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4-CHLORO-O-CRESOL

CAS No: 1570-64-5

EINECS No: 216-381-3

Summary Risk Assessment Report

2002 **Special Publication I.01.43**

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SUMMARY RISK ASSESSMENT REPORT

2002

Denmark

Rapporteur for the risk assessment report on 4-chloro-o-cresol is the Danish Environmental Protection Agency.

Responsible for the risk evaluation and subsequently for the contents of this report is the Rapporteur.

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PREFACE

The report provides a summary, with conclusions, of the risk assessment of the substance 4-chloro-o-cresol. It has been prepared by Denmark in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references, the reader is referred to the original risk assessment report that can be obtained from European Chemicals Bureau[1]. The present summary report should preferably not be used for citation purposes.

[1] European Chemicals Bureau – Existing Chemicals - http://ecb.jrc.it

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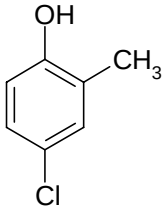
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTITY OF THE SUBSTANCE

CAS-No.:	1570-64-5
EINECS-No.:	216-381-3
IUPAC Name:	4-chloro-2-methylphenol
Synonyms:	4-chloro-o-cresol
	para-chloro-ortho-cresol (PCOC)
Trade Name:	4-chloro-o-cresol
Molecular formula:	$C_7 H_7 Cl O$
Structural formula:	



Molecular weight:	142.59

1.2 PURITY/IMPURITIES, ADDITIVES

Purity:	approx. 97% w/w	
Impurities:	2-chloro-6-methylphenol (OCOC, CAS: 87-64-9)	<1.0%
	2-methylphenol (OC, CAS: 95-48-7)	<1.0%
	2,4-dichloro-6-methylphenol (DCOC, CAS: 1570-65-6)	<2.0%
	4-chloro-2,6-dimethylphenol	<0.5%
	4-chlorophenol	<0.5%
	5-chloro-2-methylphenol	<0.2%
Additives	None	

1.3 PHYSICO-CHEMICAL PROPERTIES

Physical state:	solid at 25°C, 1 atm
Melting point:	46-50°C
Boiling point:	231°C
Relative density:	1.2 g/cm^3 at 50°C
Vapour pressure:	26.66 Pa at 20°C
Water solubility:	2,300 mg/l at 20°C
Octanol/water (K_{ow}):	log K_{ow} = 3.09
pK_a	9.71
Flash point	evaporates without ignition, open cup
Flammability	not flammable
Explosivity	unlikely (structural considerations)
Oxidising properties	non-oxidising

2 GENERAL INFORMATION ON EXPOSURE

4-Chloro-o-cresol (PCOC) is used in the industry as an intermediate in the synthesis of the phenoxy herbicides MCPA, MCPB and mecoprop (MCPP). From the industrial production, processing and formulation PCOC is emitted to air and wastewater. The produced pesticides contain PCOC as impurity (normally <1%, and 0,5% estimated as realistic worst case). The use of the pesticides in the agriculture as herbicides results in exposure to soil of PCOC as an impurity and degradation product.

As MCPA is transformed to PCOC, and PCOC has a high vapour pressure, the atmosphere will receive a contribution from application of the above mentioned pesticides.

The tonnage of substance in EU has been estimated to a total of 15,000 tons per year based on the production volumes presented by the manufacturers and supported by the production and consumption figures of the herbicides MCPA, MCPB and MCPP. Main points of emissions are at manufacturing sites of the substance where PCOC is used as an intermediate for manufacturing of the phenoxyherbicides (i.e. PCOC processing and phenoxyherbicides formulation sites) and where these herbicides are used in agriculture.

3 ENVIRONMENT

Performing a Mackay fugacity level I calculation (Mackay & Paterson 1990) results in an environmental compartment distribution of 33% in air, 56% in water, 6% in soil and 5% in sediment.

