FOREWORD INTRODUCTION

1,2-DICHLOROPROPANE

CAS N°: 78-87-5

SIDS Initial Assessment Report

From

SIAM 17

Arona, Italy, 11-15 November 2003

1. Chemical Name:	1,2-dichloropropane
2. CAS Number:	78-87-5
3. Sponsor Country:	Switzerland National SIDS Contact Point in Sponsor Country: Dr Georg Karlaganis Swiss Agency for the Environment, Forests and Landscape CH–3003 Berne, Switzerland
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	1,2-Dichloropropane ICCA/HPV Consortium Contact: Dr. L.H. Pottenger, The Dow Chemical Company, Midland, MI, USA.
• Process used	The industry consortium reviewed the underlying data and prepared the updated IUCLID (including Robust Summaries of key studies), SIAR, and SIAP. The sponsor OECD member country (Swiss CA) reviewed and commented on the resulting documents.
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	ICCA nomination
7. Review Process Prior to the SIAM:	The agreed draft dossier was submitted to OECD, posted on the CDG and comments were returned to the Swiss CA and the industry consortium 2 weeks prior to SIAM 17.
8. Quality check process:	Jointly by industry and government: Independent checking by two different government agencies (health and environment), discussion with industry
9. Date of Submission:	2006-01-23
10. Date of last Update:	2005-12-29
11. Comments:	

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 $\mu g/m^3$ 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.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 78-87-5
IUPAC Name: 1,2-dichloropropane
Molecular Formula: $C_3H_6Cl_2$
Structural Formula: $CH_3CHClCH_2Cl$
Molecular Weight: 112.99
Synonyms: propylene dichloride; PDC; dichloropropane; DCP

1.2 Purity/Impurities/Additives

1,2-Dichloropropane is produced at a purity of 99%, with the following identified impurities (ppm): H_2O (200 ppm); acidity (50 ppm); iron (15 ppm); oxygenated organic compounds (1200 ppm).

1.3 Physico-Chemical properties

1,2-Dichloropropane, a highly flammable liquid, has the following physico-chemical properties (Table 1).

Table 1. Summary of Physico-Chemical Properties.

Property	Value[1]	Comments/Reference
Physical state	liquid	
Melting point	-100.4°C	Mackay *et al.* (1993)
Boiling point	96.4°C (94.0 to 96.8)	Experimentally derived preferred value from DIPPR (1985); Mackay *et al.* (1993)
Relative density	1.155 g/cm^2 at 20°C (1.149 to 1.160)	Mackay *et al.* (1993)
Vapour pressure	66.2 hPa @ 25°C (66.17 to 71.98)	Mackay *et al.* (1993)
Water solubility	2800 g/m^3 at 25°C (1297-2820 g/m^3)	Mackay *et al.* (1993)
Partition coefficient/ log Kow (n-octanol/water)	2.00 (1.99-2.28)	Mackay *et al.* (1993)
Henry's law constant	274 Pa·m^3·mol^{-1} (25°C) (192.52-273.51)	MacKay and Yeun (1983); Ashworth, R.A. *et al*. (1988)
Organic carbon/water partition coefficient, Koc	68	QSAR-calculated, EPISuite (PCKoc V.1.66)
Flash point	21°C (open cup) 13-15°C (closed cup)	Merck (1989); Langer (1986); Rassaerts and Witzel (1975)
Stability in water	15.8 yr @ 25°C	Mackay *et al.* (1993)
Conversion factor	1 ppm= 4.70 mg/m^3	IARC (1999)

[1] = presented as preferred value or mean (range in parentheses)

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

1,2-Dichloropropane is produced by the chlorination of propylene. The largest volume currently produced is as a co-product during the production of propylene oxide *via* the chlorohydrin process. In addition, propylene dichloride is also a co-product made during the production of allyl chloride. PDC is produced in North America, Europe, Asia/Pacific, and Latin America. The total annual global production volume of PDC for 2001 is estimated to be 350 kilotonnes (about 770 million pounds). The following table gives an overview of estimated regional production volumes of PDC from 2001.

Table 2.1.1. Estimated Regional Production of 1,2-Dichloropropane.

Region	Estimated Percentage of Global Production
North America	64-69
Latin America	9-10
Europe	19-25
Japan	2-3

Currently PDC is used as a raw material in the production of many other chemicals, such as propylene, carbon tetrachloride, and tetrachloroethylene. No consumer uses of PDC are attributed to the ICCA/HPV sponsor producers. Most of the industrial uses for PDC are site-limited, involving transfer *via* pipelines to either storage tanks or other production facilities on-site. There is some transport *via* both rail and ship to facilities located elsewhere.

The major producers, and the sponsors of this dossier, are listed in Table 2.1.2 below.

Table 2.1.2. Major Producers of 1,2-Dichloropropane.

Producer Company
Asahi Glass, Ltd.
BP Koeln GmbH
The Dow Chemical Company
Solvay
Syndial SpA (formerly Enichem, SpA)*

*This former producer no longer produces or uses 1,2-dichloropropane.

Historically, PDC was formulated with the active ingredient 1,3-dichloropropene, and this mixture was approved for use as a grain and a soil fumigant. It was still listed in the 1987 Eighth Edition of the Pesticide Manual as a component of D-D MIX (Shell Chemicals), and Nematox (Siapa). Manufacture of the product Vidden D (The Dow Chemical Company) was discontinued in 1984. PDC-containing formulations were effective against soil nematodes, and were applied to many crops including cotton, peanuts, sweet potatoes, sugar beets, strawberries, tobacco, tomatoes, and other vegetable crops (CEH, 2001). The registration for this use of PDC in the USA was discontinued in the 1980's (starting in 1984; last registration dropped in 1989). In the EU, it is not clear if PDC has been used recently for this application. However, all existing authorizations lapsed in July 2003 because PDC was not notified under regulation 451/2000 EC. Thus, PDC has not been used as a soil fumigant in the U.S. for almost twenty years and is no longer used in that application in the EU since July 2003. The situation in Asia/Pacific is less clear, however, and some registered

agricultural uses may remain in some countries. Information from a soil fumigant association indicates that there are no longer any soil fumigant uses of PDC in Japan.

Other uses are mentioned for PDC in some review articles or reports (IPCS, 1993; Sittig, 1980; Baruffini *et al*., 1989). These include the following: solvent for fats and oils, gum processing, lead scavenger for anti-knock fluids, rubber making and vulcanization, preparation of scouring compounds, furniture finishing, dry cleaning fluid, paint remover, and metal degreasing. At least some of these applications, such as a lead scavenger, are outdated given the phasing out of leaded gasoline and the prevalence of unleaded gasoline; it is possible that other uses have been discontinued also. The Swiss product register lists 6 uses for PDC, mainly for industrial use as detailed in the Table 2.1.3 below. Overall a total of 46 consumer and industrial products are included. The 2 uses listed for consumer products all contain ≤5% PDC, with half containing less than 0.01% PDC.

Table 2.1.3. Distribution of Uses for PDC Based on the Swiss Product Register.

	Consumer		**Total Consumer**	**Industrial**		**Total Industrial**	**Overall Total**
Uses:	≤ 0.01%	≤ 5%		≤ 10%	≤ 50%		
Paints, laquers and varnishes	2		2	4	9	13	15
Additives					2	2	2
Adhesive, cement, surfacer or sealer				1	4	5	5
Metal curing agent				1		1	1
Solvents, degreaser, dilutor, stripper				6	5	11	11
Car care		2	2	5	5	10	12
Total	2	2	4	17	25	42	46

There were no entries for PDC in the Danish Product Register (1999-2002), and no products containing PDC listed on the Danish market, underscoring its limited use in consumer products. Based on one producer's information, the co-product/raw material uses account for over 99.5% of total PDC production in the USA and Europe, thus the remaining uses account for less than 0.5% of PDC production in those regions.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

PDC emissions data are reported to the U.S. EPA on a yearly basis as part of the Toxic Release Inventory (TRI) program. The information reported for PDC for the past several years is provided in Table 2.2.1 below, obtained from the EPA website.

Table 2.2.1. PDC Emissions Reported *via* the EPA TRI Program from 1997-2001.

Reporting Year	Air (lbs)	Water (lbs)	Soil (lbs)	Total (lbs)
1997	378,454	2,609	30	393,463
1998	298,150	1,122	32	299,571
1999	249,655	9,242	30	265,783
2000	263,838	431	382	264,656
2001	140,490	2,403	79	142,972

Given the volatility of PDC, and the emissions data from the U.S. EPA TRI monitoring database, there is some potential for exposure to the general population from airborne levels. Examples of monitoring data from the 1980's indicate that PDC was present in trace amounts in ambient air from big cities, up to 1.5 µg/m^3 (0.3 ppb), with maxima of 3.4 µg/m^3 (0.7 ppb) (IPCS, 1993). Similar values were reported by Singh *et al*. (1992) from air monitoring of 4 major US cities with mean PDC concentrations ranging from 24-163 ppt (5-35 ng/m^3), and overall values ranging from <2-724 ppt (<0.4-154 ng/m^3).

Monitoring data from wells and surface water in the US and in the EU have demonstrated the presence of PDC in from 1-50% of samples tested (IPCS, 1993). Where detectable, the concentrations have ranged from 0.1 µg/l up to 440 µg/l, with most studies reporting maximum levels of <50 µg/l. These data were published mostly from the late 1980's, just after the soil fumigant use of PDC was discontinued. More recent analyses of groundwater by the US Geological Survey for the period 1986-1999 point to concentrations in the range <0.2-19.4 µg/l, with the large majority (1911 out of 1926 total samples) containing no detectable PDC (limit of detection 0.2 µg/l) (Moran *et al*., 2002). Analysed concentrations in 13 of the 15 'positive' samples were in a range 0.2-5.0 µg/l, and >5 µg/l for the remaining two samples. Despite its use as a grain and soil fumigant, published data on crops indicate that PDC was not detected.

2.2.2 Photodegradation

Based on a review of the available data for PDC and for its structural analogue,1,2-dichloroethane, Kurland (2004) evaluated the potential of PDC to contribute to global warming (GWP), to photochemical ozone creation (POCP), and to ozone depletion (ODP), including a review of the available data on hydroxyl radical reaction rate for PDC. Photodegradation will account for some removal of PDC from the atmosphere. This is based on a calculated hydroxy radical reaction rate of 5.2 x10-13 cm3molecule-1s-1(Yujing and Mellouki, 2001), which was in excellent agreement with a measured value of 4.6±0.6 x10-13 cm3molecule-1s-1 (Atkinson, R., 1987; Kwok and Atkinson, 1995). The lifetime (τ=1/(k[OH]) of PDC, was estimated by using a global tropospheric 24-hour average OH radical concentration of 1x106 molecule cm-3 (Hein et al., 1997) and the measured bimolecular rate constant at room temperature. The tropospheric lifetime of 25 days is in good agreement with another reported value of 27 days (Tauzon et al., 1984) and is relatively short. Kurland (2004) concluded that the products of oxidation of PDC will not result in the introduction of chlorine into the stratosphere, and that potential contributions of 1,2-dichloropropane to GWP, POCP, or ODP, were negligible.

2.2.3 Stability in Water

A hydrolysis constant of 5.0 x 10^{-6} per hours (pH 7-9, 25°C) with a calculated half-life of 15.8 yr has been derived for PDC in water (MacKay *et al*., 1993).

2.2.4 Transport between Environmental Compartments

Based upon the EPISuite Level III Fugacity Model, PDC is expected to stay primarily in air, as is shown in Table 2.2.4, with the assumption of emissions to air only (according to U.S. EPA TRI Database, >99.9% of reported PDC emissions are to the atmosphere).

Table 2.2.4. Predicted Environmental Partitioning of 1,2-Dichloropropane.

Compartment	Level I	Level III
Air	98.02	98.8
Water	1.82	0.98
Soil	0.16	0.20
Biota	<0.01	ND
Sediment	ND	<0.01

Advection in air accounts for 89.2%, and reaction in air for 10.6%, of the removal rate. Advection and reaction in water, sediment, and soil, account for 0.2% of removal rate.

2.2.5 Biodegradation

No biodegradation of PDC was detected when PDC (150 mg/l) was incubated aerobically with municipal activated sludge (1,000 mg/l mixed liquor suspended solids) for 28 days in an OECD 302B (modified EMPA Zahn-Wellens test), conducted according to GLP requirements (Gonsior *et al*., 2002). However, there are published examples of acclimated municipal and other systems where PDC does undergo biodegradation, including addition of co-factors (acetate and methanol), and enrichment of cultures (Hauck and Hegemann, 1999; Hardy *et al*., 1999). It is unknown if such conditions exist or if biodegradation occurs in the environment.

2.2.6 Bioaccumulation

Data from an OECD 305C guideline study on bioaccumulation, conducted in carp at 0.4 and 0.04 mg PDC/L, demonstrated limited or no potential for PDC to bioaccumulate (BCF = 0.5-7; MITI, 1992). The published data present only limited methodological details. This low/no potential for bioaccumulation is supported by a calculated BCF of 1.29 (Howard, 1990; McKay *et al*., 1993).

2.2.7 Other Information on Environmental Fate

PDC is not expected to adsorb significantly to organic matter in soil, sediment, or suspended solids in wastewater or surface waters, based on a modelled value for Koc of 68 (Davis, 2004). The low Koc value suggests that PDC is expected to have high mobility in soil. The Henry's Law constant of 274 Pa m^3 mol^{-1} indicates that PDC is expected to volatilize from soil and to a lesser extent from water surfaces.

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure of workers *via* inhalation in production and use facilities represents the most likely route for human exposure to PDC, and many countries have set occupational exposure limits (OEL). The U.S. Occupational Safety and Health Administration (OSHA) has set a Permissible

Exposure Level (PEL) of 75 ppm for PDC. The American Council of Governmental and Industrial Hygienists (ACGIH) has a recommended Threshold Limit Value (TLV) for 1,2-dichloropropane of 75 ppm, and a Short-Term Exposure Limit (STEL) of 110 ppm. Although this is not a binding occupational exposure level, typically the ACGIH TLV values are used as exposure guidelines by industries worldwide. Several EU member countries have also set OEL values, most of which concur with the 75 ppm value from ACGIH.

2.3.2 Consumer Exposure

The data provided in Table 2.1.2 on product uses in Switzerland indicates that there are very limited consumer applications of PDC. This is supported by the lack of entries over the past 4 years in the Danish Product Register, and no products containing PDC listed on the Danish market.

3 HUMAN HEALTH HAZARDS

Adequate toxicological data exist to support an assessment of the key SIDS health elements for 1,2-dichloropropane. Other information beyond the basic SIDS requirements (including toxicokinetics, irritation, sensitization, neurotoxicity, chronic toxicity, and carcinogenicity) is also available and has been included in this documentation for completeness.

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Information is available on the toxicokinetics and metabolism of [^{14}C]-PDC in F344 rats following oral administration and inhalation exposure (Timchalk *et al*., 1989). These investigations were conducted in accordance with EPA test-rule requirements and were GLP compliant. In the oral studies, animals were given either single (1 or 100 mg/kg bw) or multiple (1 mg/kg bw/day on 8 consecutive days) gavage treatments with radiolabelled ^{14}C-PDC in corn oil, while inhalation exposure involved a 6 hr head-only exposure (0, 5, 50 or 100 ppm). Elimination pathways and the time-course for excretion were evaluated by collection of excreta (urine, faeces) and exhaled air over 48 hr. Tissue distribution of radioactivity was determined after terminal sacrifice. Structural quantitation of major urinary metabolites was also carried out.

The results demonstrated rapid absorption, metabolism, and excretion irrespective of the route of exposure. Urine was the principle route of elimination (accounting for 40-65% of recovered radioactivity), followed by expired air (20-40% of recovered radioactivity). The major urinary metabolites were identified as three N-acetylcysteine conjugates of PDC, while ^{14}C-CO_2 predominated in exhaled air with smaller amounts (generally 1-10%) of unchanged parent substance. The tissues/carcass, feces, and cage wash contained less than 11%, 10%, and 4% of the recovered radioactivity, respectively. Liver contained the greatest amount of radioactivity (<0.4% of dose per g wet weight) with small amounts present in all other tissues sampled (generally <0.1% of dose per g wet wt), indicating that PDC was distributed to all tissues, including bone. Peak plasma radioactivity was generally attained 4 hr post-treatment, irrespective of route, but Area Under the Curve (AUC) values were less than dose-proportionate in the higher oral (100 mg/kg) and inhalation (50 or 100 ppm) groups, possibly indicating saturation of uptake, enhanced excretion, or a greater volume of distribution.

3.1.2 Acute Toxicity

A number of studies are available which describe the acute toxicity of 1,2-dichloropropane in animals (summarised in Table 3.1.2). Although pre-dating modern guidelines and GLP, the results indicate that PDC is of relatively low inherent toxicity in animals after ingestion, skin contact, or inhalation. Given the high vapor pressure of 1,2-dichloropropane, inhalation exposure appears the most relevant route while rapid evaporation from skin would be expected to minimize any potential for local or systemic effects following dermal contact.

Human Case-Reports

In contrast to the acute animal data, human case-reports suggest that the liver and red blood cells may be adversely affected following over-exposure by ingestion (Larcan *et al*., 1977; Thorel *et al*., 1986; Di Nucci *et al*., 1988; Lucantoni *et al*., 1992), inhalation (Pozzi *et al*., 1985) or after prolonged, combined dermal and inhalative exposure (Fiaccadori *et al*., 2003). As is typical for short case-reports such as these, quantitative exposure information is missing from many of these studies, and exposure to PDC is inferred rather than supported by analysis of the products involved; however, varying degrees of liver damage (hepatocellular necrosis, fibrosis, hypertension), increased serum transaminases, hemolytic anemia, and intravascular coagulation were reported in the subjects. In two instances the subjects died after apparently ingesting 50-180 ml of industrial cleaning products (Larcan *et al*., 1977; Di Nucci *et al*., 1988), however the doses received by the remaining cases are not known.

Table 3.1.2. Summary of Acute Toxicity Data for 1,2-Dichloropropane.

Endpoint	Species (details)	Result	Reference
Oral	Rat (Wistar)	2200 mg/kg bw	Smyth *et al*., 1962; 1969
Inhalation LC_{50}	Rat (4 hr)	2000 ppm 9.4 mg/l	Carpenter *et al*., 1949; and Smyth *et al*., 1962
	Rat (7 hr)	> 2200 ppm > 10.3 mg/l	Highman and Heppel, 1946
	Guinea pig (7 hr)	> 2200 ppm > 10.3 mg/l	Highman and Heppel, 1946
Dermal LD_{50}	Rabbit (occluded, 24 hr)	10,100 mg/kg bw	Smyth *et al*., 1962; 1969

Conclusion

As a result of the findings from the human case-reports, PDC is considered harmful by ingestion or inhalation.

3.1.3 Irritation

Skin Irritation

Studies in Animals

Results from a GLP guideline skin irritation study (minimal redness and slight edema), indicate that PDC is slightly irritating to skin (BASF, 1982).

Human Case-Reports

See below, Human Case-Reports for Sensitization.

Eye Irritation

Studies in Animals

An early eye irritation study (BASF, 1965) reported marked redness, edema and slight opacity 24 hr after instillation of 0.05 ml PDC into the conjunctival sac of a single rabbit. These effects were fully reversed after 8 days (no interim results available), and indicate that PDC is irritating to the eye.

