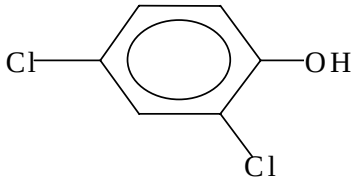
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	120-83-2
Chemical Name	2,4-Dichlorophenol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Free 2,4-dichlorophenol (2,4-DCP) does not accumulate in tissues. 2,4-DCP is a strong uncoupler for oxidative phosphorylation. It is rapidly metabolised into its glucuronate conjugate, its major metabolite, and is mainly excreted in this form via urine.
The acute oral toxicity is low: LD50 1276-1352 mg/kg b.w. when tested in CD 1 mice. The dermal toxicity is moderate: LD_{50} in Sprague Dawley rats was 780 mg/kg with molten substance at 40°C. Further occupational deaths have been reported in five cases. Accidents generally occurred in the same way: workers died after being sprayed with molten (60°C) 2,4-dichlorophenol. US-EPA concludes that contact with only 1% of the body surface may lead to death. The skin irritation tests with 2,4-dichlorophenol reports the substance to be "corrosive" to skin and risk of serious damage to the eyes is expected.

The skin sensitisation potential has not been assessed. Its evaluation may be considered as unwanted due to the necessity to avoid contact with corrosive materials. Chloracnea appears at human exposure to a mixture of chlorophenols containing 2,4-dichlorophenol.

The 2-year study (Fischer 344 rat) was chosen to establish an overall NOAEL, after prolonged treatment with 2,4-dichlorophenol, of 440 mg/kg bw/d for male and above 250 mg/kg bw/d for female, which is in agreement with the findings in the other studies. In a 90 days repeated dose toxicity study dietary administration produced bone marrow degeneration at about 800 mg/kg bw/d in females or at 1500 mg/kg bw/d in males; at 3000 mg/kg bw/d these effects were not seen. The general appearance was affected at the top dose of 3000 mg/kg bw/d.

The genetic toxicity is assessed by *in vitro* and *in vivo* studies. *In vitro*, most of the test results were negative. An i*n vivo* micronucleus test, an unscheduled DNA synthesis test and two sister chromatid exchange assays were all negative. It is concluded that the material is not genotoxic as the results of the *in vivo* tests are negative.

No evidence of carcinogenic activity was reported in rat and in mouse exposed orally for two years. These results are supported by the conclusion of the IARC: although polychlorophenols and their salts are classified in group 2B, there is evidence suggesting lack of carcinogenicity of 2,4-DCP in experimental animals (IARC, 1999).

In a two-generation study in rat (OECD Guideline 416), effects have been observed at 2000 and 8000 ppm on reproduction parameters such as a slight decrease in mean litter size and mean numbers of implantations. Transient mammary swelling was frequently observed in the F0 and F1 females after weaning of their infants. F1 males treated at 8000 ppm, presented adverse effects (delay in sexual development, increase in relative weight testis). The NOAEL for fertility is 500 ppm (33.4 mg/kg bw/d for males and 49.1 mg/kg bw/d for females).

In a one-generation study, no effect was observed via drinking water at 500 mg/kg bw/d in mice. A non-

conventional one-generation study with rats using dose levels up to 15 mg/kg bw/d did not show any significant effect on reproduction parameters. The only significant effect was an increase of some hematologic parameters (red blood cell and hemoglobin), in the F1 generation at 15 mg/kg bw/d, observed after a 14 month exposure. *In vitro* studies showed no effect on penetration of sperm in mouse ova.

In an OECD Guideline 414, no teratogenic effect was observed in rats exposed by gavage at doses up to 750 mg/kg bw/d. The NOAEL for maternal effects is <200 mg/kg bw/d, (lowest dose tested) and the NOAEL for foetal effects is 375 mg/kg bw/d.
No teratogenic effect was observed either in the OECD Guideline 416 study but some delay has been observed on pups growth and their differentiation such as eye opening at 8000 ppm. A slight increase in relative uterine weight was observed at 2000 and 8000 ppm in females weanlings, associated with an increased height of the epithelial cells in the uterine horn in F1 weanlings at 8000 ppm. It was concluded that NOAEL for growth and development of the offspring is 500 ppm (33.4 mg/kg bw/d for males and 49.1 mg/kg bw/d for females).

