b; Kuhl and Wydra, 2009a
Pisces			
Cyprinus carpio	4.89	Geometric mean of 5.3, 9.2, 2.4 mg/L (mortality)	EC, 2003b; Hooftman, 2004
Danio rerio	13.4	Mortality	
Lepomis macrochirus	12	Mortality	
Micropterus salmoides	10	Mortality	
Oncorhynchus mykiss	5.95	Geometric mean of 7.5, 3.91, 6.2, 9.0, 5.92, 4.56 mg/L (mortality)	EC, 2003b; Van der Veen, 2008; L'Haridon, 2003b; Priestly and Mullee, 2010a
Salvelinus fontinalis	8.8	Mortality	EC, 2003b
Amphibia			
Pleurodeles waltlii	20	Mortality	Caporiccio et al., 1981
Triturus helveticus	6.5	Mortality	Caporiccio et al., 1981
Xenopus laevis	8.5	Mortality	Caporiccio et al., 1981

[a] For studies with algae and *Lemna* endpoints based on growth rate are preferred over endpoints based on biomass.

Table 6 Selected chronic ecotoxicity data of chlorpropham for freshwater organisms. The bold value is used for derivation of the MPC.

Endpoints	NOEC [mg/L]	Remark	Reference
Algae[a]			
Desmodesmus subspicatus	1.17	Growth rate and yield	Vryenhoef and Mullee, 2009
Navicula pelliculosa	0.702	Growth rate and biomass	EC, 2003b
Pseudokirchneriella subcapitata	0.339	Geometric mean of 0.46, 0.197, 0.32, 0.74, 0.23, 0.83, 0.36, 0.117 mg/L (growth rate and biomass)	Ec, 2003b; Van der Veen, 2008; Hooftman, 2004; L'Haridon, 2003c; Kuhl and Wydra, 2009b
Scenedesmus quadricauda	**0.04**	Cell density	EC, 2003b
Macrophyta[a]			
Lemna minor	1.61	Growth rate and biomass	EC, 2003b
Crustacea			
Daphnia magna	1.0	Reproduction	EC, 2003b
Pisces			
Danio rerio	0.32	Larval survival	EC, 2003b

[a] For studies with algae and *Lemna* endpoints based on growth rate are preferred over endpoints based on biomass.

Table 7 Selected chronic ecotoxicity data of chlorpropham for marine species.

Endpoints	NOEC [mg/L]	Remark	Reference
Echinodermata			
Lytechinus pictus	0.124	development	Holy, 1998

4 Derivation of ERLs for water

4.1 MPC_{water} and $MPC_{saltwater}$

4.1.1 Treatment of data for freshwater and marine species

According to the new WFD-guidance, statistical testing should be performed to detect whether there are differences in sensitivity between the freshwater and marine species. Where a lack of data makes a statistical analysis unworkable, the datasets for organic substances should be pooled. This is the case for chlorpropham, where the marine dataset contains only one endpoint. The combined dataset is used for risk limit derivation.

4.1.2 $MPC_{eco,\ water}$ and $MPC_{eco,\ saltwater}$ – ecotoxicity data

NOECs are available for eight species from five taxonomic groups covering at least three trophic levels[1]. The $MPC_{eco,\ water}$ is derived by putting an assessment factor of 10 to the lowest NOEC based on growth rate of 0.04 mg/L for the alga *Scenedesmus quadricauda*, resulting in an $MPC_{eco,\ water}$ of 0.004 mg/L = 4 µg/L.

The $MPC_{eco,\ saltwater}$ is derived on the basis of the same dataset. In addition to the data for freshwater species, there is one NOEC from a specifically marine taxonomic group (Echinodermata; NOEC 0.124 mg/L). In this case an assessment factor of 50 is applied to the lowest NOEC, resulting in an $MPC_{eco,\ saltwater}$ of 0.0008 mg/L = 0.8 µg/L.

4.1.3 $MPC_{sp,\ water}$ and $MPC_{sp,\ saltwater}$ – secondary poisoning

Since the BCF value is 144 L/kg, the criterion of BCF ≥ 100 L/kg is fulfilled and the MPC via secondary poisoning is derived. Detailed toxicity data for birds and mammals are presented in Annex 2, Table A2.4. All data originate from the DAR (EC, 2003b). The data on birds cannot be used, since no effects were observed at the highest concentration tested. With respect to the mammal studies, it should be noted that a number of endpoints in Table A2.4 refer to parameters such as changes in haematology or organ weights. The link of these endpoints to population level effects is not clear, according to the guidance relevant endpoints are mortality, growth and effects on reproduction. Those endpoints are listed in Table 8 below.

[1] For a decision on the height of the assessment factor, the WFD-guidance often refers to the number of trophic levels represented in the dataset. Especially for compounds with a specific mode of action, the use of this term may be complicating because species belonging to the same trophic level may differ greatly in sensitivity because of their different taxonomic position (e.g. crustaceans and insects in case of certain insecticides). When deciding on the AF, the question whether or not the potentially most sensitive taxonomic group is represented in the dataset is more relevant than the trophic level.

Table 8 Oral toxicity data for mammals

Species	Duration	NOAEC [mg/kg fd]	AF	MPC_{oral} [mg/kg fd]
Dog	28 d	20000	300	67
Dog	60 w	2000	30	67
Mouse	18 m	4150	30	138
Rat	28 d	3000	300	10
Rat	90 d	1000	90	11
Rat	90 d	6000	90	67
Rat	2 year	600	30	20
Rat	gestation day 6-15	4000	90[a]	44
Rat	gestation day 6-19	8000	90[a]	89
Rabbit	day 6-18 after mating	4163	90[a]	46

a: although involving short-term exposure, an assessment factor of 90 is used because the compound is administered during a critical phase in embryonic development

For rats, the NOAEC values from the 90-days studies (1000 and 6000 mg/kg fd) are higher than the NOAEC from the 2 year study (600 mg/kg fd), but the larger assessment factor for the 90-days studies leads to a lower MPC_{oral} in one case. In such a situation, preference is given to the study with the longest test duration and the lowest assessment factor. The $MPC_{oral,min}$ is therefore set to 20 mg/kg fd.

The $MPC_{sp,\ water}$ and $MPC_{sp,\ saltwater}$ are derived as follows:

- The $MPC_{oral,\ min}$ is 20 mg/kg fd.
- The BCF value for water organisms is 144 L/kg. The BMF_1 is 1 (INS-Guidance Table 12).
- Combining this input and using the default parameters as given in the INS-Guidance, the $MPC_{sp,\ water}$ is 20/ (144 x 1) = 0.14 mg/L = 140 µg/L (Eq. 13 of the INS-Guidance).
- The $MPC_{oral,min}$ as described above is used as a representative for the marine environment also. To account for the longer food chain in the marine environment, an additional biomagnification step is introduced (BMF_2). Since this factor is the same as the BMF_1 (= 1), the $MPC_{sp,\ saltwater}$ is equal to $MPC_{sp,\ water}$ = 0.14 mg/L = 140 µg/L. It is not expected that chlorpropham will accumulate in the pelagic food chain.