3.1.4 Sensitization

Studies in Animals

Skin

Results from a GLP, OECD 429 guideline mouse local lymph node assay (Woolhiser et al., 2003) found no stimulation of lymphocyte proliferation in auricular lymph nodes from mice treated with up to 80% 1,2-dichloropropane, demonstrating that PDC was not a sensitizer under the conditions of this test. This lack of allergic potential in the mouse is consistent with structural considerations which provide no evidence of chemical alerts (reactive groups) that would indicate a potential to act as a sensitizer.

Human Case-Reports

Skin

Case reports provide equivocal evidence that PCD may cause allergic skin conditions after uncontrolled exposure in individuals with pre-existing dermatitis. In one study, 10 workers exposed to industrial preparations containing 10-40% 1,2-dichloropropane under conditions of poor occupational hygiene (hand cleaning using these products) exhibited an allergic response after patch testing with PDC with a threshold level of 2% (Baruffini *et al*., 1989). However, all subjects suffered from pre-existing irritant skin-lesion and hand dermatitis that quickly resolved after cessation of exposure. In another brief report (Grzywa and Rudzki, 1981), two female workers with recurrent dermatitis responded to patch testing with 1% 1,2-dichloropropane as well as other substances present in the workplace.

Conclusion

In conclusion, based on the available data, 1,2-dichloropropane is considered to provide only equivocal evidence of an ability to cause skin allergy.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Inhalation

The effects of repeated (13 week) inhalation exposure to PDC were investigated in rats, mice, and rabbits (Nitschke *et al*., 1988). This GLP compliant study evaluated macroscopic and microscopic effects following repeated exposures to 15, 50, and 150 ppm for rats and mice and 150, 500, and 1000 ppm in rabbits. Nasal respiratory changes, considered site-of-contact effects, were identified in rats and slight reductions in body weight were also reported (NOEL of 15 ppm for both). No effects whatsoever were identified in mice (NOEL of 150 ppm). Results from rabbits demonstrated slight changes in red blood cell parameters, which were indicative of a macrocytic normochromic, regenerative anemia (LOEL of 150 ppm for males; NOEL of 150 ppm for females), and site-of-contact effects in nasal tissue (NOAEL of 500 ppm).

Oral

The oral repeat dose toxicity of PDC has been investigated extensively by NTP (1986) in a series of GLP-compliant studies using male and female F344 rats and B6C3F1 mice. Key aspects of the design of these studies, along with the main findings, are summarized in Table 3.1.5. The results indicate that the liver is a target organ after gavage administration, with a chronic NOAEL of 125 mg/kg bw/day in female rats (males unaffected) and a chronic LOAEL of 125 mg/kg bw/day in male mice (females unaffected). Acanthosis of the stomach (indicative of persistent local irritation) was noted in mice (rats unaffected) with a chronic NOEL of 125 mg/kg bw/d in males and a chronic LOEL of 125 mg/kg bw/d in females. Body weight was decreased 14-24% in rats (chronic $NOEL_{males}$ = 62 mg/kg bw/d, chronic $NOEL_{females}$ = 125 mg/kg bw/d) whereas mice were unaffected (chronic NOEL = 250 mg/kg bw/d, both sexes). The overall NOAEL values following chronic administration of PDC were 62 and 125 m/kg bw/d for male and female rats respectively. No chronic NOAEL was derived for mice of either sex; the LOAEL was 125 m/kg bw/d.

Table 3.1.5. Summary of Repeat Oral Toxicity Data for 1,2-Dichloropropane in Rats and Mice (gavage administration; data from NTP, 1986).

Species	**Treatment**	**NOAEL / LOAEL (mg/kg bw/day)**	**Comments**
Rat	0, 125, 250, 500, 1000 or 2000 mg/kg bw/d for 2 wk (n = 5/sex/dose)	NOAEL = 500	All high-dose rats died during the study, with 15% decrease in bw at 1000 mg/kg bw/day (both sexes). Reddening of the renal medullae (2000 mg/kg bw/day) was the only other toxicologically-relevant effect.
	0, 60, 125, 250, 500 or 1000 mg/kg bw/d for 13 wk (n = 10/sex/dose)	NOAEL = 250	All high dose animals and 50% of males given 500 mg/kg bw/day died early. Body weight decreased 8-16% in 500 mg/kg bw/day groups. Centrilobular congestion, hepatic fatty change and centrilobular necrosis, affecting up to 50% of high dose animals, seen microscopically.
	Males: 0, 62 or 125 mg/kg bw/day for 103 wk Females: 0, 125 or 250 mg/kg bw/day for 103 wk (n = 50/sex/dose)	$NOAEL_{males}$ = 62 $NOAEL_{females}$ = 125	Survival of high dose females was significantly decreased relative to low dose and control groups (males unaffected). Body weight decreased 14-24% in high dose animals (both sexes). An increased incidence of hepatic foci of clear change and liver necrosis (high dose females only) were the only lesions of note.

Mouse	0, 125, 250, 500, 1000 or 2000 mg/kg bw/d for 2 wk (n = 5/sex/dose)	$NOAEL_{males}$ = 250 $LOAEL_{females}$ = 125	All high-dose mice died during the study, high levels of mortality also noted at 1000 mg/kg (both sexes) and 500 mg/kg (males only). No impact on body weight of survivors. Reddening of the renal medullae common in higher dose groups (both sexes), high incidence in males given 500 mg/kg, single occurrence in all lower female dose groups.
	0, 30, 60, 125, 250 or 500 mg/kg bw/d; 13 wk (n = 10/sex/dose)	NOAEL = 500	Minor (3-5%, not clearly dose-related) reduction in body weight, no histopathological lesions present.
	0, 125 or 250 mg/kg bw/day for 103 wk (n = 50/sex/dose)	LOAEL = 125	Survival of high dose females decreased relative to control (concurrent reproductive tract infection considered cause by NTP), survival of males unremarkable. Hepatocytomegaly and hepatic focal necrosis (low and high dose males), acanthosis of the stomach (high dose males, low and high dose females) and suppurative inflammation of the reproductive tract (all females, indicative of infection) were the only histopathological changes detected.

The neurological consequences of repeated oral exposure to PDC have been investigated in F344 rats (n = 15/sex/group) given 0 (corn oil), 20, 65 or 200 mg/kg bw/day for 13 weeks by gavage (Johnson and Gorzinski, 1988). The study followed U.S. E.P.A. guidelines and was conducted to the standards of GLP. Prior to treatment, and at monthly intervals during the study, all animals were assessed for a number of endpoints including functional observational battery, hindlimb grip strength, and motor activity. After a 13-week treatment, 4 rats/sex/dose were randomly selected for terminal examination (including histopathological examination of brain, spinal cord and nerve) while the remainder were retained (no further treatment) for a 9 week recovery period. Transient clinical signs (lacrimation, blinking, and decreased spontaneous motor activity) were reported on days 3-4 of treatment, and body weight was slightly decreased at week 13 in both sexes. There were no effects attributable to PDC in the functional observational battery, grip strength, or motor activity. Results from the gross and microscopic examination of the brain and nervous system revealed no treatment-related lesions. Overall, apart from a minor effect on body weight ($NOAEL_{males}$ = 20 mg/kg bw/day; $NOAEL_{females}$ 65 mg/kg bw/day), no adverse structural or functional neurological consequences were apparent in rats following 13 weeks gavage administration of PDC at doses up to 200 mg/kg bw/day.

Conclusion

Overall, results from repeat dose studies indicate that the liver is a target organ in rodents with a chronic oral NOAEL of 62-125 mg/kg bw/d in rats and a chronic LOAEL of 125 mg/kg bw/d in mice (no NOAEL established). There were no adverse systemic organ effects in rats and mice following sub-chronic exposure 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 only (NOAEL 15 ppm) in these sub-chronic inhalation studies, with site-of-contact (irritative) changes present 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; rabbits, NOAEL 500 ppm).

3.1.6 Mutagenicity

In vitro Studies

The mutagenic potential of 1,2-dichloropropane has been evaluated in a large number of microbial tests in bacteria and fungi, both in the absence and in the presence of exogenous metabolic activation (summarized by IARC, 1999). Overall, results from these tests are mixed, with both positive and negative studies (see Table 3.1.6 for *S. typhimurium* results).

Table 3.1.6. Summary of Mutagenicity Findings for 1,2-Dichloropropane in *Salmonella typhimurium* Tester Strains (modified from IARC, 1999).

***Salmonella* tester strains**	**Result**		**Dose* µg/ml**	**Reference**
	Without S9	With S9		
TA100	+	+	5000	De Lorenzo *et al*. (1977)
	-	-	3150	Oesch (1979)
	-	-	565	Stolzenberg and Hine (1980)
	+	+	2900	Principe *et al*. (1981)
	(+)	-	5000	Haworth *et al*. (1983)
	-	-	2000	NTP (1986)
TA1535	+	+	5000	De Lorenzo *et al*. (1977)
	-	-	3150	Oesch (1979)
	+	+	2900	Principe *et al*. (1981)
	(+)	-	5000	Haworth *et al.* (1983)
	-	-	2000	NTP (1986)
TA1537	-	-	3150	Oesch (1979)
	-	-	5800	Principe *et al*. (1981)
	-	-	1666	Haworth *et al*. (1983)
	-	-	2000	NTP (1986)
TA1538	-	-	5800	Principe *et al.* (1981)
TA98	-	-	5800	Principe *et al*. (1981)
	-	-	3150	Oesch (1979)
	-	-	5000	Haworth *et al*. (1983)
	-	-	2000	NTP (1986)
TA1978	-	-	25000	De Lorenzo *et al*. (1977)

+ = positive result;

(+) = weakly positive; <2-fold increase;

***** Either lowest effective dose (for positive study) or highest ineffective dose (for negative study)

However, in a GLP-compliant study with liquid pre-incubation conducted by the US National Toxicology Program, no mutagenic activity or cytotoxicity was detected when PDC (up to 2000 µg/plate) was incubated with four strains of *Salmonella typhimurium* (TA 98, TA 1537, TA 100, TA 1535) in the absence or presence of S9 fraction from Arochlor 1254-induced rats (NTP, 1986). A satisfactory response was obtained with the positive control substances, benzo(a)pyrene and MNNG. PDC was also not cytotoxic or mutagenic in these same tester strains when evaluated in the

absence or presence of S9 using a plate incorporation methodology (up to 3150 µg/plate, in the absence or presence of glutathione supplementation; Oesch, 1979). Exposure to PDC vapor (atmosphere generated by evaporation of 0.3 - 10 ml of test substance in a 20 l desiccator) also failed to produce a response in the organisms in the presence or absence of S9 and glutathione supplementation (Oesch, 1979), whereas dichloroethane (3 ml) was positive in TA100 and TA1535 under these same conditions.

Overall, PDC has returned consistently negative results in *Salmonella typhimurium* tester strains TA1537 and TA98 at up to 5800 µg/ml in the absence or presence of S9, whereas TA100 and TA1535 have returned mixed results under similar conditions.

When tested in mammalian cells *in vitro*, no increase in mutations was detected at the thymidine kinase locus in L5178Y cells after incubation with up to 1000 nl/ml 1,2-dichloropropane in the absence of rat S9 (cytotoxic at >800 nl/ml), while assays in the presence of S9 provided evidence of mutagenicity at or around the threshold for cytotoxicity (80 nl/ml) (Myhr and Caspary, 1991). In an assessment of clastogenic potential, the number of chromosomal aberrations present in CHO cells exhibited a dose-related response (reported as a 5- or >16-fold increase) after incubation with 1370 or 1580 µg/ml PDC in the absence of S9, and an approximate 4-fold increase in the number of aberrant cells exposed to 660 or 950 µg/ml in the presence of S9 (NTP, 1986). In another series of *in vitro* experiments, CHO cells exhibited a dose-related increase in sister chromatid exchanges after exposure to PDC *in vitro*, with an approximate doubling in response after incubation with 376 or 1127 µg/ml PDC, both in the presence and absence of Arochlor 1254-induced rat S9 (NTP, 1986).

In vivo Studies

Results from a recent GLP compliant OECD 474 guideline mouse micronucleus study demonstrated no evidence of cytogenetic damage in bone marrow from CD-1 mice given up to 600 mg/kg bw by gavage (corn oil vehicle) on 2 consecutive days (Spencer *et al*., 2003). Systemic toxicity (2°C drop in body temperature) was noted in high dose animals, while results from the range-finder investigation indicated that higher treatment levels (1000 mg/kg bw and above) were lethal. A satisfactory response was obtained with the positive control substance (cyclophosphamide). Based on toxicokinetic data demonstrating PDC is distributed evenly across all tissues, including bone (see Section 3.1.1), exposure of the bone marrow can be assumed for this study. The results demonstrate no potential for PDC to damage genetic material present in immature red blood cells.

Similarly, negative results were also reported from a modern, guideline rat dominant lethal assay (Hanley *et al*., 1989) performed to GLP. Male SD rats (n = 30/group) received PDC in drinking water at doses equivalent to 0, 28, 91 or 162 mg/kg bw/day for at least 13 wk. The high dose was a saturated solution of PDC in water. They were then mated with untreated females for two successive one-week periods. A positive control group (cyclophosphamide, 100 mg/kg bw, 48 hr prior to mating) was included in the study. Mating and fertility indices were comparable between the control and PDC-treated groups (96-100%), but decreased significantly in the positive controls. Slight variations in number of *corpora lutea*, number of implantations, pre-implantation losses and resorption rates were noted in the first or second week of mating in the low and high dose groups (mid-dose group not different from control), but the magnitude of the change was within the normal control ranges. In contrast, the positive control group showed a 2-fold increase in pre-implantation loss and a 10-fold increase in resorption rate. Overall it was concluded that PDC had no capacity to induce heritable mutations in male SD rats following at least 13-week oral treatment with up to 162 mg/kg bw/day.

Limited information, from a non-standard test method of unknown reliability, indicates that the number of polyploid mononuclear and binuclear hepatocytes was increased in rats following 3 days inhalation exposure to 2200 mg/m^3 PDC (Belyaeva *et al*., 1977).

Conclusion

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 or a rat dominant lethal assay. These findings indicate that PDC is not an *in vivo* somatic or germ cell genotoxicant, despite widespread distribution throughout the body.

In addition, results from adequate carcinogenicity assays in rats and mice provide supplementary information on the mutagenic potential of 1,2-dichloropropane *in vivo*. The findings (limited to liver tumors in mice and no convincing evidence of carcinogenicity in the rat) indicate that the compound is not a genotoxic carcinogen.

3.1.7 Carcinogenicity

The carcinogenic potential of PDC has been investigated in two long term oral gavage studies using F344 rats and B6C3F1 mice (NTP, 1986). Due to poor survival, statistical analysis of tumor incidence was adjusted for survival in both species.

Studies in Animals

No significant or treatment-related increase in tumor incidence was observed in male rats given 0, 62 or 125 mg/kg bw/day for 103 wk. Female rats given 125 or 250 mg/kg bw/day showed a positive trend for mammary adenocarcinoma incidence (adjusted rates: 3%, 5%, 27%), which was increased significantly in the high dose group. These were neither metastatic, anaplastic, nor highly invasive, and were diagnosed by some NTP pathologists as highly cellular fibroadenomas (NTP, 1986). Affected high dose females showed a marked decrease in survival (32% alive at study end versus 74%-86% in the control and low dose groups) and a significant reduction (>20%) in body weight, suggesting that 250 mg/kg bw/day was in excess of the Maximum Tolerated Dose for PDC; compromised metabolic, immune, or hormonal status was possible under such conditions (NTP, 1986). It is pertinent that there was no increase in liver tumors despite the occurrence of chronic histopathological changes, including foci of clear change and necrosis. Based on these findings, NTP concluded that there was no evidence for the carcinogenicity of PDC in male rats, while in females given 250 mg/kg bw for 103 wk, there was equivocal evidence of an increased incidence of mammary adenocarcinoma; these were considered borderline malignant lesions by NTP, which occurred concurrently with decreased survival and reduced body weight gain.

In mice, there was a positive trend for liver adenoma (adjusted for survival) in both sexes given 0, 125, or 250 mg/kg bw/day for 103 weeks. Tumor incidences in high dose males (45%) and both groups of treated females (17-19%) were increased significantly relative to the controls (20% in males, 3% in females). The findings in male mice occurred in the presence of hepatocytomegaly and hepatic focal necrosis in both treatment groups. The incidence of liver tumors in female mice was essentially identical in the two treated groups, despite a 2-fold difference in dose. High dose females also showed an increased incidence of thyroid tumors but this was not clearly dose-related (combined follicular cell carcinomas and adenomas, adjusted rates 3%, 0%, or 21% in control, low, and high dose groups), and occurred in the presence of liver changes (hepatocytomegaly, focal necrosis, tumors), which may have affected the metabolic and/or hormonal status of the animals. Body weights (both sexes) were unaffected by treatment, while survival at week 103 was reduced in

treated females due to reproductive tract infection (70%, 58% and 52% for control, low and high dose animals; males unremarkable). NTP concluded that there was some evidence of carcinogenicity for PDC in male and female mice, based upon an increased incidence of hepatocellular neoplasms, primarily adenomas (thyroid tumors disregarded). While the mechanism underlying these changes is unknown, the occurrence of histopathological liver lesions in male mice (LOAEL 125 mg/kg bw/day) suggests that chronic target organ toxicity may have played a contributing role in the expression of these benign tumors.

Hepatocellular adenoma is a common finding in control B6C3F1 mice. Historical control data for this lesion from contemporaneous NTP studies conducted to 1995 (corn oil, gavage, 16 studies) returned an incidence of 267/813 (33%) in males (range 14-58%) and 111/809 (14%) in females (range 2-28%) (Analytical Services Inc, 1995). Comparison of this historical control information with findings from the NTP study shows that the control incidence for males and females from this study (20%, 3%, respectively) was lower than the mean historical control data, while the incidence for high dose males (45%) and both treated females groups (17%, 19%) was below the upper bound of the historic control data. Spontaneous biological variation in the control data may therefore have influenced the results of this study.

When reviewing the rat and mouse tumor findings reported by NTP, IARC (1999) concluded that 1,2-dichloropropane is *not classifiable as to its carcinogenicity to humans (Group 3)*.

Conclusion

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.

3.1.8 Toxicity for Reproduction

Data are available from guideline, GLP studies both for effects on fertility and for effects on development.

Studies in Animals

Effects on Fertility

The effect of PDC on the reproductive performance of male and female S-D rats was investigated in a GLP-compliant, guideline, 2-generation study by Kirk *et al*. (1990). PDC was administered in drinking water at levels of 0%, 0.024%, 0.1% or 0.24% (w/v), equivalent to received doses of 20-30, 70-130 or 130-250 mg/kg bw/day, respectively, for the parental generations; females received higher doses during lactation, equivalent to approx. 60, 200 and 450-500 mg/kg bw/day. Water consumption was decreased 20-50% in the mid- and high dose groups, possibly reflecting poor palatability linked to the presence of PDC. Gestational body weight gain was reduced by approx. 20% in high dose dams and 7-13% in mid dose females. Treatment-related hepatocellular granularity, considered an adaptive change by the study pathologist, was present in males and females of both generations at all dose levels (incidence in high dose animals: $\leq$17% in females; <13% for males). All other tissues, including reproductive organs from both sexes, were unremarkable. Other key findings are presented qualitatively in Table 3.1.8.1.