PCOC is according to an experiment primarily degradable by photolysis in clean water with a half-life of 4 days. However, a re-estimation of photolysis to typical EU surface water resulted in an estimated photolytic degradation half-life of 300-700 days and therefore photolysis in water is considered negligible. The photochemical oxidation by OH-radicals estimated according to Atkinson resulted in an atmospheric half-life of 30 hours. The available biodegradation data are somewhat conflicting but based on a judgement of simulation test data on biodegradation in soil a "realistic worst-case" aerobic biodegradation half-life of PCOC in soil is estimated to be 21 days. No biodegradation has been found under anaerobic conditions. The aerobic biodegradation half-life in surface waters is based on the soil data also estimated to be 21 days. The estimated half-life in biological wastewater treatment plants is 0.7 hour resulting in an estimated removal of 88% which is in general accordance with simple mass balance estimations from one of the main manufacturers sites. The substance is considered to be ready biodegradable (borderline to inherently biodegradable). PCOC has a low to medium adsorption and may be considered mobile in some (alkaline) soils.

PCOC has been detected in water, soil, air and groundwater. In water, PCOC occurs mainly around emission sources, in air near fields applied with MCPA or MCPP, and in soil and biota after the application of the herbicides. Findings in groundwater are assumed to be the result of mobility and reduced degradation under anaerobic conditions.

The exposure assessment is primarily based on monitoring data from the two main manufacturing sites where all production and all processing of PCOC take place and where approximately 60% of the production volume is formulated. A worst-case environmental exposure scenario for a separate formulation site is included in the risk assessment.

The emissions to surface water from production sites are local and the risk assessment based on monitoring data ($C_{STP + influent}$ and actual dilution in STPs) and TGD default environmental exposure assessment for a formulation site where 10% of the production volume of phenoxy acids is formulated. Because only the STPs receiving wastewater from one of the production sites and the formulation sites are using sludge application to soil, the sludge application is considered local.

PCOC is very toxic to aquatic organisms. The acute toxicity to fish LC_{50} (96h) was observed to be 2.3 to 6.6 mg/l. The EC_{50} (48h) to daphnids were 0.29 to 1.0 mg/l. The EC_{50} (96h) to algae was 8.2 mg/l and the EC_{10} (96h) was 0.89 mg/l. The NOEC (28 days) for fish was 0.5 mg/l for histopathological changes in kidneys and liver. NOEC (21 days) for Daphnia reproduction was 0.55 mg/l. The presence of an algae EC_{10}, a long term NOEC for fish and a Daphnia reproduction test suggest that use of an assessment factor of 10 may be appropriate. The predicted no effect concentration (PNEC) is thus 0.05 mg/l. The PNEC $STP_{microorganisms}$ is obtained by using the EC_{50} for inhibition of respiration of activated sludge microorganisms and an assessment factor of 100 (0.55 mg/l). Since no ecotoxicological data are available for soil organisms the equilibrium partitioning method has been applied ($PNEC_{soil}$ = 0.36 mg/kg).

A local or regional risk for aquatic organisms is not anticipated as the predicted environment concentrations are lower than the predicted no effect concentration (regardless of whether the substance is considered readily or inherently biodegradable and whether an assessment factor of 10 or 100 is employed). Similarly risks for microorganisms in sewerage treatment plants and for sediment and soil organisms are not expected.

PCOC has a bioaccumulation potential based on log K_{ow} 3.09, but BCF found in fish was low (≤30). The risk characterisation of secondary poisoning is therefore not performed.

The substance is considered to be of no concern to aquatic organisms and microorganisms of STPs, and no further information on environmental release from production and formulation facilities is required.

4 HUMAN HEALTH

No current evidence was found for the use of PCOC as such in products, although it may formerly have been employed as a disinfectant. Direct exposure is therefore likely to be restricted to those involved in the manufacture and handling of PCOC, and in conjunction with its use in the manufacture of phenoxy herbicides. Based on limited information, exposures in the range of 0.02 - 0.7 mg/kg/day are estimated for these activities.

The main exposure of human beings to PCOC is likely to be via production, or use of phenoxy herbicides which may contain it as an impurity (<1%), or as a breakdown product following exposure of herbicides to sunlight, or to their metabolic transformation to the substance. It is difficult to quantify exposure occurring through transformation, but this is assumed to be less than 1%. During production, a realistic worst-case exposure of 0.7 mg/kg/day is indicated. In conjunction with agricultural application of herbicides, a worst-case estimate of exposure to PCOC of 0.28 mg/kg/day is obtained. Municipal gardeners may be exposed to higher levels with an estimate of 0.35 mg/kg/day suggested as a realistic worst case.