4.1.4 $MPC_{hh\ food,\ water}$ – human exposure

Chlorpropham is assigned R40, R48/22. According to the triggers as given in Table 17 of the INS-Guidance, the $MPC_{hh\ food,\ water}$ should be derived. The $MPC_{hh,\ food}$ is calculated from the ADI (0.05 mg/kg bw/d), a body weight of 70 kg and a daily fish consumption of 115 g and a maximum contribution of fish consumption to the ADI of 10%. The resulting $MPC_{hh,\ food}$ is 0.1 x 0.05 x 70 / 0.115 = 3.04 mg/kg fd. (see Eq. 15 of the INS-Guidance). Subsequently the $MPC_{hh\ food,\ water}$ is calculated using the BCF of 144 L/kg and BMF of 1 as 3.04 / (144 x 1) = 0.0211 mg/L = 21.1 µg/L (Eq. 16 of the INS-Guidance). The $MPC_{hh\ food,\ water}$ is valid for both the freshwater and the marine compartment.

4.1.5 Selection of the MPC_{water} and $MPC_{saltwater}$

The lowest of the three routes – direct ecotoxicity, secondary poisoning and human exposure via fish – is selected as the final MPC. For freshwater as well as the marine environment, direct ecotoxicity is the most critical route. The MPC_{water} is 0.004 mg/L = 4.0 µg/L, the $MPC_{saltwater}$ is 0.0008 mg/L = 0.8 µg/L.

4.2 $MPC_{dw, hh}$ – surface water for abstraction of drinking water

Chlorpropham is an organic pesticide. The drinking water standard according to Directive 98/83/EC is 0.1 µg/L. According to the WFD-guidance, a substance specific removal rate should be considered to derive the $MPC_{dw, hh}$. At present, such information is not available and water treatment is not taken into account. The $MPC_{dw, hh}$ is 0.1 µg/L.

4.3 $MAC_{eco, water}$ and $MAC_{eco, saltwater}$

L(E)C50 values are available for 16 species from six taxonomic groups including three trophic levels. The $MAC_{eco, water}$ is derived from the lowest acute toxicity value available: the EC50 of 0.43 mg/L for *Chlamydomonas eugametos*. An assessment factor of 10 can be applied, because the substance has a known mode of action with a broad spectrum of toxic action and thus representatives of the most sensitive taxonomic groups are included in the dataset. The $MAC_{eco,water}$ is 0.043 mg/L = 43 µg/L.

For indicative purposes, the derivation of a $MAC_{eco,water}$ via Species Sensitivity Distribution (SSD) was also investigated, although the dataset does not meet the criteria that are specified in the guidance. The number of taxa is lower than the minimum of eight that is required, and insects are not represented in the dataset. However, in view of the mode of toxic action insects are not expected to be particularly sensitive or insensitive. The LC50 for *Tubifex tubifex* was included in the data, although we are not sure whether testing was performed in water. *Tetrahymena* was also included, although the test was carried out in complex medium. The SSD with ETX had an accepted fit and using an assessment factor of 10, the resulting $MAC_{eco,water}$ was 73 µg/L. Although the dataset does not fulfil the requirements for ERL-derivation by means of an SSD, the outcome of this exercise supports the $MAC_{eco,water}$ derived by the assessment factor method.

The $MAC_{eco, saltwater}$ is derived on the basis of the combined dataset. Since there are no acute data from specific marine taxa, an assessment factor of 100 is applied to the lowest EC50. This results in an $MPC_{eco, saltwater}$ of 0.0043 mg/L = 4.3 µg/L.

4.4 NC_{water} and $NC_{saltwater}$

The NC_{water} is calculated by dividing the MPC_{water} by a factor of 100. The NC_{water} is 0.04 µg/L.
The $NC_{saltwater}$ is calculated by dividing the $MPC_{saltwater}$ by a factor of 100. The $NC_{saltwater}$ is 0.008 µg/L.

4.5 $SRC_{eco, water}$ and $SRC_{eco, saltwater}$

Since more than three long-term NOECs of all required trophic levels are available, the $SRC_{eco, water}$ is derived from the geometric mean of all available NOECs with an assessment factor of 1. The geometric mean is 0.48 mg/L. Therefore, the $SRC_{eco, water}$ is 0.48 mg/L = 480 µg/L. This value is also valid as $SRC_{eco, saltwater}$.

5 Conclusions

Based on the available information, environmental risk limits (ERLs) for chlorpropham in freshwater and saltwater are derived according to the methodology of the WFD and INS. An overview of the derived ERLs is presented in the table below. ERLs that are equivalent to water quality standards required under the WFD are indicated in bold.

Table 9 Environmental risk limits for chlorpropham in water

Environmental risk limit	**Value**	
	[mg/L]	**[µg/L]**
Freshwater		
$MPC_{eco, water}$	0.004	4.0
$MPC_{sp, water}$	0.14	140
$MPC_{hh\ food, water}$	0.0211	21
MPC_{water}	**0.004**	**4.0**
$MAC_{eco, water}$	**0.043**	**43**
NC_{water}	0.00004	0.04
$SRC_{eco, water}$	0.48	480
Surface water for drinking water production		
$MPC_{dw, hh}$	**100**	**0.1**
Saltwater		
$MPC_{eco, saltwater}$	0.0008	0.8
$MPC_{sp, saltwater}$	0.14	140
$MPC_{hh\ food, saltwater}$	0.0211	21
$MPC_{saltwater}$	**0.0008**	**0.8**
$MAC_{eco, saltwater}$	**0.0043**	**4.3**
$NC_{saltwater}$	0.000008	0.008
$SRC_{eco, saltwater}$	0.48	480

The Association of River Waterworks (RIWA) reports monitoring data for the rivers Rhine and Meuse. In 2009, chlorpropham was not detected on any location above the reporting limit (0.01 - 0.02 µg/L), except for Liege, where the monthly average in June was 0.031 µg/L (RIWA, 2009ab). In 2010, chlorpropham was not detected above the reporting limit at monitoring stations along the river Rhine (RIWA, 2010). According to the Bestrijdingsmiddelenatlas (www.bestrijdingsmiddelenatlas.nl), the average concentration of chlorpropham has declined from about 15 ng/L in 2001 to around 10 ng/L in 2009. In addition, there are no locations where the 90th percentile of the monitoring data exceeds the standard of 3.3 µg/L. The newly derived MPC_{water} is slightly higher, and will be compared with the average concentration. The available data thus indicate that the newly derived MPC and MAC for freshwater will not be exceeded. Monitoring data for saltwater are not available.

References

Reference list includes references used in the Annexes.

Bamdad M, Denier D, Bohatier J, Golière, C-A. 2000. Toxicity of the herbicide chlorpropham towards the freshwater ciliated protozoan *Tetrahymena pyriformis* GL. European Journal of Protistology 36: 319-325.