Table 3.1.8.1. Summary of Main Findings from a 2-Generation Reproduction Study on 1,2-Dichloropropane in Rats.

Endpoint	Concentration of PDC in drinking water					
	0.024%		0.1%		0.24%	
	F_0	F_1	F_0	F_1	F_0	F_1
Male bw	-	-	↓	-	↓	↓
Female bw (pre-mating)	-	-	-	-	↓	↓
Water intake (both sexes)	↓	↓	↓	↓	↓	↓
Gestation bw	-	-	-	↓	↓	↓
Gestation bw gain	-	(↓)	(↓)	↓	↓	↓
Gestation water intake	-	-	↓	↓	↓	↓
Gestation food intake	-	(↓)	-	(↓)	-	↓
Lactation bw	-	-	↓	-	↓	↓
Lactation bw gain	(↓)	-	↓	-	↓	-
Lactation water intake	↓	-	↓	↓	↓	↓
Lactation food intake	-	-	↓	-	↓	-
Litter size	-	-	-	-	↓	-
Postnatal survival	-	-	-	-	↓	↓
Neonatal bw	-	-	-	-	↓	↓

Key:
- no effect; (↓) slight decrease; ↓ decrease

Despite the observed effects, reproductive function was unaffected in males and females of both generations. Although neonatal body weight was decreased, and neonatal mortality increased, 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 appears secondary to maternal dehydration and a 20% reduction in gestational body weight gain, rather than a direct effect on reproduction. Live births, litter sizes and other pup parameters were unremarkable. Based on these findings, the study demonstrated a parental NOAEL of 20-30 mg/kg bw/day (0.024%; based upon body weight effects), a NOAEL in the offspring of 70-130 mg/kg bw/day (0.1%), and a reproductive NOAEL of 130-250 mg/kg bw/day (0.24%). Overall this study provides no evidence that PDC selectively targets the male or female reproductive system.

Developmental Toxicity

The potential effects of PDC on embryonal/fetal development were investigated in two species by Kirk *et al*. (1995) in two GLP-compliant guideline studies. Pregnant S-D rats were treated with 0, 10, 30 or 125 mg/kg bw/day PDC in corn oil (gavage) on gestation days 6-15 inclusive and fetuses examined on GD 20, while pregnant New Zealand White rabbits received 0 (corn oil vehicle), 15, 50 or 150 mg/kg bw/day on GD 7-19, inclusive, followed by a fetal examination on GD 28.

Clear signs of maternal toxicity were present in high dose animals of both species. Rats given 125 mg/kg bw/day exhibited clinical signs (decreased movement and muscle tone, lacrimation, salivation) on GD 6 and 7, with an approx. 25% reduction in food and water consumption and a 30% reduction in body weight gain over the entire treatment period. Rabbits given 150 mg/kg bw/day showed a statistically significant net reduction in mean body weight gain on GD 7-20

(decreased 165 g) while controls showed a net gain (49 g) during the same period. Hematological changes were also noted in high dose rabbits (not evaluated in rats), with an approx. 20% reduction in red cell counts, hemoglobin concentration and hematocrit, while platelet and white cell counts were increased by 20-25%. Fetal examination revealed a similarly low incidence of variations in control and treated groups of both species; the only treatment-related finding was a significant increase in delayed ossification of the bones of the skull in high dose rats and rabbits, indicative of a developmental delay. There was no evidence of any teratogenic effect. The NOAELs from this study are summarised in Table 3.1.8.2.

Table 3.1.8.2. Maternal and Fetal NOAELs for 1,2-Dichloropropane.

Endpoint	NOAEL (mg/kg bw/day)	
	Rat	Rabbit
Maternal toxicity	30	50
Fetal toxicity	30	50
Teratogenicity	125	150

Overall, results from these well-conducted developmental toxicity studies demonstrated the occurrence of mild fetotoxicity (delayed ossification) coincident with maternal toxicity. PDC was not teratogenic under the conditions of these investigations.

Conclusion

Overall these studies provide no evidence that PDC selectively targets the male or female reproductive systems or the developing embryo/fetus.

3.2 Initial Assessment for Human Health

Toxicokinetic studies indicate rapid absorption and widespread systemic distribution of 1,2-dichloropropane after ingestion or inhalation exposure. It is subsequently metabolized and excreted *via* the urine (conjugated metabolites) or exhaled air (predominately carbon dioxide).

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. It is irritating to the eye but causes only slight skin irritation. Results from two briefly reported case studies 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 (rats, mice) and red blood cell (rabbit) appear to be the principal target tissues following repeated exposure, with decrements in body weight gain also reported in the rat after inhalation or gavage exposure. Site-of-contact effects, consistent with repeated local irritation, have been described in stomach (oral gavage) and nasal tissue (inhalation). Neurotoxicity studies revealed no structural abnormalities nor functional deficits after sub-chronic gavage administration.

Results from *in vitro* genotoxicity tests (with and without metabolic activation) are mixed, with both positive and negative results, indicating that PDC has *in vitro* mutagenic potential. However, findings 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.

Equivocal evidence of an increase in morphologically atypical mammary tumors (adenocarcinoma or highly cellular fibroadenoma) was reported in female rats in the presence of a marked reduction in survival and body weight, while some evidence of an increased incidence of hepatic adenocarcinomas was found in male and female mice relative to concurrent (but not historic) controls in the presence of liver damage and decreased body weight (females only). Overall it is considered 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. IARC concluded that 1,2-dichloropropane is *not classifiable as to its carcinogenicity to humans (Group 3)*.

1,2-dichloropropane is not a developmental or reproductive toxicant.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The acute and chronic toxicity of PDC toward aquatic species has been investigated in fish, invertebrates, and algae, and results are summarized below and in Table 4.1. The results from these studies provide information on all key SIDS endpoints, and provide adequate reliable data to support an assessment of the key SIDS endpoints. Additional information is also available with regard to acute effects on earthworm.

Acute Toxicity Test Results

In a modern GLP-compliant guideline study using flow-through conditions and analytical confirmation of achieved concentration, Boeri (1988) obtained a 48 hr EC_{50} of 55.9 mg/l for immobilization of *Daphnia magna*.

Consistent results were obtained from the fish toxicity studies of Walbridge *et al*. (1983) and Benoit *et al*. (1982) that demonstrate that PDC is of low acute toxicity towards freshwater fish (LC_{50} ~140 mg/l). Although these studies pre-date current testing guidelines, they included analytical confirmation of achieved exposure concentrations which increases confidence in the reliability of the results obtained.

Information on the acute toxicity of 1,2-dichloropropane on the salt-water algae *Skeletonema costatum* is available from Hughes (1988). This is a modern, GLP-compliant static guideline test, however GC analysis revealed variable losses of test substance from the screw-capped test vessels over the course of the study. As a result, no direct calculation of the EC_{50} was possible. In recognition of this, Woodburn (2002a) used a time-weighted average AUC method (based on the measured dissipation rate of PDC from the test vessels) to calculate the no-effect concentration for this algal species. A $NOEC_{120\ hr}$ of 7.4 mg/l was thus obtained. In addition, Woodburn (2002b) calculated the percentage biomass inhibition and inhibition of growth rate over 72 hr based upon time-weighted average exposure concentration, and derived EC_{50} values of 16.3 mg/l and 14.7 mg/l, respectively. De Groot (2002) also re-analyzed the original data from Hughes (1988) using linear interpolation after log transformation of the results obtained over the first 3 days of the study. This approach returned 72-hr EC_{50} values of 15.1 and 15.8 mg/l for biomass and growth inhibition, respectively, and a 72-hr NOEC of 8.9 mg/l. Overall the data obtained by re-analysis of Hughes (1988) supports a 120-hr algal NOEC in the range 7.4-8.9 mg/l, with 72-hr EC_{50} values of 15.1-16.3 mg/l for biomass inhibition and 14.7-15.8 mg/l for growth inhibition.

Table 4.1. Aquatic Toxicity Results for 1,2-Dichloropropane.

Organism	Duration	LC_{50} , EC_{50}, IC_{50} mg/l	NOEC mg/l	Source
Acute effects data				
Fish				
Pimephales promelas (freshwater)	96 hr	140	-	Walbridge *et al*., 1983
*Pimephales promelas (*freshwater)	96 hr	139	-	Benoit *et al*., 1982
Invertebrate				
Daphnia magna (freshwater)	48 hr	55.9	8.3	Boeri, 1988
Algae				
Skeletonema costatum (saltwater)	120 hr	-	7.4	Hughes, 1988; Woodburn, 2002a
Growth rate inhibition Biomass inhibition	72 hr	14.7; 16.3	-	Hughes, 1988; Woodburn 2002b
Biomass inhibition Growth rate inhibition	72 hr	15.1; 15.8	8.9	Hughes, 1988; deGroot, 2002
Chronic effects data				
Fish				
Pimephales promelas (growth; freshwater)	28 days	-	6	Benoit *et al*., 1982
Pimephales promelas (survival; freshwater)	28 days	-	11	Benoit *et al*., 1982
Invertebrate				
Daphnia magna (reproduction; freshwater)	21 days	-	8.3	Boeri, 1988
Mysidopsis bahia (mortality, reproduction, growth; saltwater)	28 days	-	4.1	Ward *et al*., 1989

Chronic Toxicity Test Results

In addition to the above, chronic aquatic toxicity data are available from a fish early life-stage (ELS) test and a *Daphnia* reproduction study. In the ELS test, a chronic NOEC of 6 mg/l was obtained for growth, and a chronic NOEC of 11 mg/l for survival, when *Pimephales promelas* was exposed to PDC for 28 days under flow-though conditions (Benoit *et al*., 1982). The study included analytical verification of exposure concentration. The chronic invertebrate test, involving *Daphnia magna* (Boeri, 1988), was a GLP-compliant guideline investigation with analytical confirmation of exposure concentration. This returned a 21 day NOEC for effects on reproduction of 8.3 mg/l.

Results from a 28 day study using the marine invertebrate *Mysidopsis bahia* (Ward *et al*., 1989) gave a chronic NOEC of 4.1 mg/l for effects on mortality, reproduction and growth. The study was a GLP-compliant guideline investigation performed under flow-through conditions, with analytical confirmation of achieved exposure concentration.

Conclusions

In summary, information on the chronic toxicity of 1,2-dichloropropane toward aquatic species is available for three trophic levels (algae, fish, invertebrates), and provides consistent results for chronic NOEC values in a range 4.1 to 8.9 mg/l. The invertebrate *Mysidopsis bahia* appears to be the most sensitive species with a chronic NOEC of 4.1 mg/l.

4.2 Terrestrial Effects

Acute Toxicity Test Results

Supplemental data are available from a earthworm acute toxicity test (artificial soil, OECD guideline 207 using *Eisenia fetida*) which returned a 14-day LC_{50} of 4240 mg/kg soil (dry weight) (Neuhauser *et al.*, 1985).

4.3 Initial Assessment for the Environment

Environmental partition modelling suggests that releases of 1,2-dichloropropane into air will stay in air, where it will be removed by photodegradation and/or reaction with hydroxyl radicals. Data from PDC and a structural analogue (1,2-dichloroethane) indicate it will not lead to the introduction of chlorine into the stratosphere (negligible ozone depleting potential); in addition the potential for PDC to contribute to GWP or POCP is considered as negligible. It is not readily or inherently biodegradable when tested in standard laboratory tests; it is not expected to bioaccumulate.

Based on a modelled value for Koc of 68, PDC is expected to have high mobility in soil. The low Koc and the Henry's Law constant of 274 Pa m^3 mol^{-1} indicate that PDC is expected to volatilize from soil surfaces and to a lesser extent from water surfaces.

Results from aquatic toxicity testing indicate it is of low acute hazard toward fish, invertebrates, and alga with EC_{50} values in a range 15-140 mg/l, and with chronic aquatic NOEC values of 4.1-11 mg/l in these same species.

Results from a guideline acute toxicity test using earthworm gave an LC_{50} of 4240 mg/kg soil (dry weight).

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

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.

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S I D S

D o s s i e r

Existing Chemical	ID: 78-87-5
CAS No.	78-87-5
EINECS Name	1,2-dichloropropane
EC No.	201-152-2
TSCA Name	Propane, 1,2-dichloro-
Molecular Formula	C3H6Cl2

Producer Related Part

Company:	Dow Chemical, TERC
Creation date:	05-OCT-2004

Substance Related Part

Company:	Dow Chemical, TERC
Creation date:	05-OCT-2004

Memo:	PDC File originally from AK Mallett
Printing date:	23-JAN-2006
Revision date:	
Date of last Update:	**23-JAN-2006**
Number of Pages:	**215**
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

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13-JAN-2006

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Source: The 1,2-Dichloropropane ICCA/HPV Consortium
22-DEC-2004

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

1.1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: > 99 - % w/w
Odour: sweet, chloroform-like

Remark: stable; colorless
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

1.1.2 Spectra

1.2 Synonyms and Tradenames

1,2-Dichlorpropan

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
06-JAN-1994

alpha, beta-Dichloropropane

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

alpha, beta-Propylene dichloride

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Dichloro-1,2-propane

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Dichloropropane

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propane, 1,2-dichloro

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propylenchlorid

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propylendichlorid

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propylendichlorid-1,2

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propylene chloride

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
13-DEC-1993

Propylene dichloride

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

1.3 Impurities

EINECS-Name: oxygenated organic substances
Contents: < .4 - % w/w

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

CAS-No: 67-64-1
EC-No: 200-662-2
EINECS-Name: acetone
Contents: < .1 - % w/w

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

CAS-No: 123-38-6
EC-No: 204-623-0
EINECS-Name: propionaldehyde
Contents: < .1 - % w/w

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

CAS-No: 7732-18-5
EC-No: 231-791-2
EINECS-Name: water
Contents: <= .02 - % w/w

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

1.4 Additives

Remark: no additives
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

1.5 Total Quantity

Quantity: 350000 tonnes produced in 2001

Remark: Volume refers to production globally
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
10-JAN-2006 (1) (2) (3) (4)

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: (F) highly flammable
(Xn) harmful
Specific limits: no
R-Phrases: (11) Highly flammable
(20/22) Harmful by inhalation and if swallowed
S-Phrases: (16) Keep away from sources of ignition - No smoking
(24) Avoid contact with skin

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (5)

1.6.2 Classification

Classified: as in Directive 67/548/EEC
Class of danger: harmful
R-Phrases: (20/22) Harmful by inhalation and if swallowed

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004

Classified: as in Directive 67/548/EEC
Class of danger: highly flammable
R-Phrases: (11) Highly flammable

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
21-DEC-2004 (5)

1.6.3 Packaging

1.7 Use Pattern

Type: use
Category: Fuel additives

Remark: 1,2-dichloropropane is used as a lead additive in fuel additives. Given the reduction in use of leaded fuels, this use is minor.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
21-DEC-2004 (6)

Type: use
Category: Intermediates

Remark: Used as an intermediate in the production of chlorinated solvents (perchloroethylene/tetrachloroethylene).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (7)

Type: industrial
Category: Basic industry: basic chemicals

Remark: 1,2-dichloropropane was used as a solvent for oil, fats, caoutchouc, gum, wax and resins and also as a textile spot remover, paraffin remover, scrubbing agent ingredient, cleanser and a galvanizer. As bitumen, asphalt and tar dissolves easily in 1,2-dichloropropane it was used to manufacture construction aides and roofing.
1,2-dichlorpropane is no longer used in Western Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
22-DEC-2004 (8) (9) (10)

Type: type
Category: Non dispersive use

Remark: 1,2-dichloropropane is and was used as a nematicide, insecticide and pesticide. Formulations of 1,2-dichloropropane and 1,3-dichloropropene are used.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
22-DEC-2004 (11) (12) (13) (9) (14) (15) (10)

Type: type
Category: Wide dispersive use

Remark: 1,2-dichloropropane is and was used in a number of consumer and professional products (paints, laquers and varnishes, adhesives, solvents, degreaser, dilutor, stripper, car care). Overall, a total of 4 consumer products and 42 industrial products are listed in the Swiss product register. There were no entries for PDC in the Danish product register, and no products containing pDC listed on the Danish market, underscoring its limited use in consumer products.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
29-NOV-2005

Type: industrial
Category: Agricultural industry

Remark: 1,2-dichloropropane was used as a nematicide,insecticide and pesticide. Commercial products such as Telone II or D-D contains 94 % 3-dichloropropene and 0,2 % 1,2-dichloropropane or 52 % 1,3-dichloropropene and 29 % 1,2-dichloropropane. At this time in the German Republic (BRD) 1,2-dichloropropane in pesticides is not allowed and

is not on the market.
This use type is discontinued in the U.S. and the EU. Status in other OECD countries is unclear.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (8) (16) (17) (18)

Type: use
Category: Pesticides

Remark: 1,2 dichloropropane has been used as a nematicide, insecticide and pesticide. Formulations of 1,2-dichloropropane and 1,3-dichloropropene are applied to the above.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
21-DEC-2004 (11) (12) (13) (9) (14) (15) (19)

Type: use
Category: other: Raw Material in production of propylene

21-DEC-2004 (1)

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: MAC (NL)
Limit value: 350 mg/m3

Country: Netherlands
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (20)

Type of limit: MAK (DE)
Limit value: mg/m3

Country: Germany
Remark: No MAK-value is given. Dichloropropane is in the carcinogenic group IIIB, i.e. the compound is possibly expected to have carcinogenic potential.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (21)

Type of limit: other: ACGIH TLV (US)
Limit value: 347 mg/m3
Short term exposure
Limit value: 508 mg/m3
Schedule: 15 minute(s)
Frequency: 4 times

Country: USA
Remark: Dichloropropane is identified by other sources as a possible human carcinogen.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (22)

Type of limit: other: Odor Threshold limit in air
Limit value: 420 mg/m3

Country: USA
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (23)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

Remark: Production process:
Propylenedichloride is a co-product of the chlorohydrin process during the production of propylene oxide and of alkylchloride.

