SIDS INITIAL ASSESSMENT PROFILE

CAS No.	78-87-5
Chemical Name	1,2-dichloropropane (propylene dichloride)
Structural Formula	CH_2Cl-$CHCl$-CH_3

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Toxicokinetic data from the rat demonstrate that 1,2-dichloropropane (PDC) is rapidly absorbed and widely distributed within the body after both oral and inhalation exposure, with subsequent excretion in urine (major route of elimination) or exhaled air (carbon dioxide). Only trace amounts remained in tissues 48 hr after treatment, demonstrating its rapid elimination. Metabolic analyses showed that three N-acetylcysteine conjugates predominated in urine.

Its low boiling point and high vapor pressure suggest that evaporative losses will minimize dermal contact with liquid PDC and point to inhalation as the most relevant route of exposure.

Although results from early animal studies indicate that PDC is of relatively low inherent toxicity after ingestion (rat oral LD_{50} approx. 2000 mg/kg bw), skin contact (rabbit dermal LD_{50} approx. 10,000 mg/kg bw), or inhalation (rat 4-hr LC_{50} approx. 2000 ppm; 9300 mg/m^3), human case-reports suggest that the liver and red blood cells may be adversely affected following over-exposure. Thus PDC is considered harmful by ingestion or inhalation, is only slightly irritating to the skin but is irritating to the eye, causing redness, swelling, and slight opacity that were fully reversible after one week. Other case-reports provide equivocal evidence that it may cause allergic skin conditions after uncontrolled exposure in individuals with pre-existing skin irritation and dermatitis; however, these observations are not supported by results from a murine Local Lymph Node Assay, which were negative.

The liver is a target organ in rodents exposed repeatedly to PDC, with a chronic oral NOAEL of 62-125 mg/kg bw/d in rats (LOAEL 125-250 mg/kg bw/d) and a chronic LOAEL of 125 mg/kg bw/d in mice (no NOAEL established); centrilobular congestion, fatty change, hepatocytomegaly, and necrosis were among the changes described, along with decreased body weights. No functional or histopathological changes were reported in brain or nervous tissue from rats given PDC at doses up to 200 mg/kg bw/d by gavage as part of a 13-week neurotoxicity study. Following a 13-week inhalation exposure, no adverse systemic effects were noted in rats and mice exposed to 150 ppm PDC (NOAEL), whereas red blood cell parameters (regenerative anemia) were altered in rabbits with a LOAEL of 150 ppm in males and a NOAEL of 150 ppm in females. Body weight was slightly but statistically significantly decreased in rats (NOAEL 15 ppm) but not mice (NOAEL: 150 ppm) or rabbits (1000 ppm) in these subchronic inhalation studies. Site-of-contact effects, consistent with repeated local irritation, have been described in stomach (mouse, NOAEL/LOAEL 125 mg/kg bw/d after oral gavage, dependent on sex) and nasal tissue (rat, NOAEL 15 ppm after inhalation).

Results from *in vitro* genotoxicity tests (bacterial, fungal, mammalian systems; with and without metabolic activation) are mixed, with both positive and negative studies, indicating that PDC has *in vitro* mutagenic potential. However, results from two modern guideline, *in vivo* tests demonstrate that PDC was not active in a mouse micronucleus test (up to 600 mg/kg bw, 2 consecutive daily doses) or a rat dominant lethal assay (up to 162 mg/kg bw/d; 13-wk exposure). These findings indicate that PDC is not an *in vivo* somatic or germ cell genotoxicant.

The carcinogenic potential of PDC has been evaluated under the US National Toxicology Program, which found ‘no

evidence for carcinogenicity' in male rats (125 mg/kg bw) and 'equivocal evidence' in females (250 mg/kg bw; increased incidence of mammary tumors in the presence of a major reduction in survival), while 'some evidence of carcinogenicity' was noted for mice (both sexes), reflecting an increased incidence of hepatocellular neoplasms (primarily adenomas; 250 mg/kg bw). It is noted that the incidence of liver adenomas was within the historical control range for this strain of mouse suggesting the finding was of marginal toxicological significance. When reviewing these data, IARC concluded that 1,2-dichloropropane is *not classifiable as to its carcinogenicity to humans (Group 3)*. Overall, these considerations indicate that PDC is not a direct-acting carcinogen, that there is equivocal evidence of an increase in mammary tumors in female rats, and that other factors (such as spontaneous biological variation) may have contributed to the increased incidence of mouse liver tumors.