Caporiccio B, Tournamille J, Michel R. 1981. Etude de la toxicité aiguë de deux phénylcarbamates: le propham et le chloropropham. Comptes Rendus des Séances de la Société de Biologie 175: 496-500.

CTB. 2004. Internal summaries Gro-Stop 300 UL (dossier 3541).

Davis TD, Hardcastle WS. 1959. Biological assay of herbicides for fish toxicity. Weeds 7: 397-404.

EC. 2003a. Technical Guidance Document on risk assessment in support of Commission Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC), no. 1488/94 on risk assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Ispra, Italy: European Commission Joint Research Centre.

EC. 2003b. European Commission. Draft Assessment Report Chlorpropham. Vol B3, Sections B5 and B9.

EC. 2011. Technical guidance for deriving environmental quality standards. Final draft, January, 2011.

El-Dib MA, Aly OA. 1976. Persistence of some phenylamide pesticides in the aquatic environment - III. Biological degradation. Water Research 10: 1055-1059.

Grimwood M, Murgatroyd C, Smith C. 1995. Proposed environmental quality standards for chlorpropham in water. Final report to the Department of the Environment. DoE 3841/1.

Hess FD. 1980. A *Chlamydomonas* algal bioassay for detecting growth inhibitor herbicides. Weed Science 28: 515-520.

Hansch C, Leo A, Hoekman D. 1995. Exploring QSAR. Hydrophobic, electronic, and steric constants. ACS Professional Reference Book. Washington DC: ACS.

Holy J. 1998. Chlorpropham [isopropyl N-(3-chlorophenyl)carbamate] disrupts microtubule organization, cell division, and early development of sea urchin embryos. Journal of Toxicology and Environmental Health, Part A 54: 319-333.

Hooftman, RN. 2004. Chorpropham. TNO report CTB-2004-001-C (submitted to CTB).

Klimisch HJ, Andreae M, Tillman U. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology. 25: 1-5.

Kosanke GJ, Schwippert WW, Beneke TW. 1988. The impairment of mobility and development in freshwater snails (*Physa fontinalis* and *Lymnea stagnalis*) caused by herbicides. Comp. Biochemistry and Physiology 2: 373-379.

Kuhl R, Wydra V. 2009a. Acute toxicity of Chlorpropham 120 g/L EW to *Daphnia magna* in a static 48-hour immobilisation test. IBACON project 51222220.

Kuhl R, Wydra V. 2009b. Toxicity of Chlorpropham 120 g/L EW to *Pseudokirchneriella subcapitata* in an algal growth inhibition test. IBACON project 51221210.

L'Haridon J. 2003a. Acute toxicity in *Daphnia magna* under static conditions. CIT Project no. 24302 EAD.

L'Haridon J. 2003b. Acute toxicity in the *rainbow trout* under static conditions. CIT Project no. 24303 EAP.
L'Haridon J. 2003c. Algal inhibition test. CIT Project no. 24301 EAA.
Lepper F. 2005. Manual on the Methodological Framework to Derive Environmental Quality Standards for Priority Substances in accordance with Article 16 of the Water Framework Directive (2000/60/EC). Schmallenberg, Germany: Fraunhofer-Institute Molecular Biology and Applied Ecology. 47 pp.
Maule A, Wright SJL. 1983. Physiological effects of chlorpropham and 3-chloroaniline on some cyanobacteria and a green alga. Pesticide Biochemistry and Physiology 19: 196-202.
Nishiuchi Y. 1974. Control effect of pesticides to duckweed. Bulletin of the Agricultural Chemicals Inspectorate 14: 69-72.
Priestly SL, Mullee DM. 2010a. CIPC 120 G/L AL: Acute toxicity to rainbow trout (*Oncorhynchus mykiss*). Harlan Laboratories Ltd, project no. 0722/0112.
Priestly SL, Mullee DM. 2010b. CIPC 120 G/L AL: Acute toxicity to *Daphnia magna*. Harlan Laboratories Ltd, project no. 0722/10110.
RIWA. 2009a. Jaarrapport 2009. de Rijn. Nieuwegein, the Netherlands: Association of River Waterworks.
RIWA. 2009b. Meetgegevens Maas. http://www.riwa-maas.org/nl/kwaliteitsgegevens_hist_kwgegevens.php
RIWA. 2010. Jaarrapport 2010. de Rijn. Nieuwegein, the Netherlands: Association of River Waterworks.
Sumida S, Yoshida R, Ueda M. 1977. Studies of pesticide effects on *Chlorella* metabolism III. Effect of isopropyl 3-chlorocarbanilate (chlorpropham) on cell cycle and biosynthesis. Plant and Cell Physiology 18: 9-16.
Van der Veen MC. 2008. Chloorprofam. RIVM Report 11593A01 (submitted to Ctgb).
Van Vlaardingen PLA, Verbruggen EMJ. 2007. Guidance for the derivation of environmental risk limits within the framework of "International and national environmental quality standards for substances in the Netherlands" (INS). Bilthoven, the Netherlands: RIVM. Report no. 601782001. 146 pp.
VROM. 1999. Environmental risk limits in the Netherlands. A review of environmental quality standards and their policy framework in the Netherlands. The Hague, the Netherlands: Ministry of Housing, Spatial Planning and the Environment.
VROM. 2004. (Inter)nationale Normen Stoffen. Den Haag, the Netherlands: Ministerie van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer.
Vryenhoef H, Mullee DM. 2009. CIPC 120 G/L AL: Algal growth inhibition test. Harlan Laboratories Ltd, project no. 0722/0111.

List of abbreviations

ADI	Acceptable Daily Intake
BCF	Bioconcentration Factor
BMF	Biomagnification Factor
EC_x	Concentration at which x% effect is observed
ERL	Environmental Risk Limit
INS	International and National Environmental Quality Standards for Substances in the Netherlands
LC_{50}	Concentration at which 50% mortality is observed
MAC_{eco}	Maximum Acceptable Concentration for ecosystems
$MAC_{eco, water}$	Maximum Acceptable Concentration for ecosystems in freshwater
$MAC_{eco, saltwater}$	Maximum Acceptable Concentration for ecosystems in the saltwater compartment
Marine species	Species that are representative for marine and brackish water environments and that are tested in water with salinity > 0.5 ‰.
MPC	Maximum Permissible Concentration
MPC_{water}	Maximum Permissible Concentration in freshwater
$MPC_{saltwater}$	Maximum Permissible Concentration in the saltwater compartment
$MPC_{eco, water}$	Maximum Permissible Concentration in freshwater based on ecotoxicological data
$MPC_{eco, saltwater}$	Maximum Permissible Concentration in the saltwater compartment based on ecotoxicological data
$MPC_{sp, water}$	Maximum Permissible Concentration in freshwater based on secondary poisoning
$MPC_{sp, saltwater}$	Maximum Permissible Concentration in the saltwater compartment based on secondary poisoning
$MPC_{hh\ food, water}$	Maximum Permissible Concentration in freshwater and saltwater based on consumption of fish and shellfish by humans
$MPC_{dw, hh}$	Maximum Permissible Concentration in water used for abstraction of drinking water
NC	Negligible Concentration
NC_{water}	Negligible Concentration in freshwater
NOEC	No Observed Effect Concentration
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
SRC_{eco}	Serious Risk Concentration for ecosystems
$SRC_{eco, water}$	Serious risk concentration for freshwater and saltwater ecosystems
TGD	Technical Guidance Document
WFD	Water Framework Directive (2000/60/EC)