Emission:
The existing exposure guidelines are strictly followed during production.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (7)

1.11 Additional Remarks

Remark: Water Pollution

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 3 (strongly water polluting)
Country : Germany

Classified by : EU Commission
Labelled by : EU Commission

Class of danger : -
Country : EU
Remark : The European Union added 1,2-dichloro-propane to the "black list", which contains 129 substances of high priority chemicals. 1,2-dichloropropane is one of the 83 substances of this list with special significance for the Rhine River tributaries. At the same time these 83 substances also entered the research program of the International Rhine Commission.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
25-OCT-2004 (24) (25)

Remark: Major Accident Hazards

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
Country : Germany
Remark : appendix II, Number 114

Legislation : Gefahrgutverordnung Binnenschiffahrt (GGVBinSch)
Substance listed : yes
Country : Germany
Remark : class 3, Number 1a

Legislation : Gefahrgutverordnung Eisenbahn (Reglement international concernant le transport des marchandises dangereuses par chemins de fer/Accord europeen relatif au transport international des marchandises dangereuses par route, RID (GGVE)
Substance listed : yes
Remark : class 3, Number 3b

Legislation : Gefahrgutverordnung See (GGVSee)
Substance listed : yes
Remark : class 3.2

Legislation : Gefahrgutverordnung Strasse (GGVS)
Substance listed : yes
Country : Germany
Remark : class 3, Number 3b

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
10-JUL-2000 (26) (27) (28) (29) (30)

Remark: Air Pollution
==========

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Class of danger : 1 Number: 3.1.7 (organic substances)
Country : Germany
Remark : 1,2-dichloropropane is not listed in Appendix E of the "TA-Luft". Corresponding to Nr. 3.1.7, paragraph 3 of the "TA-Luft" 1,2-dichloropropane was added to class I. The emission concentration of class I substances can not exceed 20 mg/m3 by a mass stream of 0.1 kg/h.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
08-AUG-2000 (31)

1.12 Last Literature Search

1.13 Reviews

2.1 Melting Point

Value: = -100.4 degree C

Test substance: as prescribed by 1.1 - 1.4

Remark: Preferred value.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (32)

Value: = -100.4 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (33)

Value: = -100.4 degree C

Method: other
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
29-FEB-2004 (34)

Value: = -100 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (35)

Value: = -100 degree C

Method: other: not specified
GLP: no data

Remark: Freezing point;
Hazardous decomposition products: hydrogen chloride, chlorine, phosgene
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (36)

2.2 Boiling Point

Value: = 96.4 degree C

Year: 2001
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Preferred value. Experimental data judged acceptable by the AIChE (American Institute of Chemical Engineers) DIPPR ENVIRON 2001 database.
Reliability: (2) valid with restrictions
2g- data from a handbook or collection of data.
20-OCT-2004 (37)

Value: = 94 - 96.8 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
20-OCT-2004 (32)

Value: = 96.4 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
20-OCT-2004 (33)

Value: = 96.4 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
20-OCT-2004 (34)

Value: = 96.8 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
20-OCT-2004 (38)

Value: = 95 - 100 degree C

Method: other: DIN 53 171
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)

21-DEC-2004 (36)

Value: = 96 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (35)

Value: = 96.5 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (19)

Value: = 96.6 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (39)

2.3 Density

Type: density
Value: = 1.155 g/cm³ at 20 degree C

Test substance: as prescribed by 1.1 - 1.4

Remark: Preferred value. Mean calculated value at 20 degrees C based on data from MacKay et al. (1993).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
01-MAR-2004 (32)

Type: density
Value: = 1.1494 - 1.16 at 20 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
01-MAR-2004 (32)

Value: = 1.156 g/cm³ at 20 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (34)

Value: = 1.159 g/cm³ at 25 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (40)

Value: = 1.182 g/cm³ at 0 degree C

Method: other: not specified
GLP: no data

Remark:

Temperature	Density (g/cm3)
20	1.155
50	1.116
80	1.075

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Type: relative density
Value: = 1.16 g/cm³ at 20 degree C

Method: other: not specified
GLP: no data

Remark: Density was measured in relation to water (water=1).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

Type: relative density
Value: = 1.16 g/cm³ at 20 degree C

Method: other: not specified
GLP: no data

Remark: Density was measured in relation to air (air=1).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

Value: = 1.166 g/cm³ at 20 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (36)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: = 66.2 hPa at 25 degree C

Test substance: as prescribed by 1.1 - 1.4

Remark: Perferred value (Mackay et al. 1993) = 66.2 hPa (25 degrees C)
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
01-MAR-2004 (32)

Value: = 66.17 - 71.98 hPa at 25 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (32)

Test substance: as prescribed by 1.1 - 1.4

Remark: Vapour Pressure = 49.67 mm Hg at 25 degrees C
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
29-FEB-2004 (33)

Value: = 18 hPa at 0 degree C

Method: other (calculated): not specified
GLP: no data

Remark:

Temperature	Vapour Pressure
20	51 - 56 hPa
50	198 hPa
80	599 hPa

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (10)

Value: 51 - 56 hPa at 20 degree C

Method: other (calculated): not specified
GLP: no data

Remark: Ref. 1:

Temperature	Vapour Pressure
20	51 - 56 hPa
25	66.7 hPa
30	88.0 hPa

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (41) (42) (38)

Value: = 13.3 hPa at -6.1 degree C

Method: other (calculated): not specified
GLP: no data

Remark:

Temperature	Vapour Pressure
19.4	53.3 hPa
25	66.7 hPa
39.4	133.3 hPa
76	533.2 hPa

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (43)

Value: = 52.3 hPa at 20 degree C

Method: other (calculated): not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = 2

Test substance: as prescribed by 1.1 - 1.4

Remark: Preferred value (Mackay et al. 1993) Log Kow = 2.00
(temperature not stated)
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
11-OCT-2004 (32)

Partition Coeff.: octanol-water
log Pow: = 1.99 - 2.28

Test substance: as prescribed by 1.1 - 1.4

Remark: Temperature of determination not available.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
01-MAR-2004 (32)

Partition Coeff.: octanol-water
log Pow: = 1.99

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
01-MAR-2004 (33)

log Pow: = 1.99

Method: other (calculated): according to
Pomona-MedChem-Strukturfragment-Method
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

log Pow: = 2

Method: other (calculated): according to Hansch & Leo (1979)

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (9)

log Pow: = 2.02

Method: other (calculated): according to Hansch & Leo (1979)

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (44)

log Pow: = 2.02

Method: other (calculated): Computer calculation according to fragment method

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (45)

log Pow: = 2.16

Method: other (calculated): according to Rekker (1977)

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (46)

Year: 2004
Test substance: as prescribed by 1.1 - 1.4

Method: The following parameters were used as inputs for the PCKocWIN V1.66 software to estimate Koc:

SMILES: ClC(CCl)C
Molecular Formula: C3H6Cl2
Molecular Weight: 112.99
Remark: Preferred value for Koc.

The Koc value suggests that the chemical is expected to have very high mobility in soil.
Result: Koc = 67.7

Non-corrected Log Koc = 1.8306
First order molecular connectivity index = 2.270
Corrected Log Koc = 1.8306
Reliability: (2) valid with restrictions
2f (accepted calculation method)
29-NOV-2005 (47)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 2800 mg/l at 25 degree C

Test substance: as prescribed by 1.1 - 1.4

Remark: Preferred value.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
23-JAN-2006 (32)

Solubility in: Water
Value: = 2.8 g/l at 20 degree C

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
11-OCT-2004 (42)

Value: = 2.7 g/l at 20 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions

Data from handbook or collection of data.
11-OCT-2004 (39) (38)

Solubility in: Water
Value: = 2740 mg/l at 25 degree C

Test substance: as prescribed by 1.1 - 1.4

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
11-OCT-2004 (33)

Value: = 3 g/l at 20 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (36)

Solubility in: Water

GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Solubility of water in 1,2-dichloropropane at 20C is 1.6 g/L.
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Solubility in: other: ethanol, diethylether, benzol, and chloroform

Remark: 1,2-dichloropropane is soluble in ethanol, diethylether, benzol, and chloroform.
Reliability: (2) valid with restrictions
21-DEC-2004 (34)

2.6.2 Surface Tension

Value: = .3 mN/m at 20 degree C

GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Surface tension at 20 degrees C: 0.03 N/m
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19) (48)

2.7 Flash Point

Value: = 21 degree C
Type: open cup

Method: other: DIN 51758

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
29-FEB-2004 (40)

Value: = 13 degree C
Type: closed cup

Method: other: DIN 51755

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (49)

Value: = 15 degree C
Type: closed cup

Method: other: DIN 51755

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Value: = 16 degree C
Type: closed cup

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

2.8 Auto Flammability

Value: = 555 degree C

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
11-OCT-2004 (50)

Value: = 557 degree C

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from a handbook
11-OCT-2004 (6)

Value: = 600 degree C

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from a handbook

11-OCT-2004 (10)

Value: =

Method: other: DIN 51 794
GLP: no data

Remark: Auto-ignition temperature > 200 degrees C
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
24-JUL-2000 (36)

2.9 Flammability

Result: flammable

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (50)

Result: other: flammability limits

Method: other: not specified
GLP: no data

Remark: Upper and lower flammability limits are 12.2 (at 50 degrees C) and 3.2 %vol/vol, respectively.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

2.10 Explosive Properties

Result: other: explosive

Remark: Highly flammable vapors of 1,2-dichloropropane together with air are explosive. This mixture is heavier than air.
Explosion limit (Vol.-%) at 20 degrees C:
upper limit: 14.5
lower limit: 3.4
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (41) (50) (51)

2.11 Oxidizing Properties

2.12 Dissociation Constant

2.13 Viscosity

GLP: no data

Test substance: as prescribed by 1.1 - 1.4

Result: viscosity (mPa x s):
at 0 degree C 1.2
at 20 degrees C 0.85
at 50 degrees C 0.58
at 80 degrees C 0.44
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (10)

2.14 Additional Remarks

Remark: Vapor density: 3.9 kg/m3
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (38)

Remark: relative vapor density: 3.89 (air = 1)
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
21-DEC-2004 (39)

Remark: Thermal energy at 304 degrees C, 44300 hPa: 308.0 kJ/kg
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Remark: Thermal energy: 312.1 kJ/kg
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (34)

Remark: Specific temperature at 30 degrees C: 1.38 kJ/kg x K
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Remark: Azeotropic mixtures (at 1013 hPa):

1,2-dichloropropane with	boiling point (degrees C)	weight-% 1,2-dichloropropane in the azeotrope
water	78.0	90
methanol	62.9	47

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (19)

Remark: Azeotropic mixtures (at 1013 hPa):

1,2-dichloropropane with	boiling point (degrees C)	weight-% 1,2-dichloropropane in the azeotrope

	ethanol	74.7	42.3
	cyclohexane	80.4	16
	tetrachloromethane	76.6	16

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
21-DEC-2004 (49)

3.1.1 Photodegradation

Type: air

Test substance: as prescribed by 1.1 - 1.4

Remark: I. Lifetime of 1,2-Dichloropropane

A. Rate of Reaction of 1,2-Dichloropropane with Hydroxyl Radical
The absolute rate constant has been measured for the gas-phase reaction of hydroxyl radicals with 1,2-dichloropropane. Experiments were carried out using the pulsed laser photolysis-laser induced fluorescence technique over the temperature range 233-372 K. The kinetic data obtained were used to derive the following Arrhenius expression:

k=(2.1±0.5)x10-12 exp[-(453±76)/T] (in units of cm3molecule-1 s-1)

The quoted errors for the pre-exponential factor, A, and E/R are given by (delta)A=2Asigma(lnA) and E/R=2sigma(E/R) respectively. At room temperature, the rate constant obtained is (4.6±0.6)x10-13 cm3molecule-1s-1.

OH + CH2(Cl)CH(Cl)CH3 --> products

The rate constant obtained at 298 K was compared with the calculated one using a quantitative structure-activity relationship (QSAR.) The calculated value, 5.2 x10-13 cm3molecule-1s-1 was in excellent agreement with the experimental one.

B. Upper Limit on Rate of Reaction of 1,2-Dichloropropane with Hydroxyl Radical

The rate constant for reaction of 1,2-dichloropropane with hydroxyl radical is <4.4x10-13cm3 molecule-1sec-1 at 296 K (23°C) based on its rate relative to dimethyl ether. That does not contradict the work above, since the discrepancy is well within the experimental error of the measurements.

C. Estimation of the Lifetime of 1,2-Dichloropropane

The lifetime (t=1/(k[OH]) of 1,2-dichloropropane, was estimated by using a global tropospheric 24-hour average OH radical concentration of 1x10^6 molecule cm-3 and the measured bimolecular rate constant at room temperature. The tropospheric lifetime of 25 days is relatively short and hence one should consider the oxidation products to evaluate its atmospheric impact.

II. Products of Oxidation of 1,2-Dichloropropane

The QSAR for estimating the rate of reaction of 1,2-dichloropropane with hydroxyl radicals (3) also provides an estimate of the amount of hydrogen abstraction from each carbon atom; 60% from the central carbon, 29% from the

chloromethyl (-CH2Cl) group and 11% from the methyl group.

The products of chlorine-initiated oxidation of a similar molecule, 1,2,3-trichloropropane have been studied. 1,2,3-Trichloropropane is oxidized through ClCH2CCl(*)CH2Cl and ClCH2CHClCH(*)Cl radicals which are analogous to the major radical products of H-abstraction from 1,2-dichloropropane by HO*.

The initial radicals react with oxygen to form peroxy radicals (ROO*) which are reduced, largely by reaction with NO, to alkoxy radicals (RO*).

By analogy to the decomposition of CH2ClCCl(O*)CH2Cl, which yields a majority of 1,3-dichloroacetone by Cl atom loss and some HC(=O)Cl and ClCH2C(=O)Cl by C-C bond cleavage followed by oxidation of ClCH2*, the main products from 1,2-dichloropropane will be chloroacetone, acetyl chloride (CH3C(=O)Cl) and formyl chloride (HC(=O)Cl) as shown in the following reactions.

CH3CCl(O*)CH2Cl → CH3C(=O)CH2Cl + Cl*

CH3CCl(O*)CH2Cl → CH3C(=O) Cl + *CH2Cl

*CH2Cl —O2→ *OOCH2Cl —NO→ oOCH2Cl —O2→ HC(=O)Cl + HO2*

The minor attack at the CH2Cl group leads to an alkoxy radical that, by analogy to similar attack on 1,2,3-trichloropropane, will yield some CO2 and the CH3CHCl radical as well as uncertain amounts from other pathways leading ultimately to HCl and acetyl chloride.

CH3CHClCH(*)Cl ---> CH3CHClCH(OO*)Cl ---> CH3CHClCH(O*)Cl

CH3CHClCH(O*)Cl ---> CH3CHClC(=O)* + HCl --> --> CH3CHClC(=O)O*

CH3CHClC(=O)O* ---> CO2 + CH3CH(*)Cl ---> ---> CH3C(=O)Cl or HCl + CH3C(=O)*

II.A. Fate of Oxidation Products

II.A.1. Chloroacetone

Chlorination of acetone results in a red shift and increase of the UV absorption. The UV spectrum of chloroacetone much more closely resembles that of 1,3-dichloroacetone than acetone. Using the actinic flux (the quantity of light available to molecules at a particular point in the atmosphere) representative of a summer day at 40°N the photolysis lifetime for 1,3-dichloroacetone is between 30 minutes and 12 hours. The estimated photolysis half-life of acetone is ~80 days at the surface and ~30 days at 5 km at 40°N in the summer. Thus the half life of chloroacetone will be much shorter than that required for transport to the stratosphere.

The estimated lifetime of chloroacetone due to reaction with hydroxyl radicals in the atmosphere is 29 days based on kOH= 0.3682 x 10-12 cm3 molecule-1 sec-1 and days with an average of 1 x 106 molecules cm-3 of HOo for 12 hours of daylight. Photolysis will be the main pathway of removal of chloroacetone from the atmosphere, but reaction with HOo also is sufficient to prevent significant transport of chlorine to the stratosphere.

II.A.2. HCl, Acetyl chloride (CH3C(=O)Cl) and Formyl chloride (HC(=O)Cl)

The atmospheric fate of these compounds is expected to be incorporation into rain-cloud-fog water followed by hydrolysis and removal by wet deposition within probably 5-15 days.

Similarly, HC(=O)Cl and CH2ClC(=O)Cl, the chlorinated organic products from photooxidation of 1,2-dichloroethane, are considered to have lifetimes in the lower atmosphere which are much shorter than that required for transport to the stratosphere and so are incapable of delivering significant amounts of chlorine to the stratosphere.

III. Ozone Depletion Potential of 1,2 Dichloropropane

Based on the lifetime and the products of oxidation, emission of 1,2-dichloropropane will not put a significant amount of chlorine into the stratosphere, and the ozone depleting potential of 1,2-dichloropropane is negligible.

IV. Global Warming Potential of 1,2 Dichloropropane

The tropospheric lifetime of 1,2-dichloropropane, based on its rate of reaction with hydroxyl radicals and the average tropospheric hydroxyl concentration, is 25 days. This is very short compared to the time horizons for global climate change.

A rough comparison to 1,1,1-trichloroethane, CH3CCl3,based on a comparison of lifetimes and infrared spectra, suggests that the GWP of 1,2-dichloropropane relative to CO2 will be 7 for a time horizon of 20 years and 2 for a time horizon of 100 years.

Thus, the global warming potential of 1,2-dichloropropane is negligible.

V. Photochemical Ozone Creation Potential (POCP) of 1,2 Dichloropropane

The potential of 1,2-dichloropropane to form ozone in polluted air, although not specifically determined, is clearly low. The POCP under the 5-day European base case is in the range of 2-25 compared to 100 for ethylene.

A rough estimate of the MIR (maximum incremental reativity) of 1,2-dichloropropane indicates that it is within a factor of

two of that of ethane, which is considered to have "negligible photochemical reactivity" by the US EPA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Expert summary of available data.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (52)

Type: air

Test substance: as prescribed by 1.1 - 1.4

Remark: Photo-oxidation half-life in air, based on estimated rate constant for the vaour phase reaction with hydroxyl radicals in air, in the range 65 - 646 hr.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (32)

Type: air

Test substance: as prescribed by 1.1 - 1.4

Remark: 1,2-Dichloropropane does not have any chromophores that absorb wavelengths >290 nm, so direct photolysis will not be a significant fate process.

Vapour phase photolysis under simulated sunlight did not occur after prolonged exposure (period not stated).

Experimental determination of its rate of reaction with hydroxyl radicals gave a half-life of >23 days. A computer estimate of its half-life due to H-atom abstraction by hydroxyl radical yields a calculated half-life of 7.12 days. Typically measured data are more reliable than calculated data.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (53)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm³
Rate constant: <= .0000000000006 cm³/(molecule * sec)
Degradation: = 50 % after 27 day(s)

Method: other (calculated)
Year: 1984
Test substance: no data

Remark: No catabolic products were found.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Temperature: 22 degree C
Reliability: (2) valid with restrictions
Valid with restrictions, evaluated in report:

Kurland, J. (2003) Unpublished communication. The Dow Chemical Company, Midland, MI.

21-DEC-2004 (54)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm³
Rate constant: = .0000000000016396 cm³/(molecule * sec)
Degradation: = 50 % after 10 day(s)

Method: other (calculated)
Year: 1987
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The calculations refer to room temperature.
Reliability: (2) valid with restrictions
Valid with restrictions, evaluated in report:
Kurland, J. (2003) Unpublished communication. The Dow Chemical Company, Midland, MI.