No adverse impact on reproduction was noted in male and female rats exposed to PDC in drinking water over two generations. Although neonatal body weight was decreased, and neonatal mortality higher in litters from high-dose dams consuming up to 250 mg/kg bw/d during pregnancy or up to 500 mg/kg bw/d during lactation, this was considered secondary to dehydration and a 20% reduction in gestational body weight gain, rather than a direct effect on reproduction. Overall there is no evidence that PDC selectively targets the male or female reproductive system. Results from developmental toxicity studies in rats and rabbits were consistent with delayed fetal development (reduced ossification of the bones of the skull) in the presence of clear maternal toxicity (clinical signs, lower body weight gain) with a common maternal/fetal NOAEL of 30 mg/kg bw/d for rats and 50 mg/kg bw/d for rabbits (LOAELs of 125 and 150 mg/kg bw/d, respectively). There was no evidence of a teratogenic effect at any dose in either species.

Environment

1,2-dichloropropane is a liquid with a vapour pressure of 66.20 hPa (25°C), water solubility of 2800 mg/l (25°C), and Log Kow of 2.0.

Taking into account that PDC emissions will be mainly to air, results of distribution modelling show that PCD will stay predominantly in air (98.6%), with negligible amounts partitioning into the water compartment (1.2%). In the air, PDC has the potential to degrade through indirect photolytic processes mediated primarily by hydroxyl radicals with a calculated degradation life-time in the troposphere of approximately 25 days, however wet deposition is not likely to contribute significantly to its atmospheric fate. Based on the data for dichloroethane, oxidation of PDC will not result in the introduction of chlorine into the stratosphere, and its ozone depleting potential is negligible.

Based upon a log Pow of 2 and a measured BCF of 0.5-7, little or no bioaccumulation of PDC in environmental species is expected.

Although PDC is not readily or inherently biodegradable, published data show a co-factor dependent degradation by organisms present in acclimated municipal waste treatment systems. It is not expected to adsorb significantly to organic matter in soil, sediment, or wastewater solids, based on a Koc of 50-299.

The acute toxicity of PDC toward aquatic species has been investigated in fish (fathead minnow, 96 hr EC_{50} 140 mg/l), invertebrates (*Daphnia*, 48 hr EC_{50} 56 mg/l) and saltwater algae (72 hr IC_{50} 15-16 mg/l). Chronic data are also available for three trophic levels (fish, invertebrate, plant) with consistent chronic NOEC values in a range 4-11 mg/l. The saltwater invertebrate *Mysidopsis bahia* appears to be the most sensitive species, with a 28-d NOEC (mortality, reproduction, growth) of 4.1 mg/l.

Exposure

PDC is used primarily as a site-limited or limited-transported co-product/raw material for the manufacture of many chlorinated compounds. Estimated annual global production of PDC in 2001 was about 350 kilotonnes (about 770 million pounds). Based on information from the Swiss Product Registers, there are only 2 recognized consumer applications (likely used in the auto industry), while the Danish and French Product Registers listed no consumer applications. There is no specific information on potential consumer exposure from these 2 applications.

Agricultural use is prohibited in North America and Europe. A total of 46 industrial products were listed in the Swiss Product Register as containing PDC, including as main applications, use in 'paints, lacquers, & varnishes' and 'solvents, degreasers, diluters, & strippers'. Most OECD member countries have established occupational exposure levels for PDC of 75 ppm.

Its high volatility indicates there is some potential for exposure of the general population. Historical data indicate trace amounts in ambient air (maximum reported value identified as 3.4 µg/m^3 or 0.7 ppb), while historical aquatic monitoring data demonstrate typical maximum concentrations <50 µg/l, with a single reported maximum of 1.2 mg/l from a site following application of PDC as a pesticide. More recent analyses of groundwater by the US Geological Survey (for the period 1986-1999, *i.e.*, as agricultural uses ceased) point to concentrations in the range <0.2-19.4 µg/l, with the majority (1911 out of 1926 total samples) containing no detectable PDC (limit of detection 0.2 µg/l).

Potential exposure to PDC in the occupational setting is limited since it is handled and used predominately in closed systems. As a result of the deregistration of PDC for use in agricultural pest control products, the potential for human exposure following deliberate release of PDC to the environment is of diminishing concern.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Adequate data exist to evaluate all of the SIDS endpoints, and sufficient data are available to characterize its hazards.

Human Health:
PDC is harmful after ingestion or inhalation, slightly irritating to the skin, and is irritating to the eye. These hazards do not warrant further work given their transient (irritation) and acute (high exposure) nature. These hazards should nevertheless be noted by chemical safety professionals and users. The chemical is currently of low priority for further work because of its recognized hazard profile and anticipated low exposure.

Environment:
The chemical is currently of low priority for further work because of its low hazard profile.