Annex 1 Detailed BCF data

Legend to column headings	
Purity	refers to purity of active substance or content of active in formulation; ag = analytical grade
Test type	S = static; Sc = static closed; R = renewal; F = flow through; CF = continuous flow; IF = intermittent flow system
Test water	am = artificial medium; dtw = dechlorinated tap water; dw = deionised/dechlorinated/distilled water; nw= natural water; rw = reconstituted water; rtw = reconstituted tap water; tw = tap water
T	temperature
Ri	Reliability index according to Klimisch et al. (1997); asterisk indicates citation

Table A1.1. Bioconcentration factors for chlorpropham

Species	Species properties	Purity	Analysis	Test type	Test water	pH	Hardness $CaCO_3$	T	Exp. time	Exp. conc.	BCF (based on chlorpropham)	BCF type	Method	Ri	Notes	Ref.
		[%]					[mg/L]	[°C]		[mg/L]	[L/kg ww]					
Pisces																
Oncorhynchus mykiss	1.5- 2.5 g, 4-6 cm	>97	LSC; chlorpropham	F	tw				60 d	0.005	133	whole fish	kinetics	2	1,2,3,4,5,6	EC, 2003b (Caldwell, 2001)
Oncorhynchus mykiss	1.5- 2.5 g, 4-6 cm	>97	LSC; chlorpropham	F	tw				60 d	0.050	154	whole fish	kinetics	2	1,2,3,4,5,6	EC, 2003b (Caldwell, 2001)

Notes
1 U-^{14}C label in the phenyl ring.
2 Depuration time 14 days.
3 According to OECD guidance.
4 The water temperature, hardness and pH were not reported in the summary in the DAR.
5 The BCF values for whole fish based on total radioactivity were: 5 µg/L: 192 L/kg ww and 50 µg/L: 195 L/kg ww.
6 The lipid content of the fish was approx. 5.5%. Therefore no correction for lipid content on the BCF was carried out.

Annex 2 Detailed ecotoxicity data

Legend to column headings	
A	test water analysed Y(es)/N(o)
Test type	S = static; Sc = static closed; R = renewal; F = flow through; CF = continuous flow; IF = intermittent flow system
Purity	refers to purity of active substance or content of active in formulation; ag = analytical grade
Test water	am = artificial medium; dtw = dechlorinated tap water; dw = deionised/dechlorinated/distilled water; nw= natural water; rw = reconstituted water; rtw = reconstituted tap water; tw = tap water
T	temperature
Ri	Reliability index according to Klimisch et al. (1997); asterisk indicates citation

Table A2.1. Acute toxicity of chlorpropham to freshwater organisms

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 a.s./L]	Ri	Notes	Ref.
Bacteria																
Bacillus cereus	gram positive	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Escherichia coli	gram negative	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Klebsiella aerogenes	gram negative	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Pseudomonas aeruginosa	gram negative	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Sarcina urea	gram positive	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Staphylococcus albus	gram positive	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Streptococcus faecalis	gram positive	N	S	a.s.	ag	am		37		16 h	NOEC	growth inhibition	≥10	3	20	El-Dib and Aly, 1976
Cyanobacteria																
Anabaena cylindrica		N	S	a.s.	99	am		30		80 min	EC50	nitrogenase inhibition	12.9	3	14	Maule and Wright, 1983
Anacystis nidulans		N	S	a.s.	99	am		30		10 min	EC50	oxygen production	13.2	3	13	Maule and Wright, 1983

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 a.s./L]	Ri	Notes	Ref.
Algae																
Chlamydomonas reinhardii		N	S	a.s.	99	am		25		10 min	EC50	oxygen production	30.5	3	13	Maule and Wright, 1983
Chlamydomonas eugametos	10^5 cells/mL	N	S	a.s	tg	am	6.7	25		48 h	EC50	cell density	0.43	2	1, 22	Hess, 1980
Chlorella ellipsoidea		N	S	a.s.		am		24		6 d	EC50	growth rate	0.50	3	21	Sumida et al., 1977
Desmodesmus subspicatus	5 x 10^4 cells/mL	N	S	Chlorpropham 1% DP	1.0	am		23 ± 2	243	72 h	EC50	growth rate	>1.0	4	16,19	Van der Veen, 2008 (Rudolf, 2005)
Desmodesmus subspicatus	5 x 10^4 cells/mL	N	S	Chlorpropham 1% DP	1.0	am		23 ± 2	243	72 h	EC50	biomass (AUGC)*	>1.0	4	16,19	Van der Veen, 2008 (Rudolf, 2005)
Desmodesmus subspicatus	6.2 x 10^3 cells/mL	Y	S	Chlorpropham 1% DP	1.0	am	8.8-9.4	23 ± 2	243	72 h	EC50	growth rate	2.1	4	4,17,19	Van der Veen, 2008 (Rudolf, 2005)
Desmodesmus subspicatus	6.2 x 10^3 cells/mL	Y	S	Chlorpropham 1% DP	1.0	am	8.8-9.4	23 ± 2	243	72 h	EC50	biomass (AUGC)*	0.77	4	4,17,19	Van der Veen, 2008 (Rudolf, 2005)
Desmodesmus subspicatus	4.4 x 10^3 cells/mL	Y	S	CIPC 120 G/L AL	11.7	am	7.1-7.3	24 ± 1	-	72 h	EC50	growth rate	3.04	2	1,4	Vryenhoef and Mullee, 2009
Desmodesmus subspicatus	4.4 x 10^3 cells/mL	Y	S	CIPC 120 G/L AL	11.7	am	7.1-7.3	24 ± 1	-	72 h	EC50	yield	2.34	2	1,4	Vryenhoef and Mullee, 2009
Navicula pelliculosa	1 x 10^4 cells/mL	Y	S	a.s.	98.8	am	7.3-7.5	23 ± 2	-	96 h	EC50	growth rate	1.65	2	4,7	EC, 2003b (Firth, 2001)
Navicula pelliculosa	1 x 10^4 cells/mL	Y	S	a.s.	98.8	am	7.3-7.5	23 ± 2	-	96 h	EC50	biomass (AUGC)*	1.00	2	4,7	EC, 2003b (Firth, 2001)
Pseudokirchneriella subcapitata		N	S	a.s.	99.3	am	8.0-8.8	22.5	-	96 h	EC50	growth rate	3.3	2	3,4	EC, 2003b (Hanstveit, 1989)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlor-IPC 400 EC	40	am	7.0-8.1	23 ± 2	-	96 h	EC50	biomass (AUGC)*	1.1	2	2,4,6	EC, 2003b (Migchielsen, 2001)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlor-IPC 400 EC	40	am	7.0-8.1	23 ± 2	-	96 h	EC50	growth rate	1.9	2	2,4,6	EC, 2003b (Migchielsen, 2001)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlorproham 400 G/L EC	40.6	am	7.5 ± 0.3	23	34	72 h	EC50	growth rate	2.14	2	6,4	Van der Veen, 2008 (L'Haridon, 2005)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlorproham 400 G/L EC	40.6	am	7.5 ± 0.3	23	34	72 h	EC50	biomass (AUGC)*	0.869	2	6,4	Van der Veen, 2008 (L'Haridon, 2005)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 300 HN	31.2	am	7.8-8.2	23	24	72 h	EC50	growth rate	>1.1	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)