21-DEC-2004 (55)

Type: air
Light source: Sun light
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 2000000 molecule/cm³

Method: other (calculated)
Year: 1982
Test substance: no data

Remark: The photochemical decrease of 1,2-dichloropropane was laboratory tested. The decrease was calculated at 10.2 % per day with conditions of average temperature of 27 degrees C and 12 hours of sunlight.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

21-DEC-2004 (56)

Type: air
Light source: Sun light

Remark: The direct photolysis of 1,2-dichloropropane is not relevant in the troposphere, as 1,2-dichloropropane does not absorb simulated sun light higher than 290 nm.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

21-DEC-2004 (57)

Type: other: Silica
Light source: Sun light

Method: other (measured): Stability Test

Year: 1980
GLP: no data
Test substance: no data

Remark: In presence of activated Silica the photomineralization of 1,2-dichloropropane was examined.
Activated Silica was exposed for 96 hours to a Hg-high pressure lamp (simulated sun light Lambda > 290 nm) through Pyrexglas. The determination of the photomineralization was tracked by CO2-formation.
It was observed that the oxidative degradation (build of CO2 and Cl-) of 1,2-dichloropropane which is adsorbed on the surface of the Silica, highly depends on the activation of the Silica (surface catalyzed photolysis). In non-activated Silica a buildup of 1.8 % CO2 and 3 % Cl- was determined; in activated Silica buildup was 45.9 % CO2 and 60.7 % Cl-. The activation highly influences the mineralization. This points to the fact that the photooxidative decrease of CO2 takes place at the surface and not in the gaseous phase. It is yet to be known if these lab results remain the same in nature for 1,2-dichloropropane, which can adsorb to aerosol surfaces, dusts, sands etc.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (58)

Type: water

Method: other (measured): Stability Test
Year: 1988
GLP: no data
Test substance: no data

Remark: The catabolism of 1,2-dichloropropane has been tested in Pyrex vessels containing demineralized water. As Pyrex absorbs wave-length < 290 nm, the sunlight spectrum of the troposphere was simulated during the irradiation. The transformation rate was 4 % after 180 minutes irradiation with 5.65 mg 1,2-dichloropropane/l starting concentration and was 8 % after 120 min irradiation with a starting concentration of 10.17 mg 1,2-dichloropropane/l. This results in the half-life times estimated at ca. 50.9 hours and 16.6 hours.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (59)

Type: water
Light source: Xenon lamp
Light spect.: = 450 nm
DIRECT PHOTOLYSIS
Halflife t1/2: = 5.8 minute(s)

Method: other (measured): Stability Test
Year: 1992
GLP: no data

Test substance: other TS: purity = 97 %

Remark: An unbuffered sample (with pH-values between 4.5 and 6.6) was irradiated using titandioxide (1 g/l) as a photo catalyst. To keep the titandioxide in solution, it was stirred with a magnetic stir. For control there was a solution without titandioxide kept in darkness.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (60)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH7: ca. 15.8 year at 25 degree C
t1/2 pH9: ca. 15.8 year at 25 degree C

Test substance: as prescribed by 1.1 - 1.4

Remark: Calculated half-life of 15.8 years.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (32)

Type: abiotic
t1/2 pH7: ca. 283 month at 25 degree C

Method: other: Stability Test
Year: 1988
GLP: no data
Test substance: no data

Remark: In sea water (at a pH-value of 8.3) the half-life time of 1,2-dichloropropane shortens to 60 months (5 years). Hydrolysis produces 1-Chlor-2-propanol and HCl.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The tests were treated with demineralized water.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (59)

Type: abiotic

GLP: no data
Test substance: no data

Remark: The hydrolysis rate constant (KN) of 1,2-dichloropropane is 7.2 x 10E-4 h-1 at 25 degrees C under natural conditions.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (45)

Type: abiotic

GLP: no data
Test substance: no data

Remark: Under relevant conditions to the environment there was no hydrolytical decrease established.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (61)

3.1.3 Stability in Soil

Type: laboratory

Method: other: Dissipation Test
Year: 1974

Remark: The half-life time was tested on an average of 2 sand grounds (organic compounds 7.7% and 1.9%; pH value 4.3 and 5.0) and 2 clay grounds (organic compounds 1.5% and 1.8%; clay content 7.9% and 17.4%; pH value 7.7 and 7.6). The grounds were enriched with 1,2-dichloropropane in closed glass vessels (9 times bimonthly). Twenty-seven months after the last addition of 1,2-dichloropropane the organic chloride content of the grounds was analyzed to determine the reduction of 1,2-dichloropropane. There was no control with contaminated or sterilized ground (only ground without the 1,2-dichloropropane enrichment).
Result: The following average half-life times were obtained:

Temp (degrees C)	Half-life time (days)
2	74
15	52
20	41

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
23-JAN-2006 (62)

Type: other: soil-air (calculation)

Year: 1976

Remark: 1,2-dichlorpropane was applied in open vessels that were placed outside in a sandy-clay ground layer 3 cm thick, in 12 cm depth.
Result: 1,2-dichlorpropane evaporated by 99% in 10 days. Volatile catabolic products could not be detected.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
21-DEC-2004 (63)

3.2.1 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: ground water
Concentration: = .2 - 19.4 µg/l
Method: Limit of detection = 0.2 ug/l

Remark: Samples of untreated ground water from 1,926 rural, self-supplied domestic wells in the USA were analyzed for VOCs, including 1,2-dichloropropane, during 1986-1999. Reviewer's comment: this period covers the phase-out (1984-1989) and subsequent delisting of PDC as a soil fumigant in the USA, including a 10-yr follow-up period.

Data were complied from two sources:
* Samples analyzed by the USGS National Water-Quality Laboratory between 1993-1999 as part of the US Geological Survey's National Water-Quality Assessment Program. Samples were analyzed using purge and trap gas chromatography-mass spectrometry.

* Samples analysed as part of an ambient ground water/source water quality monitoring program conducted by local, State and other Federal agencies between 1986-1995. Analysis was performed by a US-EPA certified laboratory (variety of methodologies, not reported).

Results from these analyses were included in the report only if the analytical limit of detection was 0.2 ug/l or less (i.e. 0.2 ppb or below).

PDC was present in 15/1926 samples at detected concentrations of 0.2-19.4 ug/l, with a median of 0.5 ug/l (500 ppt).

The analyzed concentration was greater than 5 ug/l in 2 of these 15 samples, and exceeded 10 ug/l in one of those 15, essentially 1 out of 1926 total samples analyzed.

Reviewer's comment: by inference, 13/15 of the 'positive' samples contained PDC at a concentration of 0.2-5 ug/l. The vast majority of samples (1911/1926 = 99.2%) contained no detectable PDC (at a limit of detection of 0.2 ug/l or 200 ppt).

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: 1,2-dichloropropane was present at concentrations of 0.2-19.4 ug/l in 15 of 1926 ground water sources from the USA analyzed during the period 1986-1999. Only two samples contained PDC at concentrations in excess of 5 ug/l. The vast majority of samples (1911/1926 = 99.2%) contained no detectable PDC (at a limit of detection of 0.2 ug/l).
Reliability: (2) valid with restrictions
Monitoring studies conducted by US government agency
25-OCT-2004 (64)

Type of measurement: background concentration
Medium: air
Method: Limit of detection at or below 2 ppt

Remark: Measurements of urban air concentrations of 24 selected VOCs,

including
1,2-dichloropropane, were conducted over periods of approx. 2 wk at 4 urban locations in the USA during the mid-1980s:

- San Jose, CA ("Silicon Valley"); April, August and December 1985 (total 35 days of sampling)
- Downey, CA; February 1984 (total 10 d)
- Houston TX; March 1984 (total 9 d)
- Denver CO; March-April 1984 (total 8 d)

Air samples were collected using a stainless steel manifold, 5 m above ground level. In the majority of locations, samples were collected 3-5 min over 1-2 hr whereas a 2 hr integrated collection regime was employed at San Jose. On average 500 ml ambient air was collected at each location, cryoconcentrated (liquid argon) and analyzed immediately by electron capture detector GC. The analytical equipment was calibrated once or twice each day using appropriate concentration standards. External audit (Northrop Services Inc., under contract to US-EPA) indicated a precision of +/-15% and accuracy of +/-30%

Reviewer's comment: no limit of detection was given for PDC however, based on results obtained, this would appear to be 2 ppt or below.

The following arithmetic mean ambient air concentrations (ppt, parts per trillion; range in parenthesis) were reported:

San Jose, CA: 31 (9-70), 25 (9-61), 24 (9-35)
Downey, CA: 35 (<2-157)
Houston TX: 158 (<2-724)
Denver CO: 163 (<2-312)

Reviewer's comment: the authors do not discuss these findings, which were generally one order of magnitude below the analyzed concentration of other VOCs reported in this study.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: The concentration of 1,2-dichloropropane in ambient air was in a range <2-157 ppt at two locations in California, <2-312 ppt in Denver, CO and <2-724 ppt in Houston, TX. Arithmetic mean concentrations were consistently less than 1 ppb (between 24 and 163 ppt).

Reliability: (2) valid with restrictions
Research investigation, suitable for assessment.

25-OCT-2004 (65)

Type of measurement: background concentration
Medium: air

Remark: In 1980 1,2-dichloropropane measured a maximum concentration of 6.93 ug/m3 taken in 350 samples from the air in Terschelling Island, The Netherlands.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (66)

Type of measurement: background concentration
Medium: air

Remark: From February - April 1984 the average of 7 samples showed 0.03 ug 1,2-dichloropropane/m3 air (mimimum 0.02 ug, maximum 0.04ug) found in Portland, Oregon, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: < 0.02 ug/m3
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (67)

Type of measurement: background concentration
Medium: air

Remark: From 1970 - 1980 minimum 0.10 ug, maximum 0.52 ug and an average of 0.27 ug 1,2-dichloropropane/m3 was found in 396 air samples in cities and suburbs in the USA. During the same time minimum 0.006 ug, maximum 0.51 and an average 0.47 ug 1,2-dichloropropane was found in headwaters in the USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (68)

Type of measurement: background concentration
Medium: air

Remark: 1,2-dichloropropane was qualitatively found in interior air of a new office buildng in the USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (69)

Type of measurement: background concentration
Medium: air

Remark: On March 29, 1982, 2.00 ug 1,2-dichloropropane/m3 was found in the pristine continental troposphere in Gaulihuette near Grindelwald, Switzerland. On April 1, 1982 1.90 ug 1,2-dichloropropane/m3 was found in Ankenbelli in the Swiss Alps. In June 1982, in the marine troposphere above the Azores, 1.9 - 7.0 ug 1,2-dichloropropane m/3 was found (n=5) and above Madeira 0.95 ug 1,2-dichloropropane/m3 was found (n=4).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: < 0.85 ug/m3
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
22-DEC-2004 (70)

Type of measurement: background concentration
Medium: air

Remark: On March 14, 1991 analysis of the air in Rome tested 0.47 ug 1,2-dichloropropane m/3 air.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 0.01 ug/m3
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (71)

Type of measurement: background concentration
Medium: air

Remark: In July 1978 the atmosphere of nine apartment houses in "Old Love Canal" (Niagara, New York, USA) were tested and two cases of 1,2-dichloropropane were found.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (72)

Type of measurement: background concentration
Medium: air

Remark: From May 1980 - April 1981 in the cities of Houston, St. Louis, Denver, Riverside, States Island, Pittsburgh and Chicago, an average between 0.11 and 0.38 ug 1,2-dichloropropane/m3 per location was found (9 - 10 samples/location).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (56)

Type of measurement: background concentration
Medium: air

Remark: On December 16, 1981 a single measure of 0.85 ug 1,2-dichloropropane/m3 air was found and on January 8, 1982 a single measure of 1.26 ug 1,2-dichloropropan/m3 air was found on the outskirts of Ulm, Germany. On May 25, 1982 the average of 2 measures showed concentrations of 1.70 ug 1,2-dichloropropane/m3 in the air. On June 25, 1982 a single measure showed 3.10 ug 1,2-dichloropropane/m3 in the city of Ulm. On February 26, 1982, 2 measures showed a concentration of 2.0 ug 1,2-dichloropropane/m3 in the unpolluted area from Weiherkopf near Sonthofen (pristine continental troposphere) in the Allgaeuer Alps in Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Proof limit: < 0.85 ug/m3
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
22-DEC-2004 (70)

Type of measurement: background concentration
Medium: surface water

Remark: From April 08 - 26, 1986 a concentration of < 2 ug/l

1,2-dichloropropane was found in the Potomac River (Virginia, USA).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (73)

Type of measurement: background concentration
Medium: surface water

Remark: On October 29, 1981, traces of 1,2-dichloropropane were found in the wilderness of Lake Crawford (Canada).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (74)

Type of measurement: background concentration
Medium: surface water

Remark: From April - July 1989 in an agricultural area in Big Creek near Ontario, Canada, 44 samples were taken in four locations, 11 samples at a time and no 1,2-dichloropropane was found.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 0.16 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (75)

Type of measurement: background concentration
Medium: surface water

Remark: From 1986 - 1989 an average of <= 1 ug of 1,2-dichloropropane was found in the upper, lower and middle courses and tributaries of the Rhine River.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (76) (77) (78) (79)

Type of measurement: background concentration
Medium: surface water

Remark: From November 8 - 22, 1988 Rhine River water in Mainz/Wiesbaden, Germany was tested and no 1,2-dichloropropane was detected
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 20 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (80)

Type of measurement: background concentration
Medium: surface water

Remark: In the water of Lake Haringvliet near Stellendam, the Netherlands, 1,2-dichloropropane/l was found on a monthly average respectively:
-January - March 1991 - 0,2 mg
-April - May 1991 - 0,3 mg
-June - July 1991 - < 0,1 mg
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (81)

Type of measurement: background concentration
Medium: surface water

Remark: In 1980 and 1981 concentrations of 1,2-dichloropropane lower than 7 ug/l were found in the German rivers of Elbe, Ems, Leine and Weser. In 1982, concentrations of 1,2-dichloropropane remain the same in the Ems, Leine and Weser rivers. In 1982 concentrations of 1,2-dichloropropane between <7 ug/l and 87 ug/l were found in the Elbe River.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (82)

Type of measurement: background concentration
Medium: surface water

Remark: From June - October 1978, an average concentration of 0.1 - 1.0 ug/l 1,2-dichloropropane (detection frequency of 3 %) in the Rhine River near Maassluis, the Netherlands. From 1979 - 1982 the average concentration in this location was also 0.1 - 1.0 ug/l. In October 1978 an average of 3 ug/l 1,2-dichloropropane was found in the Rhine near Lobith (detection frequency of 3 %).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (83) (84)

Type of measurement: background concentration
Medium: surface water

Remark: In 1988 and 1989 an average concentration of 0.1 ug/l 1,2-dichloropropane (corresponding to the maximum) was found in the Rhine River near Hagestein, Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (85)

Type of measurement: background concentration
Medium: surface water

Remark: From November 1975 - January 1976 an average concentration

of 0.04 ug/l 1,2-dichloropropane was found in the lower Rhine River in Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (86)

Type of measurement: background concentration
Medium: surface water

Remark: In 1986, 1987 and 1989 an average concentration of 1 ug/l 1,2-dichloropropane was found and in 1988 a measurement of 1.3 ug/l 1,2-dichloropropane was found in the Wupper River in Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (76) (77) (78) (79)

Type of measurement: background concentration
Medium: surface water

Remark: From 1981 - 1982 an average concentration of < 0.15 ug/l 1,2-dichloropropane was found in the Elbe River near Schnackenburg, Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (87)

Type of measurement: background concentration
Medium: other: rain water

Remark: Rainwater in Portland Oregon, USA was tested and no 1,2-dichloropropane was found.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: There was no detection limit given.
The samples were collected during rainfall. The concentrations have been determined at the same time in the gaseous and aqueous phases.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (67)

Type of measurement: background concentration
Medium: other: rain water

Remark: On July 31, 1982, 86 samples of drained rainwater from 19 cities in the U.S. were taken from 11 rivers. The only location detecting 1,2-dichloropropane was in Eugene, Oregon where 3 ug were found.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The proof frequency was 1 %.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (88)

Type of measurement: background concentration
Medium: other: sediment

Remark: In May - June 1980, sediment samples found 0.2 - 0.4 ug 1,2-dichloropropane/kg (related to wet weight, average of 5 samples or an unknown number of mixed samples) in the outlets of Lake Pontchartrain on the Mississippi River (mouth of the Gulf of Mexico).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (89)

Type of measurement: background concentration
Medium: ground water

Remark: Between July 1985 and December 1986 in the ground water of flat-grounded wells in 206 agricultural areas in Germany, maximum of 5.1 ug 1,2-dichloropropane has been found (total number of samples 1534).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (14)

Type of measurement: background concentration
Medium: ground water

Remark: Between April - July 1989 1,2-dichloropropane was not found in 33 samples of spring water (11 samples each, taken in 3 places) of the drainage area of Big Creek, an agricultural area in southwest Ontario, Canada).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 0.16 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (75)

Type of measurement: background concentration
Medium: other: drinking water

Remark: From November 1975 - January 1976, an average of 0.40 ug/l 1,2-dichloropropane was found in filtrate on the river banks of the lower Rhine River in Germany and the Rhine River filtrate was measured 0.09 ug/l 1,2-dichloropropane.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (86)

Type of measurement: background concentration
Medium: other: drinking water

Remark: From 1979 - 1982, < 0.1 ug 1,2-dichloropropane/l was found

in drinking water processed from Rhine River water in the Netherlands.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (83)

Type of measurement: background concentration
Medium: other: drinking water

Remark: A maximum of 0.96 ug 1,2-dichloropropane/l was found in ground water used as drinking water in the USA (186 samples, 5 positive).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (90)

Type of measurement: background concentration
Medium: other: drinking water

Remark: From August - September 1979, a maximum of 1 ug 1,2-dichloropropane/l was found in drinking water samples from waterworks in Canada.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (91)

Type of measurement: background concentration
Medium: other: drinking water

Remark: On October 29, 1981, a maximum of 0.21 ug/l 1,2-dichloropropane was found in the drinking water of Port Robinson, Canada and on this same date it was found that the concentration of 1,2-dichloropropane was below the limit of detection in the drinking water in Niagara Falls and Burlington, Canada.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: LOD: 0.03 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (74)

Type of measurement: background concentration
Medium: other: drinking water

Remark: In July 1978, maximum 1.2 ug/l 1,2-dichloropropane was found (lowest measured concentration) in 1 of 9 drinking water samples tested in Love Canal, Niagara Falls, New York, USA. From 1964 - 1979, trace levels of 1,2-dichloropropane were found in 14 drinking water samples in Niagara Falls and Buffalo, New York, USA.(7 % positive samples)
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to

determine reliability.
25-OCT-2004 (72) (92)

Type of measurement: background concentration
Medium: biota

Remark: It is expected that a person of 70 kg absorbed 18.5 ug 1,2-dichloropropane/day in 1980 in the Netherlands, assuming a tidal volume of 20 m3/day and an absorption rate of 50 %.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (66)

Type of measurement: background concentration
Medium: biota

Remark: Blood samples tested in 22 people found 0.51 ug 1,2-dichloropropane/l of blood (n=4).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: LOD: < 0.05 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (93)

Type of measurement: background concentration
Medium: biota

Remark: Human hair showed qualitative absorption of 1,2-dichloro-propane.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Number of samples, locality and period of analysis: no information
LOD: no information
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (94)

Type of measurement: background concentration
Medium: biota

Remark: From May - June 1980, 1,2-dichloropropane was not found in samples of oyster and mussels (average of 5 samples and mixed samples) from drains in Lake Pontchartrain (mouth of Mississippi and Gulf of Mexico).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Proof limit: no information
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (89)

Type of measurement: background concentration
Medium: food

Remark: 1,2-dichloropropane was not found in milk and milk products tested in the Netherlands (number of samples not given).