Similarly, some consumer exposure should also be expected, as the same herbicides can be used in lawn treatment and similar gardening activities. While no detailed information was found on such exposures, it may be amount to 0.07 mg/kg per event. Assuming a really worst case of five events per year, the total yearly dose of PCOC would be 0.35 mg/kg/year corresponding to $9.6 \cdot 10^{-4}$ mg/kg/day.

Indirect exposure via the environment resulting from partitioning into air/water/soil and biomagnification in food sources is low at a regional level, combined secondary exposure estimate being in the range of $1.40 \cdot 10^{-5}$ mg/kg/day of PCOC. Local indirect exposure estimates are about $1.2 \cdot 10^{-4}$ mg/kg/day.

The acute toxicity of PCOC (LD_{50} oral rat 2650-3196 mg/kg, LD_{50} dermal rat 2240 mg/kg, LC_{50} inhal. rat 4h 0.9 mg/l or >30 mg/l) does not give rise to immediate concern, particularly considering that the substance (crystalline needles) is unlikely to form aerosols or dusts, and that PPE is mandated during handling of the substance.

PCOC is corrosive in high concentrations, and has been assigned risk phrase R-35 (“Causes severe burns”) by the manufacturers which should provide adequate warning to those handling it in industrial settings. No consumer exposure is expected at concentrations which could approach that required for corrosivity. No sensitisation was observed in a Guinea pig maximisation test and no case studies indicating sensitisation of persons handling the substance were found.

There were no effects on reproduction according to OECD screening test 422 at doses of up to 600 mg/kg for a total of 40 days.

In 28-day repeat dose studies in rats, the best NOAEL appears to be 200 mg/kg, with a LOAEL of 800 mg/kg where salivation after dosing and ruffled fur was seen in some animals. At this dose, levels of serum alanine-aminotransferase were increased in males, and effects were seen on blood parameters (reduced thromboplastin times, reduction of leukocyte and erythrocyte counts). Liver weights in females were increased, but no histopathological changes were seen in this, or any other organs examined. Decreased adrenal weights were also seen in females at 200 mg/kg and above, but were unaccompanied by histopathological changes.

PCOC has not been investigated for carcinogenicity. Two older tests were positive for mutagenicity, one *in vivo* (mouse micronucleus test) and one *in vitro* in a single strain (TA97) of Salmonella in the Ames test (while showing no activity in other strains in a number of separate tests). Repeated testing with TA97 gave unequivocally negative results. A repeat of the micronucleus test according to current guidelines also gave clearly negative results. On the balance, it is not felt that there is evidence for PCOC being a mutagen.

The estimated human local indirect exposure of $1.2 \cdot 10^{-4}$ mg/kg/day is well below the repeated dose toxicity (NOAEL 200 mg/kg/day).

For the population with the highest potential exposure (production workers assuming inhalation exposure at 5 mg/m^3 for eight hours) a margin of safety of 285 (200 mg/kg/0.7 mg/kg/day) is obtained with regard to the repeat dose NOAEL. For agricultural workers engaged in spraying phenoxy herbicides the ratio is 200 mg/kg /0.28 mg/kg, or 714. For municipal gardeners (0.35 mg/kg/day) a margin of safety of 571 is obtained. Consumers may be exposed to 0.07 mg/kg/day once, or a few times yearly. All other exposure scenarios result in much higher margins of safety.

5 RESULTS

( )	**i)**	There is a need for further information and/or testing.
(X)	**ii)**	There is at present no need for further information and/or testing or for risk reduction measures beyond those for which are being applied already.
(...)	i**ii)**	There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

With regards to the environment, the latest information from the manufacturers on release and monitoring data result in the conclusion that no further information and/or testing is needed as the endpoints do not give rise to concern beyond the need for Classification and Labelling.

With regard to effects on human health, an older positive *in vivo* mutagenicity assay was not confirmed by a test performed according to current guidelines. Other mammalian toxicity endpoints do not give rise to concern beyond the need for Classification and Labelling. While exposure can occur indirectly through the use of pesticides, PCOC itself appears to be used exclusively as an intermediate in the chemical industry.