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 a.s./L]	Ri	Notes	Ref.
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 300 HN	31.2	am	7.8-8.2	23	24	72 h	EC50	biomass (AUGC)*	>1.1	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP EC (300)	31.2	am	8.1-8.3	21-23	24	72 h	EC50	growth rate	>1.4	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP EC (300)	31.2	am	8.1-8.3	21-23	24	72 h	EC50	biomass (AUGC)*	>1.4	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 120 EW	11.8	am	7.7-9.0	21.5-23	-	72 h	EC50	growth rate	0.90	2	6,4	Hooftman, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 120 EW	11.8	am	7.7-9.0	21.5-23	-	72 h	EC50	biomass (AUGC)*	0.49	2	6,4	Hooftman, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Gro-Stop Innovator (300 UL)	32.4	am	7.7-8.3	22-23	-	72 h	EC50	biomass (AUGC)*	1.1	2	6,4	CTB, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Gro-Stop Innovator (300 UL)	32.4	am	7.7-8.3	22-23	-	72 h	EC50	growth rate	1.8	2	6,4	CTB, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Nogerma Vloeibaar 500	49.3	am	7.4-8.6	23-23.6	-	72 h	EC50	growth rate	1.36	2	4,7	L'Haridon, 2003c
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Nogerma Vloeibaar 500	49.3	am	7.4-8.6	23-23.6	-	72 h	EC50	biomass (AUGC)*	0.86	2	4,7	L'Haridon, 2003c
Pseudokirchneriella subcapitata	0.5 x 10^4 cells/mL	Y	S	Chlorpropham 120 g/L EW	11.7	am	8.0-9.6	23-24	24	72 h	EC50	growth rate	1.13	2	6,4	Kuhl and Wydra, 2009b
Pseudokirchneriella subcapitata	0.5 x 10^4 cells/mL	Y	S	Chlorpropham 120 g/L EW	11.7	am	8.0-9.6	23-24	24	72 h	EC50	biomass (AUGC)*	0.62	2	6,4	Kuhl and Wydra, 2009b
Scenedesmus quadricauda	-	N	S	Aliacine 400EC	40	am	8.0-8.8	25	-	72 h	EC50	growth rate	0.45	3	4,8	EC, 2003b (Kita, 1997)
Protozoa																
Tetrahymena pyriformis	1 x 10^4 cells/mL	N	S	a.s.		am		28		6 h	EC50	growth rate	0.69	3	10	Bamdad et al., 2000
Macrophyta																
Lemna minor	4 fronds/plant	Y	R	a.s.	>97.5	am	6.5-7.7	25 ± 2	-	7 d	EC50	growth rate	3.82	2	1,4,9	EC, 2003b (Bogers, 2000)
Lemna minor	4 fronds/plant	Y	R	a.s.	>97.5	am	6.5-7.7	25 ± 2	-	7 d	EC50	biomass	1.67	2	1,4,9	EC, 2003b (Bogers, 2000)

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 a.s./L]	Ri	Notes	Ref.
Lemna minor	4 fronds/plant	Y	R	a.s.	98.8	am	6.6-10.4	25 ± 2	-	14 d	EC50	growth rate	3.14	2	4,7	EC, 2003b (Firth, 2001)
Lemna minor	4 fronds/plant	Y	R	a.s.	98.8	am	6.6-10.4	25 ± 2	-	14 d	EC50	biomass	2.65	2	4,7	EC, 2003b (Firth, 2001)
Mollusca																
Lymnea stagnalis	eggs	N	S	a.s.	pa					20 d	EC50	egg development	1.5	3	15	Kosanke et al., 1988
Annelida																
Tubifex tubifex		N		a.s.			7.5	20		48 h	LC50	mortality	3.8	4	1,24	Grimwood et al., 1995 (Applegate et al., 1957)
Crustacea																
Daphnia magna	<24 h	N	S	a.s.	99.3	rw	7.7-8.1	20	262	48 h	EC50	mobility	4.0	2	4	EC, 2003b (Adema and Van Drongelen-Sevenhuijsen 1989)
Daphnia magna	<24 h	Y	S	a.s.	98.1	rw	8.0-8.5	20	148	48 h	EC50	mobility	3.7	2	4,7	EC, 2003b (Sved et al., 1992)
Daphnia magna		N	S	Aliacine 400EC	40	rw	7.3	21	152	48 h	EC50	mobility	8.4	2	4	EC, 2003b (Kita, 1997)
Daphnia magna	Neonates	Y	S	Chlor-IPC 400 EC	40	rw	7.3-7.9	20-21	-	48 h	EC50	mobility	2.6	2	2,4,6	EC, 2003b (Migchielsen, 2001)
Daphnia magna		N	S	a.s.		rw			-	24 h	EC50	mobility	6.5	3	11	Caporiccio et al., 1981
Daphnia magna	<24 h	Y	S	Chlorpropham 1% DP	1.0	rw	7.7-8.1	20 ± 2	250	48 h	EC50	mobility	>0.62	4	4,7,19	Van der Veen, 2008 (Rudolf, 2005)
Daphnia magna	<24 h	Y	S	Gro-STOP 300 HN	31.2	rw	8.2 ± 0.2	20 ± 2	250	48 h	EC50	mobility	2.3	2	4,7	Van der Veen, 2008 Bogers and Van der Waard, 1996)
Daphnia magna	<24 h	Y	S	Gro-STOP EC (300)	30	rw	8.1 ± 0.2	18-20	250	48 h	EC50	mobility	4.3	2	6,4	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Daphnia magna	<24 h	Y	R	Chlorpropham 400 G/L EC	40.6	rw	8.1-8.7	20 ± 2	306	48 h	EC50	mobility	3.59	2	6,4	Van der Veen, 2008 (l'Haridon, 2005)
Daphnia magna	<24 h	Y	S	GRO-STOP 120 EW	11.8	rw	8.0-8.1	18.6-19.6	250	48 h	EC50	mobility	0.47	2	6,4	Hooftman, 2004 (Migchielsen, 2002)