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: LOD: no information
period of analysis: no information
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (95)

Type of measurement: background concentration
Medium: food

Remark: 1,2-dichloropropane was not found in 231 food stuffs tested (probably in the area of Kansas City, Missouri, USA).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Proof limit: no information
period of analysis: no information
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (96)

Type of measurement: concentration at contaminated site
Medium: air

Remark: In 1986 - 1987, concentrations of 1 - 198 ug/m3 1,2-dichloropropane were found in 9 locations in ground air above a disorganized dump (approximately 12 years old). The dump was located on top of a former brick factory where special and domestic waste was stored until 1974. From 1975 - 1978 the dump was filled with earth and rubble and in 1983 it was partially cultivated.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (97)

Type of measurement: concentration at contaminated site
Medium: air

Remark: From April 1986 - April 1987, 0.9 - 2.0 ug 1,2-dichloro-propane/m3 air was found in 5 districts with large volumes of traffic (19000-72000 cars/day) in Hamburg, Germany. The annual average of 0.19 - 1.6 ug 1,2-dichloropropane/m3 was measured in industrial areas.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (98)

Type of measurement: concentration at contaminated site
Medium: air

Remark: In 1980, a maximum of 7.1 - 14.1 ug/m3 1,2-dichloropropane was found in the industrial areas of the cities of Delft and Vlaardingen, the Netherlands. On the average, 1,2-dichloropropane measured 0.28 - 0.65 ug/m3 (350 samples/location).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (66)

Type of measurement: concentration at contaminated site
Medium: air

Remark: In 1983/84, 1.20 ug 1,2-dichloropropane was measured in the air (average from 310 samples in 10 localities) of the industrial city of Philadelphia, PA, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (99)

Type of measurement: concentration at contaminated site
Medium: air

Remark: In March 1980, 1,2-dichloropropane was found lower than the proof limit in the industrial area (oil factory) of Beaumont, Texas, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 0.20 ug/m3
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (100)

Type of measurement: concentration at contaminated site
Medium: air

Remark: From January - February 1977, 0.2 ug 1,2-dichloropropane/m3 was found in the chemical/industrial area of Iberville Parish, Louisiana, USA (11 samples, 6 positive).
In February 1978, 1.4 ug/m3 1,2-dichloropropane was found in the air of 1 in 6 cellars tested in apartment houses near a dump in Niagara Falls, New York, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (101)

Type of measurement: concentration at contaminated site
Medium: air

Remark: From 1964 - 1979 traces of 1,2-dichloropropane were found in the industrial area of Niagara Falls, New York, USA (9 samples, 22 % positive). In the same time, a maximum of 3.999 ug 1,2-dichloropropane/m3 was found in the industrial areas of Baton Rouge, Louisiana, USA (39 samples, 38 % positive).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (92)

Type of measurement: concentration at contaminated site
Medium: air

Remark: From 1983 - 1988, 4 - 198 ug 1,2-dichloropropane/m3 was found in the gas of an industrial sludge dump in Bielefeld-Brake, Germany.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (102)

Type of measurement: concentration at contaminated site
Medium: surface water

Remark: Between September 22, 1981 and November 16 - 22, 1981, 0.22 - 0.44 ug/l of 1,2-dichloropropane was found in 5 of 82 measurements in Lake Ontario, Canada, contaminated by industrial and communal affluents. In 41 of these measurements, 1,2-dichloropropane was lower than the detection limit. On September 22, 1981, 0.01 - 0.055 ug/l 1,2-dichloropropane was found in 9 of 17 industrial areas tested on the Niagara River in Canada.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Detection limit: 0.02 ug/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (103)

Type of measurement: concentration at contaminated site
Medium: surface water

Remark: In February 1976, > 1 ug/l 1,2-dichloropropane was found from 30 samples taken in the longitudinal profile of the communal and industrial areas surrounding the Delaware River in the USA (detection frequency of 10 %).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (104)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: In 1988 in the Netherlands, after applying 170 kg 1,3-dichloropropane (containing 0.85 kg 1,2-dichloropropane)/ha, 0.1-200 ug 1,2-dichloropropane/l was found in 15 of 22 ground water samples of sand grounds containing arable land for growing potatoes.
In the remaining 7 samples, 1,2-dichloropropane concentrations were lower than the proof limit. After treating sand grounds growing flower bulbs (containing humus), with 600 kg 1,3-dichloropropane (containing 3 kg 1,2-dichloropropane)/ha, 6 of 8 ground water samples showed 1-14 ug 1,2-dichloropropane/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Proof limit: 0.1 ug/l
Ground water 6 meters deep in an agricultural used area was

analyzed. The area was treated with 1,3-dichloropropane, which contained until 1983 34 % of 1,2-dichloropropane; from 1984, it contained 0.5 %.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (105)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: A concentration of > 100 ug/l 1,2-dichloropropane was found in ground water at Suffolk County, New York, USA after the use of Telone (a mixture of 1,3-dichloropropane and 1,2-dichloropropane).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (106)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: In April 1978, a concentration of 10 ug/l 1,2-dichloropropane was found in the ground water after 1,3-dichloropropane (Telone II, 92 %, application amount 140 l/ha) was used as a ground fumigate for 83 and 104 days and 6 ug/l 1,2-dichloropropane was found after 138 days of use. In October 1978, 5 ug 1,2-dichloropropane/l was found in Suffolk County, New York, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The fumigate was applied in 8 - 12 cm depth of ground in a mud floor or clay-mud floor with sand and gravel drainage.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (107)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: 1 - 50 ug 1,2-dichloropropane was found after 1,2-dichloropropane was used as a nematicide on surfaces of 4 states in the USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (12)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: A maximum of 1200 ug 1,2-dichloropropane/l was found after 1,2-dichloropropane was used as a pesticide in 75 wells in 9 locations in California, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to

determine reliability.
25-OCT-2004 (11)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: 1,2-dichloropropane was found in well water 30 m deep under a factory producing colors.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Country and period of analysis: no information
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (108)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: In May 1988, 3.2 - 11.0 ug 1,2-dichloropropane/l was found in the aquifer near a dump close to Ottawa, Ontario, Canada.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (109)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: 0.5 - 43 ug 1,2-dichloropropane/l was found in 8 in 13 ground water samples under dumps in Minnesota, USA. Also 1.1 ug 1,2-dichloropropane/l was found under a second urban dump.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (110)

Type of measurement: concentration at contaminated site
Medium: other: drinking water

Remark: In September/November 1987, maximum 19.0 ug/l, minimum 0.7 ug/l (average 4.6 ug/l) was found in all 8 drinking water samples tested in East Windsor, Suffield and Bolton, USA after 1,2-dichloropropane containing pesticide was used. An average of 10 ug 1,2-dichloropropane/l was found in 12 wells of which drinking water was taken after 1,2-dichloropropane containing pesticides was used in the USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (11) (111)

Type of measurement: concentration at contaminated site
Medium: other: leachate

Remark: Samples in 3 places were tested after domestic and

industrial wastewater was brought in a dump in the USA. These 3 samples contained < 10 ug 1,2-dichloropropane/l in the water leakage. Two other places showed 18 and 37 ug 1,2-dichloropropane/l in the water leakage.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (112)

Type of measurement: concentration at contaminated site
Medium: other: leachate

Remark: 2.0 - 81 ug 1,2-dichloropropane/l was found in the dump water leakage of 3 official communal dumps of which some industrial waste was deposited in Minnesota, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (110)

Type of measurement: concentration at contaminated site
Medium: biota

Remark: 1,2-dichloropropane was not detected after samples of exhaled air, urine and blood were taken from 9 persons in early July 1979 in the Love Canal dump area in Niagara Falls, New York, USA.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (72)

Type of measurement: concentration at contaminated site
Medium: biota

Remark: The usual amount of 1,3-dichloropropane-1,2-dichloropropane mixture (D-D-mixture, containing 23 % 1,2-dichloropropane) labeled radioactive, was used and potatoes were planted 5 months after ground treatment.
At the time of planting, ground radioactivity was estimated at 5 - 10 % of the applied radioactivity. Four months later the potatoes were gathered and the radioactivity was 5 % of the applied amount. 0.007 mg 1,2-dichloropropane/kg was found in the potatoes.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
25-OCT-2004 (63)

Type of measurement: concentration at contaminated site
Medium: ground water

Remark: In April/May 1978, no 1,2-dichloropropanewas found inwell water tested on days 10, 13, 26 and 49, after adding 80 ml/m2 of the pesticide Ditrapex, containing 24 % 1,2-dichloropropane. The pesticide was administered at 25 cm

to ground covered with foil in the greenhouses. In the same time period, 130 ug 1,2-dichloropropane/l was found on day 10 after adding 75 ml Ditrapex/m2 to drainage water.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Test condition: Detection limit: 5,78 ug/l

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

25-OCT-2004 (15)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

Media: other: dynamic distribution in air-sediment-soil-water

Method: Calculation according Mackay, Level III

Year: 2004

Method: Input Parameters for Level III:
Molecular Mass (g/mol): 112.99
Temperature (°C): 20
Log Kow: 2.0
Vapor Pressure (Pa): 6620 (49.7 mmHg)
Henry's LC: 0.00282 atm-m3/mole (Henry database)

Half-lives (hr) Based upon Biowin (ultimate) and AOPWin
Air: 581
Water : 900
Soil: 1800
Sediment: 8100

Level III Emissions: 1,000 kg/hr to air only.
According to U.S. EPA TRI Database, >99.9% of reported PDC emissions are to the atmosphere.

Result: Distribution of PDC in the environment based on Level III model:

Compartment	Distribution (%)
Air	98.8
Water	0.979
Soil	0.197
Sediment	0.00378

Advection in air accounts for 89.2% of removal rate

Reaction in air accounts for 10.6% of removal rate

Advection and reaction in water, sediment, and soil account for 0.2% of removal rate

Source: The 1,2-Dichloropropane Consortium

Conclusion: Level I and III models predict that PDC will be predominately transported to the atmosphere, with little or no potential for deposition to soil and water. Advection is the predominant removal mechanism in the atmosphere.

Reliability: (2) valid with restrictions

2d (accepted calculation method)
Flag: Critical study for SIDS endpoint
29-NOV-2005 (113)

Media: other: static distribution in air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I
Year: 2003

Result: Compartment Level I amount, %
Air 98.0
Water 1.82
Soil 0.161
Sediment 3.6E-03
Suspended particles 1.1E-04
Fish 9.1E-06
Conclusion: In a static fugacity-driven distribution model without advection or reaction, 1,2-dichloropropane is expected to distribute mainly to air (98 %) with water (1.8 %), soil (0.16%), sediment (3.6E-03%), suspended particles (1.1E-04%) and fish (9.1E-06%) being serially less important compartments.
Reliability: (2) valid with restrictions
Widely used and accepted computer distribution model, reliability 2.
Flag: Critical study for SIDS endpoint
29-NOV-2005 (114)

Media: other: dynamic distribution in air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level III
Year: 2003

Result: Dynamic distribution, Level III amount, %
Emissions, kg/h, to air water soil sediment
3000 0 0 0
Compartment
Air 98.5
Water 1.3
Soil 0.2
Sediment 5.3E-03
Residence time, h 90.9

0 3000 0 0
Compartment
Air 16.9
Water 82.7
Soil 0.04
Sediment 0.34
Residence time, h 369
0 0 3000 0
Compartment
Air 41.3
Water 3.7
Soil 55.0
Sediment 0.015
Residence time, h 216

Model conditions
degradation rates (Half-lives): air = 600 h; water, soil,

sediment = 1.0E11 h (negligible). Data temperature = 25°C; water solubility = 2800 mg/l, vapour pressure = 6620 Pa; log Kow = 2.00; melting point = -100.4°C.

Conclusion: The Level III dynamic distribution model highlights the importance of the emission pathway. For realistic emissions only to air, the main distribution is expected to air (98.5%) and secondarily to water (1.3%) and soil (0.2%), while sediment (5.3E-03%), suspended particles (7.9E-05%) and fish (6.4E-06%) are unimportant.

Reliability: (2) valid with restrictions
Widely used and accepted computer distribution model, reliability 2.

Flag: Critical study for SIDS endpoint

29-NOV-2005 (114)

Media: other: NaCl - air
Method: other (measurement)
Year: 1989

Result: A partition coefficient of 2.75 for 1,2-dichloropropane in 0.9% NaCl/air was calculated at a temperature of 37 degrees C.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

29-NOV-2005 (115)

Media: other: olive oil - air
Method: other (measurement)
Year: 1979

Result: A partition coefficient of 747 and 428 for 1,2-dichloropropane in olive oil/air was calculated at 37 degrees C.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (116)

Media: other: olive oil - blood
Method: other (calculation)
Year: 1979

Result: A partition coefficient of 70 for 1,2-dichloropropane in olive oil/blood was calculated at 37 degrees C.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (116)

Media: other: olive oil - water
Method: other (calculation)
Year: 1979

Result: A partition coefficient of 138 for 1,2-dichloropropane in olive oil/water was calculated at 37 degrees C.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (116)

Media: water - air
Method: other (calculation)
Year: 1984

Remark: The calculated Henry constant is 212.78 Pa x m3 x mol-1 at 20 degrees C.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (117)

Media: water - air
Method: other (measurement)

Remark: A Henry constant at 20 degrees C for 1,2-dichloropropane was calculated at 192.52 - 273.51 Pa x m3 x mol-1 and at 25 degrees C, at 361.73 Pa x m3 x mol-1.
According to Thomas (1982) as 1,2-dichlorpropane is a light volatile substance, a transition from aqueous solution of 1,2-dichloropropane evaporates in the atmosphere.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (118) (42)

Media: water - air
Method: other (measurement)
Year: 1980

Remark: A water solution, enriched with 1 mg 1,2-dichlorpropane/l, had a high of 1,6 cm. It was stirred at 24 degrees C with a magnetic stirrer at 100 +/- 10 U/min.
Result: In a simulation experiment 1,2-dichloropropane was de-gassed out of an aqueous solution in the laboratory and after 8 minutes it had evaporated by 50 %.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (119)

Media: water - air
Method: other (measurement)
Year: 1984

Result: A relative transfer coefficient of 0.57 for 1,2-dichloropropane was determined in a laboratory experiment in a circulating current (speed 1 m x s-1, 1 m depth). Based on this coefficient, the half-life time for the evaporation of 1,2-dichloropropane was approximately 6 hours.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (120)

Media: water - air
Method: other (measurement)
Year: 1984

Result: The Henry constant in a closed system calculated at 10 degrees C 124 Pa x m3 x mol-1, at 15 degrees C 128 Pa x m3 x mol-1, at 25 degrees C 362 Pa x m3 x mol-1 and at 30 degrees C 290 Pa x m3 x mol-1.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (118)

Media: water - air
Method: other (measurement)
Year: 1979

Result: An 8-hour volatility laboratory experiment in a "wind-wave-tank" resulted in a Henry-constant calculated as 274 Pa x m3 x mol-1 at 20 degrees C . A general liquid-mass- transfer-coefficient KOL of 28.9 - 93.9 x 10E6 m x s-1 was determined at wind speeds of 5.96 - 13.2 m x s-1.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (42)

Media: water - air
Method: other (calculation)
Year: 1984

Remark: The diffusion loss from the water surface was < 5 - 10 %.
Result: A Henry constant of 213 Pa x m3 x mol-1 at 20 degrees C was calculated.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (117)

Media: water - air
Method: other (measurement)
Year: 1975

Remark: The de-gassing was calculated in a simulation experiment (stirred with a propeller, temperature: 25 degrees C, 200 rotations/minute).
Result: Dilling et al. (1975) made tests on other chlorinated hydrocarbons. Relating to these tests the half-life time of evaporation of 1,2-dichloropropane out of water is <= 50 minutes. The half-life time of evaporation of 1,2-dichloropropane out of water can differ from one to several hours depending on environmental conditions.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (61)

Media: water - air
Method: other (measurement)
Year: 1979

Result: The partition coefficient of 1,2-dichloropropane water/air is 5.4 at a temperature of 37 degrees C.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (116)

Media: water - air
Method: other (calculation)
Year: 1980

Remark: The partition coefficient between water and gaseous phase (Kw/g) was calculated.
Result: The partition coefficient Kw/g is
at 15 degrees C 13 ug/ml water x (ug/ml gas)-1
at 20 degrees C 11 ug/ml water x (ug/ml gas)-1
at 29 degrees C 7 ug/ml water x (ug/ml gas)-1
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (62)

Media: water - soil
Method: other (measurement)
Year: 1980

Remark: A measurement of 75 ml Ditrapex/m2, which contains 24 % 1,2-dichloropropane, was brought in through closed lysimeter (cross-section 12 cm) 1.25 m long, 25 cm deep.
Result: During 26 days of 1600 mm precipitation, 1.43 % of the total amount of applied 1,2-dichloropropane was found in water leakage.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (15)

Media: water - soil
Method: other (calculation)
Year: 1980

Result: For 1,2-dichloropropane, a ground sorption coefficient Koc 299.14 can be calculated on a basis of n-Octanol/water partition coefficient log Pow 2.02 according to the formula of Kenaga and Goring (1980) log Koc = 1.377 + 0.544 (log Pow).
Therefore, according to Blume (1990) low ground sorption is

expected.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from a handbook
10-JAN-2006 (121) (122)

Media: water - soil
Method: other (calculation)
Year: 1982

Result: A ground sorption coefficient of 50 was calculated on the basis of the n-Octanol/water partition coefficient Pow 105 according to the formula Koc - 0.48 x Pow.
According to Blume (1990) the expectation is from very low to low ground sorption.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Data from a handbook
10-JAN-2006 (121) (45)

Year: 2004

Method: The following parameters were used as inputs for the PCKocWIN V1.66 software to estimate Koc:

SMILES: ClC(CCl)C
Molecular Formula: C3H6Cl2
Molecular Weight: 112.99
Remark: Preferred value for Koc.

The Koc value suggests that the chemical is expected to have very high mobility in soil.
Result: Koc = 67.7

Non-corrected Log Koc = 1.8306
First order molecular connectivity index = 2.270
Corrected Log Koc = 1.8306
Test substance: as prescribed by 1.1 - 1.4
Attached doc.: 2f (accepted calculation method)
Reliability: (2) valid with restrictions
10-JAN-2006 (47)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Concentration: 150 mg/l related to Test substance
Contact time: 28 day(s)
Result: under test conditions no biodegradation observed

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 2002
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Reaction mixtures were prepared by adding 150 mg/L PDC directly to activated sludge (1,000 mg/L mixed liquor suspended solids) in a defined mineral medium. The test vessels were sealed to minimize the loss of PDC due to volatilization. Oxygen concentrations in the headspace of the vessels were monitored and oxygen gas was added as necessary to ensure that aerobic conditions were maintained.

Abiotic control mixtures were prepared by adding PDC to activated sludge inhibited with mercuric chloride. Positive control mixtures were prepared with aniline added to activated sludge to confirm the viability of the microbial inoculum. Toxicity controls were prepared with aniline and PDC in activated sludge to determine if the test compound was inhibitory to the microbiol inoculum. The reaction mixtures were continuously mixed and incubated at 22 ± 1 °C for 28 days.

Reaction mixtures were sampled after 0, 1, 2, 7, 14, 21, and 28 days to measure PDC and dissolved organic carbon (DOC) concentrations remaining in the mixtures. PDC concentrations in the reaction mixtures were determined by gas chromatography with flame ionization detection (GC-FID). Removal of aniline was determined by dissolved organic carbon (DOC) analyses of the reaction mixtures.