The hormone disruption potential of 2,4-DCP was shown in only one *in vitro* test considered to be invalid. In another *in vitro* tests on estrogenic activity (competitive binding and response to proliferation culture) results were negative. In the 2-generation reproductive toxicity in rat, some findings, such as increased uterine weight in females weanlings, females showing mammary swelling after weanling of their pups, slight delay of the age of sexual development in males and reduced numbers of implantation sites and litters sizes, could coincide with known estrogenic effects. One of the possible interpretations is that 2,4-DCP might alter endogenous sex hormone concentrations by a specific mechanism through which the estrogenic phenotype appears in treated animals. However, the study didn't show any changes in serum concentrations of pituitary or sex steroid hormones (FSH, LH, Prolactin, Estradiol, Progesterone) in the treated females at necropsy after weaning of the offspring. Furthermore, results were also negative in two *in vivo* tests (a uterotrophic assay and a Hershberger assay), thus endocrine disruption potency of 2,4-DCP could not be evidenced.

Environment

2,4-DCP is a white solid in crystal or needle forms. It has a low vapour pressure at room temperature (0.16 hPa at 25 °C). The water solubility of 2,4-DCP is 4.5 g/l at 25 °C, but since the pKa is 7.89, which falls in the pH range of environmental waters (approximately 6-9), the extent of dissociation of 2,4-DCP may vary significantly. The measured log Pow is 3.21-3.25 at 20°C.

Based on its vapour pressure, 2,4-DCP is expected to have a low volatility from dry soil surfaces. In contrast, photodegradation should be an important means of removing 2,4-DCP from clear surface water. Atmospheric oxidation half-life is estimated by QSAR to be 3.6 days. Hydrolysis is not expected to occur: halogenated aromatics and phenols are generally resistant to hydrolysis. Mechanisms other than photodegradation and microbial degradation, as adsorption by organic matter present within the sediments, catalysis at the surface of silica or oxidation, may also be involved in the disappearance of 2,4-DCP from water. Since the pKa is around 7.8, 2,4-DCP will exist in water and sediment in a partially dissociated state which may affect its transport and reactivity. Similarly in soil, the ionised form (in alkaline soil) is poorly adsorbed, whereas the neutral form (acid soil) is expected to undergo more adsorption. Adsorption will also increase with increasing organic matter content.

Biodegradation studies have shown that 2,4-DCP was not readily biodegradable, but it was inherently degradable only in the presence of adapted microflora, both in aerobic and anaerobic conditions. Anaerobic degradation of 2,4-DCP produced 4-chlorophenol as the major product. The BCFs of 7.1 to 69 in carp suggest that bioaccumulation in aquatic organisms is low.

Aquatic effects

In acute toxicity studies, the lowest LC_{50} values are 1.7 mg/L for freshwater fish and 1.4 mg/l for *Daphnia magna*. For aquatic plants, results on Lemna are available, leading to EC_{50} (7d) = 1.5 mg/L (endpoint: vegetative frond reproduction). In chronic toxicity studies, a NOEC of 0.29 mg/l for a fish, of 0.41 mg/L for Lemna (endpoint: vegetative frond reproduction) and a NOEC of 0.21 mg/l (endpoint: reproductivity rate) for *Daphnia magna* have been obtained. In a non-standard valid test on net spinning behaviour of the Trichoptera larvae, A LOEC value of 0.0035 mg/l was derived.

Despite the numerous consistent data available on fish, Daphnia and algae, issued from acute and chronic toxicity studies, due to the uncertainties on ecological relevance of the endpoint of the Trichoptera study, no final decision

was made regarding PNEC derivation.

Tests with activated sludge resulted in EC50 values of 32 – 73 mg/l. Tests with *Pseudomonas putida* and *Tetrahymena pyriformis* resulted in EC50 values of 133 and 4.5 – 12.6 mg/l, respectively. Test with nitrifying bacteria resulted in a EC50 value of 0.15 mg/l. This latter value could be used for the derivation of a PNEC.

Terrestrial effects

The LC50 for earthworm is 125 mg/kg dw and for plants the EC50 is 316 mg/kg dw. The EC10 in a 34 day test with *Folsomia candida* was 0.7 mg/kg dw.

Exposure

The production volume of 2,4-dichlorophenol was 2000 to 5000 tonnes per year in France.

The use is non-dispersive, as an intermediate for synthesis in chemical industry. The product is not dispersed or transported outside of the site in the Sponsor country, the process functions in a closed system. The principle hazard for manufacturers or users can be burns by accidents at debottlenecking with a temperature higher than 60°C. In closed systems if there is a leak the penetrating odour of 2,4-dichlorophenol gives an alert.

The possible sources of 2,4-DCP in the environment are through the degradation of 2,4-D (2,4-dichlorophenoxy acetic acid, herbicide), or potentially chlorination of phenol-containing water.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for human health (acute toxicity, corrosivity, toxicity to reproduction) and the environment. Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country. The main source for 2,4-DCP measured in the environment appears to be through degradation of the pesticide 2,4-D.

In other programmes: an EU evaluation (in relation to the Community Strategy for Endocrine Disrupters) is ongoing for the environment.