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 a.s./L]	Ri	Notes	Ref.
Daphnia magna	<24 h	Y	S	Gro-Stop 300 UL	32.4	rw	7.9-8.2	18-22	-	48 h	EC50	mobility	2.5	2	6,4	CTB, 2004 (Migchielsen, 2002)
Daphnia magna	6 - 24 h	Y	S	Nogerma Vloeibaar 500	49.3	rw	7.9-8.2	19.5-20.3	255-272	48.h	EC50	mobility	0.98	2	4,7	L'Haridon, 2003a
Daphnia magna	<24 h	Y	S	CIPC 120 G/L AL	11.7	rw	7.8-8.0	21-22	250	48 h	EC50	mobility	3.51	2	6,4	Priestly and Mullee, 2010b
Daphnia magna	6-22 h	Y	S	Chlorpropham 120 g/L EW	11.7	rw	7.8-8.0	21	250	48 h	EC50	mobility	0.37	2	6,4	Kuhl and Wydra, 2009a
Pisces																
Cyprinus carpio	2.9 cm, 0.89 g	Y	R	Chlor-IPC 400 EC	40		7.0-7.5	21-22	250	96 h	LC50	mortality	5.3	2	2,4,6	EC, 2003b (Migchielsen, 2001)
Cyprinus carpio	7.5 cm	N	S	Aliacine 400EC	40		7.3	21	109	96 h	LC50	mortality	9.2	2	4	EC, 2003b (Kita,1997)
Cyprinus carpio	2.3 ± 0.24 cm, 0.33 ± 0.14 g	Y	S	GRO-STOP 120 EW	11.8	rw	7.4-8.2	20.5-21.4	250	96 h	LC50	mortality	2.4	2	6,4	Hooftman, 2004 (Migchielsen, 2002)
Cyprinus carpio	2.3 cm, 0.15 g	Y	S	Gro-Stop 300 UL	32.4	rw	7.2-8.1	21	250	96 h	LC50	mortality	11	3	4, 18	CTB, 2004 (Migchielsen, 2002)
Danio rerio	2.5 cm, 0.23 g	N	R	a.s.	99.3	rw	7.5-8.2	25	262	96 h	LC50	mortality	13.4	2	3,4	EC, 2003b (Adema and Van Drongelen-Sevenhuijsen, 1989)
Lepomis macrochirus	7.5-12.5 cm	N	S	a.s.		nw	6.6-7.4	25 ± 1	25-30	48 h	LC50	mortality	12	2	1	Davis and Hardcastle,1959
Micropterus salmoides	7.5-12.5 cm	N	S	a.s.		nw	6.6-7.4	25 ± 1	25-30	48 h	LC50	mortality	10	2	1	Davis and Hardcastle,1959
Oncorhynchus mykiss	4.7 cm, 1.4 g	Y	S	a.s.	99.3	rw	8.3	16	230	96 h	LC50	mortality	7.5	2	1,2,4,5	EC, 2003b (Bogers, 1993)
Oncorhynchus mykiss	5 ± 1 cm	Y	S	Chlorpropham 1% DP	1.0	tw	7.8-8.2	15 ± 2	94	96 h	LC50	mortality	>0.42	4	4,7,19	Van der Veen, 2008 (Rudolf, 2007)
Oncorhynchus mykiss	4.0-5.5 cm, 0.95 g	Y	R	Chlorpropham 400 G/L EC	40.6	dtw	7.7-8.0	13.6-14.5	153-159	96 h	LC50	mortality	3.91	2	6,4	Van der Veen, 2008 (L'Haridon, 2005)
Oncorhynchus mykiss	5.6 ± 0.6 cm, 2.55 ± 1 g	Y	S	Gro-Stop 300 HN	31.2	tw	8.0-8.7	14 ± 1	230	96 h	LC50	mortality	6.2	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Oncorhynchus mykiss	4.91 cm, 1.97± 0.2 g	Y	S	Gro-STOP EC (300)	30	tw	7.7-8.7	14.4-15.3	230	96 h	LC50	mortality	9.0	2	4,7	Van der Veen, 2008 (Bogers, 1996)
Oncorhynchus mykiss	4.2 cm, 0.77 g	Y	S	Nogerma Vloeibaar 500	49.3	dtw	7.5-8.1	13.3-14.3	156-161	96 h	LC50	mortality	5.92	2	4,7	L'Haridon, 2003b

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 a.s./L]	Ri	Notes	Ref.
Oncorhynchus mykiss	4.2 cm, 0.93 g	Y	S	CIPC 120 G/L AL	11.7	dtw	7.2-8.1	13-14	140	96 h	LC50	mortality	4.56	2	4,7	Priestly and Mullee, 2010a
Salvelinus fontinalis	7.4 cm	N	S	Aliacine 400EC	40		7.3	15	109	96 h	LC50	mortality	8.8	2	4	EC, 2003b (Kita,1997)
Amphibia																
Pleurodeles waltlii	larvae	N	S	a.s.		rw				24 h	LC50	mortality	20	2	12	Caporiccio et al., 1981
Triturus helveticus	adults	N	S	a.s.		rw				24 h	LC50	mortality	6.5	2	12	Caporiccio et al., 1981
Xenopus laevis	larvae	N	S	a.s.		rw				24 h	LC50	mortality	8.5	2	12	Caporiccio et al., 1981

* AUGC = Area Under the Growth Curve

Notes
1 Results based on nominal concentrations.
2 The mean measured concentrations were > 80% of the nominal concentrations.
3 DMSO was used as vehicle.
4 According to OECD guidance.
5 Glycerine PEG ricinoleate was used as vehicle.
6 Results based on nominal concentrations; drop in concentration < 20% during the experiment.
7 Results based on mean measured concentrations.
8 The report was very deficient in data. Replicate results were not reported, therefore no correct EC50 could be calculated.
9 Test solutions were refreshed after 2 and 4 days. In some test solutions with low concentration (0.046 – 0.46 mg/L) the concentration dropped under 67% in the aged solutions. Nevertheless, it was accepted that results were based on nominal concentrations.
10 The ciliate was grown axenically in PPYS medium. Cell density was counted with a Coulter counter. The EC50 was determined by the evaluator from the graphical results of the author. Since the org. C content of the medium was too high, an Ri3 was given.
11 According to AFNOR T90 -301. Test duration too short. Ri = 3
12 20 larvae or 10 adults were kept in 500 mL of water.
13 6-Day old cultures were harvested and suspensions of the cells were incubated with NaHCO3 in the presence of chlorpropham. The oxygen formation was followed for 5-10 min in illuminated suspensions. The exposure period was too short, therefore an Ri=3 was given.
14 6-Day old cultures were harvested and suspensions of the cells were incubated with acetylene. The nitrogenase activity was measured by GLC determination of ethylene production during 80 min.
15 The author gives an EC50 of 15 mg/L but from the data an EC50 = 1.5 mg/L seems more appropriate. Insufficient experimental data are given (no temperature, pH, type of test solution) (Ri = 3).
16 Chlorpropham concentration and pH not measured.
17 Test results based on mean measured concentrations.
18 No concentration measurements were done at t=96 h. A reliable estimation of the LC50 was not possible (Ri = 3).
19 Data in the report were expressed in terms of formulation. Content of chlorpropham in formulation was considered to be too low for extrapolation from 1% to 100% a.s. The data are not used for MAC derivation (Ri = 4).
20 Tested in nutrient broth (therefore Ri = 3). At 10 mg/L no inhibitory or toxic effect was observed.