PDC and DOC concentrations were reported as the arithmetic mean of analyses from duplicate reaction mixtures.

Result: No biodegradation of PDC was observed in the test. No difference was observed in loss of PDC in viable mixtures compared to abiotic controls over 28 days.

Aniline (reference compound) was extensively degraded in positive control mixtures (96% in 14 days), thereby confirming the viability of the microbial inoculum. Extensive degradation of aniline in toxicity control mixtures containing PDC (98% in 14 days) showed that PDC was not inhibitory to the inoculum under the test conditions.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: PDC did not meet the criteria of inherent biodegradability under the conditions of a modified OECD Method 302B test.

Reliability: (1) valid without restriction
GLP guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (123)

Type: aerobic
Inoculum: activated sludge
Concentration: 1 mg/l related to Test substance
Degradation: = 0 % after 28 day(s)
Result: other: not readily biodegradable

Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1981
GLP: no data
Test substance: other TS: purity = 65 %

Remark: A mixture with the main component 1,2-dichloropropane was

analyzed. Other compounds of the mixture were:
1,3-dichloropropene 25 %
2,3-dichloropropene 10 %
1,1-dichloropropane trace
3,3-dichloropropene trace

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Temperature: 21 degrees C
Reliability: (3) invalid
Invalid. Other test material.
21-DEC-2004 (124)

Type: aerobic
Inoculum: other: BASF-activated sludge
Concentration: mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 96 % after 3 hour(s)
Result: other

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: No conclusion can be made about biodegradation from this study because of the high volatility of 1,2-dichloropropane.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Invalid. Not reliable due to uncertainty concerning the volatilization of test material.
21-DEC-2004 (125)

Type: aerobic
Inoculum: Nitrosomonas sp. (Bacteria)
Concentration: .048 mg/l related to Test substance
Degradation: = 75 % after 1 hour(s)
Result: other: biodegradable

Method: other: Biodegradation Test
Year: 1990
GLP: no data
Test substance: no data

Remark: Bacterial suspensions of bacteria living in the ground were analyzed and no degradation products were given.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: pH-value: 7.7
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (126)

Type: aerobic
Inoculum: Pseudomonas fluorescens (Bacteria)
Concentration: 100 mg/l related to Test substance
Degradation: = 3 % after 24 hour(s)

Method: other: Biodegradation Test
Year: 1988
GLP: no data
Test substance: no data

Remark: A decrease of 1,2-dichloropropane caused by an isolated bacterium from enriched water and ground samples from a contaminated industrial dump with 1,2-dichloroethane and 1,2-dichloropropane was tested. This bacteria in mineral-salt medium uses 1,2-dichloropropane. The carbon and energy sources, glucose (0.5 %) and yeast extract (0.005 %), were added to the starting concentration of 1,2-dichloropropane. The decrease of 1,2-dichloropropane concentration in the medium was the measured parameter. The microbial decrease was given in average of 3 samples.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: In order to record the microbial decrease of 1,2-dichlorpropane, it was incubated in a shaker at 25 degrees C.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (127)

Type: aerobic
Inoculum: other: Nitrosolobus multiformis
Concentration: .048 mg/l related to Test substance
Degradation: = 40 % after 1 hour(s)

Method:
Year: 1990
GLP: no data
Test substance: no data

Remark: Bacterial suspensions (living bacteria in the ground) were analyzed after the addition of 1 mM NH4Cl.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: pH-value: 7.7
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (126)

Type: aerobic
Inoculum: other: influent and effluent of chemical industrial waste water
Concentration: 182 mg/l related to Test substance

Method: other: Biodegradation Test
Year: 1983
GLP: no data
Test substance: no data

Remark: The elimination of 98.9 - 99.2 % according to the 1,2-dichlorpropane concentration in the drain was attributed to the stripping.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The analysis took place in a 3 l sludge reactor. The "entering concentrations" of 1,2-dichlorpropane were established after 5 days.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (128) (129)

Type: aerobic
Inoculum: other: effluent from a university sewage treatment plant
Concentration: 70 mg/l related to Test substance

Method: other: Filtration Test
Year: 1981
GLP: no data
Test substance: no data

Remark: The decrease of 1,2-dichloropropane was tested on a pilot machine using the meadow filtration method. Grass was planted on the filtration area (ground temperature was 20 - 22 degrees C). For 2 months before testing, they brought in the effluent sewage from a university. The established 1,2-dichloropropane elimination was 74 %. The question remains if 1,2-dichloropropane was eliminated through evaporation or from a biological decrease. In a "Leaching test" only "non-spiked" waste water was used. One day after the "Leaching test" began 1,2-dichloropropane was no longer found in the water samples along the filtration installation. We can conclude that a reversal adsorption did not take place.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Temperature of the waste water: 25 - 29 degrees C, Waste water rush rate: 0.17 m3/m x hour
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (130)

Type: aerobic
Inoculum: other: domestic waste water, adapted
Concentration: 10 mg/l related to Test substance
Degradation: = 81 % after 7 day(s)

Method: other: Flask-screening procedure of Bunch and Chambers
Year: 1967
GLP: no data
Test substance: no data

Remark: Evaporation of 3 %. This analysis is non-reliable due to insufficient controls.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: closed statistical test at 25 degrees C in dark
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (131)

Type: aerobic
Inoculum: other: domestic waste water, adapted
Concentration: 5 mg/l related to Test substance
Degradation: = 89 % after 7 day(s)

Method: other: Flask-screening procedure of Bunch and Chambers
Year: 1967
GLP: no data
Test substance: no data

Remark: Evaporation of 3 %. This analysis is non-reliable due to

insufficient controls.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: closed statistical test at 25 degrees C in darkness
Reliability: (3) invalid
Invalid. Not reliable due to insufficient controls.
21-DEC-2004 (131)

Type: aerobic
Inoculum: other: domestic waste water, non adapted
Concentration: 10 mg/l related to Test substance
Degradation: = 42 % after 7 day(s)

Method: other: Flask-screening procedure of Bunch and Chambers
Year: 1987
GLP: no data
Test substance: no data

Remark: This analysis is unreliable due to insufficient controls.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Invalid. Not reliable due to insufficient controls.
21-DEC-2004 (131)

Type: aerobic
Inoculum: other: BASF-activated sludge
Concentration: mg/l related to Test substance
Degradation: = 0 % after 7 day(s)
Result: other

Method: other: not specified
GLP: no data

Remark: No additional information is provided.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (132)

Type: anaerobic
Inoculum: other: medium loam
Concentration: 71 mg/l related to Test substance
Degradation: = 29 % after 140 day(s)

Method: other: Biodegradation Test
Year: 1976
GLP: no data
Test substance: other TS: purity > 99 %, [2-14C]-1,2-dichloropropane

Remark: The degradation grade value is percent of radioactivity. It relates to the acetone extract of ground sample. The clay ground contained 7 % organic compounds and 30 % humidity. No information was given about controls concerning contaminated or sterilized ground. The amounts of evaporated 1,2-dichloropropane in vessels were not analyzed.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: closed system, without ventilation
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (63)

Type: anaerobic
Inoculum: other: sandy soil
Concentration: 71 mg/l related to Test substance
Degradation: = 20 % after 84 day(s)
Kinetic: 560 day(s) = 27 %

Method: other: Biodegradation Test
Year: 1976
GLP: no data
Test substance: other TS: purity > 99 %, [2-14C]-1,2-dichloropropane

Remark: The degradation grade value is percent of radioactivity. It relates to the acetone extract of the ground sample. The clay ground contained 2 % organic compounds and 15 % humidity. No information was given about controls concerning contaminated or sterilized ground. The amounts of evaporated 1,2-dichloropropane in closed vessels were not analyzed.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: closed system, without ventilation
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (63)

Inoculum: other: sludge
Concentration: 100 mg/l related to Test substance
Degradation: = 0 % after 14 day(s)

Method: other: Biodegradation Test
Year: 1974
GLP: no data
Test substance: no data

Remark: 1,2-dichlorpropane is not easily biodegradable.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (133)

3.6 BOD5, COD or BOD5/COD Ratio

Method:
Year:
Method:
Remark: Chemical oxygen consumption (CSB) analysis, following the uniform procedures to test water and waste water, determined that 1,2-dichloropropane can only be oxidized in small quantities by chrome (IV), catalyzed with silver ions. During the oxidation of dichromate, 12 % of the theoretical CSB value was found without silver ions and 24.5 % with silver ions. 1,2-dichloropropane does not oxidize in the presence of manganese (VII). Oxidation was 0 % of the theoretical value in the presence of permanganate.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to

determine reliability.
26-OCT-2004 (134)

3.7 Bioaccumulation

BCF: < 1 - 1.29

Test substance: as prescribed by 1.1 - 1.4

Remark: Reported BCF values are < 1.0 (Fish, meaured) and 1.26 - 1.29 (calculated)
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
23-JAN-2006 (135) (32)

Species: other: carp (fish)
Exposure period: 42 day(s) at 25 degree C
BCF: .5 - 7

Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: 1981

Remark: According to the bioconcentration factor (BCF), no or little bioaccumulation is expected.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: pH-value: 7; oxygen content: ca. 7 ppm, flow-through system, direct intake through gills and epithelium.

Test concentration 0.4 and 0.04 mg/L of PDC in water.
Reliability: (2) valid with restrictions
Valid with restrictions; limited methodological detail available, guideline study.
21-DEC-2004 (133)

BCF: = 6.9

Test substance: as prescribed by 1.1 - 1.4

Remark: Based on a log Kow =2.0, the BCF was estimated using the following equation: log BCF = 0.77 log Kow - 0.7
Reliability: (4) not assignable
23-JAN-2006 (113)

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:**
LC50: = 139

Year: 1982
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Only brief details are available for this study, which was conducted as a preliminary to an Early Life Stage test.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Valid with restrictions.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (136)

Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50: = 140

Method: other: US EPA (1975) The Committee on Methods for Toxicity Tests with Aquatic Organisms: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians. Ecological Research Series (EPA-660/3-75-009)
Year: 1983
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: Test organisms and housing
Laboratory-reared Fathead minnows were used in these studies. The fish were 30 - 35 days old at the time of the test.

Test conditions
Testing was carried out at 25 degrees C in all-glass aquaria with a working volume 41 l. Water from Lake Superior was used as the exposure medium. Fifty fish were randomly assigned to 12 exposure tanks, comprising five test concentrations plus a control, in duplicate. A 'saturator system' was used to prepare a stock solution of PDC, and the lower exposure concentrations prepared at a dilution spacing of 0.6 (however the actual exposure concentrations used are not stated in the paper). Fish were not fed during the period of the test. Water flow through the tanks was greater than 10 tank volumes per day. Dissolved oxygen, hardness and alkalinity were determined at least once daily on a control, intermediate and high exposure tank. Fluorescent lighting and a 16 hr photoperiod was used (48 lumens at the water surface).

Analysis
GC with 63Ni electron capture detection was used to quantify

the concentration of PDC in the test solutions.

Determination of LC50
The LC50 concentration was determined using the Trimmer Spearman-Karber method for estimating median lethal concentrations (Hamilton, MA et al. (1977) Environ Sci Technol, 11, 714; ibid (1978) 12, 417).

Statistics
No further statistical methods were applied to these data.

Result: The pH of the test solutions was 6.7 - 7.6, dissolved oxygen 7.6 - 9.2, hardness 45.0 - 45.5 mg/l CaCO3, alkalinity 35.6 - 43.3 mg/l CaCO3).

Recovery of PDC from the exposure solutions was 99 +/- 4%.

General signs of toxicity included lethargy and anaesthesia.

LC50 values (with 95% CI) were as follows:

24 hr = 194 mg/l (184 - 205)
48 hr = 154 mg/l (144 - 166)
72 hr = 141 mg/l (132 - 151)
96 hr = 140 mg/l (131 - 150)

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: The LC50 of PDC in Fathead minnow (Pimephales promelas) under flow through conditions was 140 mg/l (CI = 131 - 150).
Reliability: (2) valid with restrictions
Test procedure in accordance with national standard methods and described in sufficient detail.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (137)

Type: flow through
Species: Limanda limanda (Fish, marine)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 61

Method: other: Acute Toxicity Test
Year: 1951
GLP: no data
Test substance: no data

Remark: The test was made with non-standardized sea water with nominal concentration of 1 - 10 mg/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: open vessels, no feeding, temperature: 12 - 18 degrees C, oxygen content: 5 mg/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (138)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 7 day(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 116

Method: other: Prolonged Toxicity Test
Year: 1981
GLP: no data
Test substance: no data

Remark: Toxicity was tested on animals 2 - 3 months old.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The test solution was renewed daily, temperature: 21 - 23 degrees C, oxygen content: 5 mg/l, hardness: 25 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (139)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 320

Method: other: Acute Toxicity Test
Year: 1975
GLP: no data
Test substance: no data

Remark: The LC50-value was tested based on the nominal concentration.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: open vessels, no information on feeding, ventilation started after 24 hours, temperature: 23 degrees C, pH-value: 7.6 - 7.9, hardness: 55 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (140)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 360

Method: other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA
Year: 1975
GLP: no data
Test substance: other TS: purity >= 80 %

Remark: The LC50-value was tested based on the nominal concentration.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: open vessels, feeding, temperature: 21 - 23 degrees C, pH-value: 6.5 - 7.9, hardness: 32 - 48 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (141)

Type: static

Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 280

Method: other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA
Year: 1975
GLP: no data
Test substance: other TS: purity >= 80 %

Remark: The LC50-value was tested based on the nominal concentration. The 95% confidence level was 220 - 340 mg 1,2-dichloropropane/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: open vessels, feeding,temperature: 21 - 33 degrees C, pH-value: 6.5 - 7.9, hardness: 32 - 48 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (141)

Type: static
Species: Menidia beryllina (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 240

Method: other: Acute Toxicity Test
Year: 1975
GLP: no data
Test substance: no data

Remark: The LC50-value was tested based on the nominal concentration.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: open vessels, no information on feeding, continuous ventilation, addition of synthetic sea salt mixture (specific density of the salt solution 1.018), temperature : 20 degrees C, pH-value: 7.6 - 7.9, hardness: 55 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (140)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 127

Method: other: Acute Toxicity Test
Year: 1985
GLP: no data
Test substance: other TS: purity = 99 %

Remark: The 95% confidence level was 119 - 135 mg 1,2-dichloropropane/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: no information on vessels and feeding, temperature: 25

degrees C, pH-value: 7.5, hardness: 45 mg CaCO3/l
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (142)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: flow through
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 8.3
EC50: = 55.9

Method: other: EPA OTS 797.1330
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: The acute LC50 of PDC in Daphnia magna was determined as part of an invertebrate chronic toxicity study.

Test organism and conditions
Daphnia magna brood stocks were acclimated under static conditions (period not stated) and fed Selenastrum capricorneutum daily throughout the test. Culture medium was carbon-filtered dechlorinated tapwater (hardness 160-180 mg/l CaCO3; pH 8.1-8.3; conductivity 480-624 umho/cm; 8.5-9.4 mg/l oxygen). All glassware was solvent/acid washed prior to use. The test method was based upon EPA OTS 797.1330.

Ten daphnids per treatment level were housed inside a glass exposure chamber, which was placed in a 600 ml glass beakers containing 500 ml of medium. The beakers were loosely covered to reduce volatilisation of PDC from the test solution. The test was conducted at 20 +/- 2 degrees C with a 16 hr light / 8 hr dark cycle but no aeration. Dissolved oxygen, conductivity, pH and temperature in each vessel were recorded at 24 hr intervals during the test.

The calculated nominal concentration of PDC in the test vessels was 0, 7.5, 12.0, 21.0, 36.0 and 60.0 mg/l. The medium inside the test vessels was replaced with fresh medium on average 42 times per day. Samples of test medium were removed from the replicate vessels on days 0, 7, 14 and 21 and analysed using GC (limit of detection 0.02 mg/l).

The number of live daphnids and occurrence of sub-lethal effects (immobilisation, abnormal behaviour, abnormal appearance) were recorded daily.

Statistical analysis
The data were analysed using ANOVA and Dunnett's test, and Probit, moving average and binomial techniques used to calculated the 24 hr and 48 hr LC50.
Result: Mean, measured concentrations of PDC in the test vessels were 0, 8.3, 15.8, 21.5, 39.5 and 72.9 mg/l.

Physico-chemical parameters recorded daily throughout the 21 days of this flow-through study were as follows:
Oxygen: 8.5-9.4 mg/l
pH: 8.1-8.3
Conductivity: 480-624 umho/cm
Temperature: 20.0-21.5 degrees C

Daphnids exposed to 72.9 mg/l DCP were unable to maintain their position in the water column immediately after being placed in the test vessels, while those exposed to 39.5 mg/l were immobilised from day 2. Sub-lethal effects (smaller size, lighter colour) were noted in daphnids exposed to 21.5 mg/l.

There was no mortality at 24 hr or 48 hr in vessels containing 8.3 - 39.5 mg/l PDC. 10-20% mortality was recorded at 24 hr, and 90 - 100% at 48 hr, after exposure to 72.9 mg/l.

The calculated 24 hr and 48 hr LC50 values for lethality in Daphnia magna under flow-through conditions were >72.9 mg/l and 55.9 mg/l, respectively.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the flow-through conditions used in this test, the 48 hr LC50 of PDC in Daphnia magna was 55.9 mg/l.
Reliability: (2) valid with restrictions
GLP guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (143)

Species: Crangon crangon (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50 : > 100

Method: other: Acute Toxicity Test
Year: 1968
GLP: no data
Test substance: no data

Remark: The nominal concentration was tested and the highest level was 100 mg 1,2-dichloropropane/l.
The LC50-value was tested on adult animals.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: static test in sea water, closed vessels, temperature: 15 degrees C, constant ventilation, photoperiod: 24 hours darkness
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (144)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50 : = 45

Method: other: Acute Toxicity Test for Daphnia
Year: 1984

GLP: no data
Test substance: no data

Remark: The LC50-value was tested based on the nominal concentration.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: static test, no feeding, temperature: 22 degrees C
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (145)

Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: < 22
LC50 : = 99

Method: other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA
Year: 1975
GLP: no data
Test substance: other TS: purity > 80 %

Remark: The stated LC50-value applies to the nominal concentration. The 95% confidence level was 58 - 600 mg 1,2-dichloropropane/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: static test, temperature: 22 degrees C, pH-value: 7.4 - 9.4, hardness: 173 mg CaCO3/l, closed system, no indication on feeding
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (146)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: < 22
LC50 : = 52

Method: other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, US EPA
Year: 1975
GLP: no data
Test substance: other TS: purity > 80 %

Remark: The stated LC50-value applies to the nominal concentration. The 95 % confidence level was 42 - 68 mg 1,2-dichloropropane.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Static test, temperature: 22 degrees C, pH-value: 7.4 - 9.4, hardness: 173 mg CaCO3/l, closed system, no information on feeding.
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (146)

Species: Mysidopsis bahia (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50 : > 26.65

Method: other: Acute Toxicity Test
Year: 1988
GLP: yes
Test substance: other TS: purity = 99.9 %

Remark: The tests were made in animals < 24 hours in a flow-through system. The average, actual concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentrations. The authors attribute this to the evaporation. The stated LC50-value was calculated in appliance to the actual concentration.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered seawater (salinity: 20 - 21 o/oo), with feeding, temperature: 25 degrees C, photoperiod: 14 hours light, 10 hours darkness.
Reliability: (2) valid with restrictions
Valid with restrictions; GLP, guideline study.
21-DEC-2004 (147)

Species: Mysidopsis bahia (Crustacea)
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50 : = 24.79

Method: other: Acute Toxicity Test
Year: 1988
GLP: yes
Test substance: other TS: purity = 99.9 %

Remark: The tests were made in animals < 24 hours in a flow-through system. The average actual concentrations per dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentration. The authors attribute this to the evaporation. The stated LC50-value, referred to the actual concentration with a 95 % confidence level, was calculated as
4.92 - infinity mg/l.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered sea-water (salinity: 20 - 21 o/oo), with feeding, temperature: 25 degrees C, photoperiod: 14 hours light, 10 hours darkness.
Reliability: (4) not assignable
Valid with restrictions; GLP, guideline study.
22-DEC-2004 (147)

Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes

LC50 : = 24.79

Method: other: Acute Toxicity Test
Year: 1988
GLP: yes
Test substance: other TS: purity = 99.9 %

Remark: The tests were made in animals < 24 hours in a flow-through system. The average, actual concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentrations. The authors attribute this to the evaporation. The stated LC50-value was calculated in appliance to the actual concentration.
The mortality after 96 hours averaged between 5 % with 4.92 mg/l (actual) concentration and 55 % with the highest tested (actual) concentration of 26.55 mg/l. The LC50-value was applied to the actual concentration of 4.92 - infinite mg/l with a 95 % confidence level.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered sea-water (salinity: 20 - 21 o/oo), with feeding, temperature: 25 degrees C, photoperiod: 14 hours light, 10 hours darkness.
Reliability: (4) not assignable
Valid with restrictions; GLP, guideline study.