21 Fifty mL of nutrient solution with 2% glucose was inoculated with 0.5 mL pre-cultured cell suspension. Cells were grown in the presence of chlorpropham for 6 days at 200 lx. The increase in cell density was less than 16 x in 3-4 days. The amount of light and the growth rate was considered to be too small for reliable results (Ri = 3). The evaluator calculated the EC50 value from the graphical results of the author.
22 Test conducted in shake cultures. Cell numbers were determined with a Coulter counter.
23 The test was probably carried out in water.
24 It is not sure whether testing was performed in water. Ri = 4.

Table A2.2. Chronic toxicity of chlorpropham to freshwater organisms

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 a.s./L]	Ri	Notes	Ref.
Algae																
Desmodesmus subspicatus	6.2 x 10^3 cells/mL	Y	S	Chlorpropham 1% DP	1.0	a.m.	8.8-9.4	23 ± 2	243	72 h	NOEC	growth rate	0.18	4	4,7,13	Van der Veen, 2008 (Rudolf, 2005)
Desmodesmus subspicatus	4.4 x 10^3 cells/mL	Y	S	CIPC 120 G/L AL	11.7	am	7.1-7.3	24 ± 1	-	72 h	NOEC	growth rate, yield	1.17	2	6,4	Vryenhoef and Mullee, 2009
Navicula pelliculosa	1 x 10^4 cells/mL	Y	S	a.s.	98.8	am	7.3-7.5	23 ± 2	-	96 h	NOEC	growth rate, biomass	0.702	2	4,7	EC, 2003b (Firth, 2001)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlor-IPC 400 EC	40	am	7.0-8.1	23 ± 2	-	96 h	NOEC	growth rate, biomass	0.46	2	4,6	EC, 2003b (Migchielsen, 2001)
Pseudokirchneriella subcapitata	-	N	S	a.s.	99.3	am	8.0-8.8	22.5	-	96 h	NOEC	biomass	0.1	2	3,4,5	EC, 2003b (Hanstveit, 1989)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Chlorproham 400 G/L EC	40.6	am	7.5 ± 0.3	23	34	72 h	NOEC	growth rate, biomass	0.197	2	6,4	Van der Veen, 2008 (L'Haridon, 2005)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 300 HN	31.2	am	7.8-8.2	23	24	72 h	NOEC	growth rate, biomass	0.32	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP EC (300)	31.2	am	8.1-8.3	21-23	24	72 h	NOEC	growth rate, biomass	0.74	2	4,7	Van der Veen, 2008 (Bogers and Van der Waard, 1996)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	GRO-STOP 120 EW	11.8	am	7.7-9.0	21.5-23	-	72 h	NOEC	growth rate	0.23	2	6,4	Hooftman, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Gro-Stop Innovator (300 UL)	32.4	am		22-23	-	72 h	NOEC	growth rate	0.83	2	6,4	Migchielsen, 2002 (CTB, 2004)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Gro-Stop Innovator (300 UL)	32.4	am		22-23	-	72 h	NOEC	biomass	0.46	2	6,4	CTB, 2004 (Migchielsen, 2002)
Pseudokirchneriella subcapitata	1 x 10^4 cells/mL	Y	S	Nogerma Vloeibaar 500	49.3	am	7.4-8.6	23-23.6	-	72 h	NOEC	growth rate, biomass	0.36	2	4,7	L'Haridon, 2003c
Pseudokirchneriella subcapitata	0.5 x 10^4 cells/mL	Y	S	Chlorpropham 120 g/L EW	11.7	am	8.0-9.6	23-24	24	72 h	NOEC	growth rate, biomass	0.117	2	6,4	Kuhl and Wydra, 2009b
Scenedesmus quadricauda		N	S	Aliacine 400EC	40	am	8-8.8	25	-	72 h	NOEC	cell density	0.04	2	4,8	EC, 2003b (Kita, 1997)
Macrophyta																
Lemna minor	4 fronds /plant	Y	R	a.s.	>97.5	am	6.5-7.7	25 ± 2	-	7 d	NOEC	biomass	0.46	2	4,9	EC, 2003b (Bogers, 2000)

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 a.s./L]	Ri	Notes	Ref.
Lemna minor	4 fronds/plant	Y	R	a.s.	98.8	am	6.6-10.4	25 ± 2	-	14 d	NOEC	growth rate, biomass	1.61	2	4,7	EC, 2003b (Firth, 2001)
Lemna paucicostata		N	S	EC formulation	40(?)	am		25	-	7 d	NOEC	growth	4	3	12	Nishiuchi, 1974
Crustacea																
Daphnia magna	<24 h	Y	R	a.s.	98.1	rw	7.6-8.4	20	-	21 d	NOEC	reproduction	0.45	3	4,10	EC, 2003b (Bogers, 1995)
Daphnia magna		Y	R	a.s.	97.7	rw	7.6-8.7	20-21	186	21 d	NOEC	reproduction	1.0	2	6,4	EC, 2003b (Hooftman,1999)
Pisces																
Danio rerio	fertilised eggs	Y	R	a.s.	97.7	rw	7.8-8.4	25 ± 1	186	34 d	NOEC	larval survival	0.32	2	1,2,4,11	EC, 2003b (Hooftman,1999)

Notes
1 Results based on nominal concentrations.
2 *t*-Butyl alcohol was used as vehicle.
3 DMSO was used as vehicle.
4 According to OECD guidance.
5 Growth at 0.32 mg/L was significantly inhibited. Therefore a NOEC of 0.1 mg/L is selected as endpoint value.
6 Results based on nominal concentrations; drop in concentration < 20% during the experiment.
7 Results based on mean measured concentrations.
8 Growth at 0.32 mg formulation/L was inhibited for 30%.
9 Test solutions were refreshed after 2 and 4 days. In some test solutions with low concentration (0.046 – 0.46 mg/L) the concentration dropped under 67% in the aged solutions. Nevertheless, it was accepted that results were based on nominal concentrations.
10 There are several deficiencies in the test. Ten test animals per treatment instead of forty (OECD Guideline 202). In view of this low number of test animals, the statistical analysis on mortality data is considered not relevant. From the available data a nominal NOEC for reproduction of 0.45 mg/L could be derived. These results are however not reliable and not useful for risk evaluation.
11 ELS test.
12 The content of the formulation was not reported (Ri = 3).
13 Data in the report were expressed in terms of formulation. Content of chlorpropham in formulation was considered to be too low for extrapolation from 1% to 100% a.s. The data are not used for MAC derivation (Ri = 4).

Table A2.3. Chronic toxicity of chlorpropham to marine organisms

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Salinity [‰]	Exp. time	Criterion	Test endpoint	Value [mg a.s./L]	Ri	Notes	Ref.
Echinodermata																
Lytechinus pictus	fertilised eggs	N	S	a.s.		am		18		8 h	NOEC	aberrant mitotic spindles, cytoskeletal and developmental deficits	0.124	2	1	Holy, 1998

Notes

1 Eggs were exposed to 0.124, 1.24 and 12.4 mg a.s./L in artificial seawater. No EC50 could be derived because only qualitative data were available. Due to the life stage of the organism the results can be considered as a chronic test result.

Table A2.4. Oral toxicity of chlorpropham to birds and mammals

Species	Species properties	Test compound	Purity [%]	Application route	Exp. Time	Criterion	Test endpoint	Value [mg a.s./kg diet]	Ri	Notes	Ref.
Aves											
Colinus virginianus		a.s.	98.1	diet	5 d	LC50	mortality	>5170	2	1	EC, 2003b (Campbell and Lynn, 1992)
Coturnix coturnix japonica		a.s.	98.6	diet	5 d	LC50	mortality	>5000	2	1	EC, 2003b (Van Dreumel, 1997)
Colinus virginianus	7 months old, ♀,♂	a.s.	98.8	diet	22 w	NOEC	reproduction	≥1000	2	4	EC, 2003b (Johnson, 2001)
Mammalia											
Dog	Beagle,♀, ♂	a.s.	98.6	diet	14 d	NOEC	organ weights, haematology clinical signs	5000 ≥ 25000	2	1,4	EC, 2003b (Schoenmaker and Nesselrooy, 1998)
Dog	Beagle, ♀, ♂	a.s.	97.1	diet	28 d	NOEC	spleen weight, thyroid activity food consumption, weight	200 20000	2	4,5	EC, 2003b (Wedig, 1990)
Dog	Beagle, ♀,♂	a.s.	98.6	capsule	90 d	NOEC	blood and organ changes body weight gain	1000 ≥ 25000	2	1,4	EC, 2003b (Schoenmakers and Frieling,1998)
Dog	Beagle, ♀,♂	a.s.	96.2	diet	60 w	NOEC	effects on thyroid body weight gain	200 2000	2	4,5,8	EC, 2003b (Wedig, 1992)
Mouse	♀,♂	a.s.	96.2/97.1	diet	90 d	NOEC	blood, reticulocytes body weight	1743 ≥ 3486	2	5,6	EC, 2003b (Krohmer, 1996)
Mouse	♀,♂	a.s.	98.6	diet	90 d	NOEC	increased met-Hb and Heinzbodies body weight gain	<1000 ≥ 300	2	1	EC, 2003b (Jonker, 1998)
Mouse	CD1 albino, ♀,♂	a.s.	96.2	diet	18 m	NOEC	changes in spleen and bone-marrow mortality	830 4150	2	1,6,9	EC, 2003b (Botta, 1992; Krohmer, 1992)
Rabbit	New Zealand White,♀	a.s.	98.6	gavage	d 6-18 after mating	NOEC	maternal decreased food consumption and mortality, increased spleen weight; slightly retarded foetal weight and ossification	8325	2	1,3	EC, 2003b (Waalkens-Berendsen, 1998)
Rabbit	New Zealand White,♀	a.s.		gavage	d 6-18 after mating	NOEC	maternal decreased food consumption embryotoxicity	8325 4163	2	1,3	EC, 2003b (James et al., 1983)
Rat	Wistar, ♀,♂	a.s.	98.6	diet	28 d	NOEC	red blood cell parameters, reticulocytes body weight	<600 3000	2	1	EC, 2003b (Schoenmakers et al., 1998)

Species	Species properties	Test compound	Purity [%]	Application route	Exp. Time	Criterion	Test endpoint	Value [mg a.s./kg diet]	Ri	Notes	Ref.
Rat	Sprague-Dawley, ♀,♂	a.s.	96.2	diet	90 d	NOEC	red blood cells body weight gain	340 6000	2	2,5	EC, 2003b (Wedig, 1990)
Rat	Wistar, ♀,♂	a.s.	98.6	diet	90 d	NOEC	blood cell count and Met-Hb body weight gain, clinical signs	120 ≥ 3000	2	1,2	EC, 2003b (Schoenmakers et al., 1998)
Rat	Sprague-Dawley, ♀,♂	a.s.	96.2	diet	2 y	NOEC	changes in liver, spleen and bone-marrow body weight gain	<600 600	2	2,5	EC, 2003b (Krohmer, 1992; Botta, 1993)
Rat	Sprague-Dawley, ♀,♂	a.s.	98.8	diet	2 gen. (90 d)	NOEC	F1 parental body weight and organ changes; off-spring body weight and survival reduction, changes in spleen	1000	2	7	EC, 2003b (Schroeder, 1983)
Rat	Wistar/HAN, ♀	a.s.	99.3	gavage	d 6-15 of gestation	NOEC	maternal decreased growth and food consumption; reduced foetal weight and retarded ossification	4000	2	1,2	EC, 2003b (Becker and Biedermann, 1990)
Rat	Sprague-Dawley, ♀	CIPC on Hi-Sil	40.2	gastric intubation	d 6-19 of gestation	NOEC	maternal body weight gain; maternal spleen weight foetal weight, fertility	800 < 800 8000	2	1,2	EC, 2003b (Tasker, 1983)

Notes
1 According to OECD guideline.
2 Recalculated from mg/kg bw/d with a conversion factor of 20.
3 Recalculated from mg/kg bw/d with a conversion factor of 33.3.
4 Recalculated from mg/kg bw/d with a conversion factor of 40.
5 According to US-EPA guideline.
6 Recalculated from mg/kg bw/d with a conversion factor of 8.3.
7 Carried out similar to OECD 416.
8. Effect on body weight gain not significant, likely due to palatability problems.
9. Significant higher mortality at 1000 mg/kg bw in males only.

Annex 3 SCOPUS profile

1. TITLE-ABS-KEY(effect* OR bioassay* OR toxic* OR ecotoxic* OR mortalit* OR sensitiv* OR phytotox* OR assessment* OR reproduct* OR lethal* OR response* OR growth OR teratogen*) OR TITLE-ABS-KEY(ec50* OR ec20* OR ec10* OR lc50* OR lc20* OR lc10* OR noec* OR loec* OR matc OR tlm OR chv OR ecx OR bioassay*) OR TITLE-ABS-KEY(bioconcentrat* OR bioaccumulat* OR uptake OR depuration OR food-web OR trophic OR biomagnificat* OR BCF* OR BAF* OR FWMF* OR TMF* OR BMF* OR BSAF*) OR TITLE-ABS-KEY(sorpt* OR adsorpt* OR freundlich OR koc* OR kd* OR kp* OR kf* OR partition-coefficient*)

2. TITLE-ABS-KEY(chlorpropham OR chloorprofam) OR CASREGNUMBER(101-21-3)

#1 AND #2

Published by:

National Institute for Public Health and the Environment
P.O. Box 1 | 3720 BA Bilthoven
The Netherlands
www.rivm.com