22-DEC-2004 (147)

Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50 : > 26.65

Method: other: Acute Toxicity Test
Year: 1988
GLP: yes
Test substance: other TS: purity = 99.9 %

Remark: The tests were made in animals 3 - 4 days old in a flow-through system. The average, actual concentrations/dilution were between 76 % (with 6.5 mg 1,2-dichloropropane/l nominal) and 53 % (with 50 mg 1,2-dichloropropane/l nominal) of the nominal concentration. The authors attribute this to the evaporation. The stated LC50-value was calculated in appliance to the actual concentration.
The mortality after 96 hours averaged 0 % (with 4.92 mg 1,2-dichloropropane/l) and 30 % (with 10.88 and 26.55 mg 1,2-dichloropropane/l). These results estimated the LC50-value.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The animals were exposed to 5 different concentrations of 1,2-dichloropropane (nominal: 6.5, 10.8, 18, 30 and 50 mg/l) in covered glass aquariums with natural, filtered sea-water (salinity: 20-21 o/oo), with feeding, temperature: 25 degrees C, photoperiod: 14 hours light, 10 hours darkness.
Reliability: (4) not assignable
Valid with restrictions; GLP, guideline study.

22-DEC-2004 (147)

Species: other aquatic crustacea: Eliminius modestus
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50 : = 53

Method: other: Acute Toxicity Test
Year: 1975
GLP: no data
Test substance: no data

Remark: The test medium did not follow standardized conditions, therefore, only a limited comparison is possible.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Static test, closed vessels
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (138)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Skeletonema costatum (Algae)
Endpoint: biomass
Exposure period: 120 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 7.4 - 18 measured/nominal

Method: EPA OTS 797.1050
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Test organism and conditions
Skeletonema costatum in logarithmic growth phase and grown on synthetic marine algal assay nutrient medium was used as the inoculum for the test. All glassware was thoroughly cleaned with non-phosphate detergent, then rinsed with hydrochloric acid, deionised water and medium prior to use. Assays (volume 25 ml) were conducted in 125 ml Erlenmeyer flasks fitted with Teflon-lined screw-capped lids. One set of replicate flasks was prepared for each study day, and discarded after sampling.

Range finding test
A range finding test was conducted to determine concentrations to be used in the definitive study. Assays were conducted in duplicate, with nominal concentrations of 1, 10, 100 and 1000 mg/l. Exposure was for 5 days. Analysis of PDC content was performed on study days 0, 3 and 5.

Definitive test
Five test concentrations (10, 18, 32, 56 and 100 mg/l) and a control were prepared in triplicate. Analysis of the PDC content of the flasks (GC-FID) was carried out on study days 0, 2, 3, 4 and 5. Algal biomass (Coulter counter, 3 counts per replicate) was determined on days 2, 3, 4 and 5 of the exposure phase, and again during a recovery phase (see

below). A parallel set of control flasks with foam stoppers was also prepared to monitor algal growth under conditions open to the atmosphere.

Microscopic counts of individual cells (improved Neubauer hemacytometer) were also made on one flask each of the highest test concentration, an intermediate test concentration and a control on day 5 of the study.

The cultures were incubated at 20 (+/-2) degrees C with illumination of 4306 (+/-646) lux with a photoperiod of 14 hr light:10 hr dark. Flasks were shaken manually on each sampling day.

Determination of algistatic and algicidal effects
Aliquots from the 56 mg/ml and 100 mg/ml vessels (where culture counts were similar to or lower than the initial inoculum level) were either subcultured into fresh medium and cell growth determined on days 2, 6 and 9 (recovery experiment), or stained with Evans Blue stain and examined microscopically (living cells exclude stain).

AUC calculation to estimate PDC content of test medium
Due to the highly variable results obtained from the analytical determinations, the measured water dissipation rates for PDC in algal medium were determined by Woodburn and used to calculate the overall residual amounts of test substance present in the flasks. This was expressed as the time weighted average (TWA) concentration, and was based upon the area under the concentration curve. It follows methods developed in Annex 6 of the updated OECD Guideline 202, part II (Daphnid reproduction test, revised January 1996). The integrated area is considered by OECD to be the best expression of the dose to which aquatic organisms are exposed over the selected time period. Further information is given in Attachment 4.3AUC.

Statistical analysis
Analysis of variance and two multiple range tests (Tukey's test, Scheffe's test) were applied to the cell count data.

Remark: Although closed vessels were used, significant loss of PDC from the test vessels was evident. While a general trend of decreasing algal growth with increasing nominal exposure concentration was apparent, the analysed concentrations for each nominal value were sufficiently variable to preclude determination of an EC50 value from the data. The data were, however, adequate for derivation of a NOEC value. The reliability of this determination has been enhanced through additional 'area under the curve' calculations performed subsequently by scientists from the laboratory performing the study.

Result: Analytical results
Mean analysed concentrations on day 1 were in a range 57-75% of nominal. From day 2 onwards, however, there was little consistency either between results obtained within a set of replicate flasks or between the analysed and nominal concentrations. It was concluded that significant losses had occurred despite use of screw-capped vessels.

Calculated TWA concentrations

The calculated TWA concentrations for PDC on exposure days 3, 4 and 5 are shown in Attachment 4.3a. The application of first-order kinetics to the dissipation of PDC in algal media is presented in Attachment 4.3b.

Cell counts
Mean values for the three replicate flasks were highly variable, reflecting the analytical results. This information is summarised in Attachment 4.3c. No clear concentration-response relationship is evident, as would be expected given the analytical results, although there was a trend of reduced algal growth in the two highest nominal test concentrations.

Comparison of mean cell counts from the screw-capped- and foam stoppered controls revealed a 65-73% reduction in growth in the capped vessels.

Microscopic counts were lower than counts obtained using the Coulter counter, however this did not appear to have any significant impact on the overall interpretation of the data.

Little growth occurred in algal populations from the two highest test concentrations during the recovery period. Growth in the control samples was also poor, suggesting that insufficient cells had been used to inoculate the recovery vessels. No conclusion could therefore be reached concerning possible algistatic and algicidal effects of PDC.

Microscopic examination of Evans blue stained cells from the 56 mg/l and 100 mg/l vessels was inconclusive since it was difficult to discriminate between stained and unstained cells. Approx. 8% of cells from the 56 mg/l culture, and 20% of cells from the 100 mg/l culture, appeared dead.

Determination of IC50 value
No scientifically valid estimate of the IC50 for PDC was possible given the highly variable results obtained for algal growth and analysed concentration.

No Observed Effect Concentration
ANOVA and multiple range tests indicated that there were no significant differences between mean cell counts in the 10 mg/l and 18 mg/l nominal concentrations and the controls on any of the exposure days. In contrast, mean cell counts obtained from the other concentrations did differ significantly from controls. The authors conclude that the 5 day NOEC for PDC in Skeletonema costatum is 18 mg/l (nominal).

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Attached doc.:

Attachment 4.3 AUC

Use of AUC calculation to estimate concentrations of PDC in algal medium

Application of first order kinetics allow for the calculation of exposure concentrations of PDC at time ‘t’:

$\mathbf{C = C_0 e^{-kt}}$ (1)
Where C is the concentration of PDC (ug/l) at time t, C_0 is the initial concentration (ug/l) at time 0, k is the rate constant for decay of dissipation ($time^{-1}$), and t is time.

Integrating the concentration as a time-weighted average dose over time 't' produces:

$\mathbf{C_{twa} = 1/t \int C_0 e^{-kt}}$ (2)

Integrating between time 0 and 't', where C_{twa} is the time weighted average concentration over time 't', the analytical solution for equation (2) is:

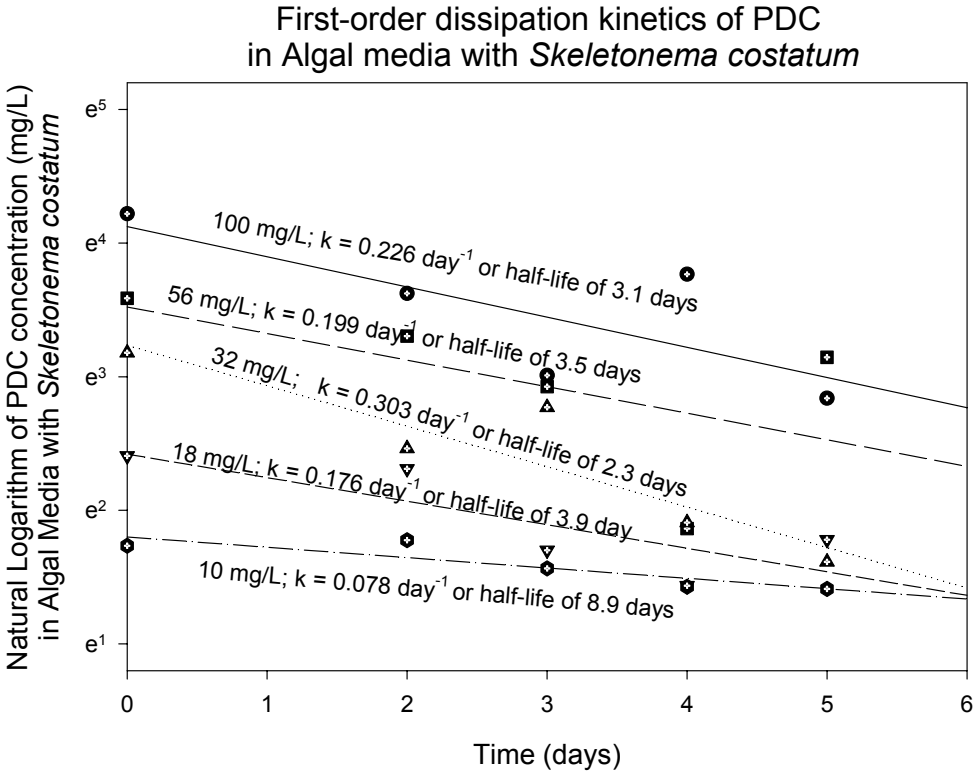
$\mathbf{C_{twa} = (-C_0/kt)(e\text{-}kt^{-1} - 1)}$ (3)

Attachment 4.3a.doc

TWA Concentrations and calculated first-order rate constants for PDC in algal media with *Skeletonema costatum*.

Nominal Dose Level	TWA Concentration for PDC (mg/L)			First-order	
(mg/L)	Day 3	Day 4	Day 5	k value (day^{-1})	half-life (d)
10	5.06	4.87	4.70	0.078	8.9
18	8.62	7.97	7.38	0.176	3.9
32	15.78	13.93	12.37	0.303	2.3
56	27.18	24.89	22.87	0.199	3.5
100	49.33	44.71	40.70	0.226	3.1

Attachment 4.3b.doc



Attachment 4.3c.doc

Percent inhibition (relative to control) of growth of Skeletonema costatum, from Hughes (1988a)

	Percent inhibition *			
Nominal Concn (mg/l)	**Day 2**	**Day 3**	**Day 4**	**Day 5**
10	-6.6	7.0	13.5	4.7
18	4.7	-0.3	7.9	15.7
32	21.6	52.2	33.3	25.3
56	44.1	68.7	61.3	70.1
100	40.9	69.9	80.8	75.3

* A negative value indicates growth

Conclusion: Under the conditions of the test, the 5-day NOEC for PDC in Skeletonema costatum was 18 mg/l based on nominal values, and 7.4 mg/l using analysed concentrations and a TWA technique to integrate the dose to which the algae were exposed.

Reliability: (2) valid with restrictions
Guideline study using accepted calculation method, acceptable with restrictions.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (148) (149) (150)

Species: Skeletonema costatum (Algae)
Endpoint: other: biomass and growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:**
EC10: calculated
EC50: = 14.7 - 16.3

Method: other: calculation
Test substance: as prescribed by 1.1 - 1.4

Method: Algal biomass- and growth measurements from the algal toxicity study in Skeletonema costatum study reported by Hughes (1998) were used by Woodburn (2002a,b) to derive a 120 hr NOEC and a 72 hr EC50 value, based upon calculated time-weighted average concentrations of PDC in the test medium. [For details of the TWA calculation, see attachment 4.3 AUC and Attachment 4.3a).

Result: Attachment 4.3d tabulates the percentage biomass inhibition- and inhibition of growth rate reported by Hughes (1988) against the TWA concentration of PDC in the test system calculated by Woodburn (2002a).

The figures in Attachment 4.3d present graphical plots of this information.

Based on this analysis, the 72 hr EC50 (biomass) for PDC in Skeletonema costatum is 16.3 mg/l, while the 72 hr EC50 (growth) is 14.7 mg/l.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 4.3 AUC.doc

Use of AUC calculation to estimate concentrations of PDC in algal medium

Application of first order kinetics allow for the calculation of exposure concentrations of PDC at time 't':

$$\mathbf{C = C_0 e^{-kt}} \quad (1)$$

Where C is the concentration of PDC (ug/l) at time t, C_0 is the initial concentration (ug/l) at time 0, k is the rate constant for decay of dissipation ($time^{-1}$), and t is time.

Integrating the concentration as a time-weighted average dose over time 't' produces:

$$\mathbf{C_{twa} = 1/t \int C_0 e^{-kt}} \quad (2)$$

Integrating between time 0 and 't', where C_{twa} is the time weighted average concentration over time 't', the analytical solution for equation (2) is:

$$\mathbf{C_{twa} = (-C_0/kt)(e\text{-}kt^{-1} - 1)} \quad (3)$$

Attachment 4.3a.doc

TWA Concentrations and calculated first-order rate constants for PDC in algal media with *Skeletonema costatum*.

Nominal Dose Level (mg/L)	TWA Concentration for PDC (mg/L)			First-order k value (day^{-1})	half-life (d)
	Day 3	Day 4	Day 5		
10	5.06	4.87	4.70	0.078	8.9
18	8.62	7.97	7.38	0.176	3.9
32	15.78	13.93	12.37	0.303	2.3
56	27.18	24.89	22.87	0.199	3.5
100	49.33	44.71	40.70	0.226	3.1

Attachment 4.3d.doc
TWA of PDC and inhibition of biomass area under the curve with *Skeletonema costatum*

Day TWA Concentration*	Biomass %inhibition
(mg/l)	On day 3 (%)
Control	
5.0	-3.1
8.6	5.1
15.8	56.6
27.2	92.0
49.3	89.1

*TWA concentration = Time-weighted average concentration for respective timeframe

Day 3:
E_bC50 value = 16.3 mg/L

TWA of PDC and inhibition of growth rate with *Skeletonema costatum*

Day 3 TWA Concentration*	Growth rate inhibition (%)
(mg/L)	Day 0 - 3

Control	
5.0	6.1
8.6	-0.2
15.8	62
27.2	97
49.3	100

*TWA concentration = Time-weighted average concentration for respective timeframe

Day 0-3:
E_rC50 = 14.7 mg/L

Conclusion: Based on this re-analysis, the 72 hr EC50 for 1,2-dichloropropane in Skeletonema costatum is 14.7-16.3 mg/l.
Reliability: (2) valid with restrictions
Reanalysis of data using accepted calculation methods.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (151)

Species: Skeletonema costatum (Algae)
Endpoint: other: biomass and growth rate
Exposure period: 72 hour(s)

Unit: mg/l **Analytical monitoring:**
NOEC: = 8.9 calculated
EC10: calculated
EC50: = 15.1 - 15.8

Method: other: calculation
Test substance: as prescribed by 1.1 - 1.4

Method: The cell density measurements from Hughes (1988) were used to calculate the biomass integral (day 3) and growth rate (days 0-3) for each test flask.

These results were used to determine the mean biomass integral and mean growth rate for each test concentration. The inhibition (%) of the biomass integral and the inhibition (%) of the growth rate were then calculated for each test concentration.

Linear interpolation, with concentration on a logarithmic scale (base = 10), was used to determine the EC50 over 0-72h for biomass integral and growth rate inhibition.

Details of the calculations used are given in Attachment 4.3e.

Result: Although the variation in the measured concentrations between replicates was relatively high a good concentration-response relationship was obtained after 3 days of exposure (see Attachment 4.3e).

Using linear interpolation, with mean measured concentrations on a logarithmic scale (base = 10), the EC50 over 0-72h for biomass integral and growth rate were 15.8 and 15.1 mg/l, respectively.

The No Observed Effect Concentration (NOEC), based on biomass integral at test termination, was determined with Williams' Test (Williams, 1972). Based on mean measured concentrations this revealed a NOEC of 8.9 mg/l.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 4.3e.doc

The biomass integral was calculated according to the formula:

$$An = \frac{N1 - N0}{2} \times t1 + \frac{N1 + N2 - 2N0}{2} \times (t2 - t1) + \frac{Nn-1 + Nn - 2N0}{2} \times (tn - tn-1)$$

where

An	=	biomass integral on day n (area under the growth curve)
N0	=	cell density at t0
N1	=	cell density at t1
Nn	=	cell density on day n (cells/ml)
t1	=	time of first measurement after beginning of test
tn	=	time of nth measurement after beginning of test

The growth rate (μ) was calculated according to the formula:

$$\mu = \frac{\ln (Nn/N0)}{tn - t0}$$

Biomass integral inhibition (%) on day 3

Nominal Concentration[A] (mg/l)	Biomass integral inhibition On day 3 (%)
0 (n.d.)	0
10 (5.5)	-3.1
18 (8.9)	5.1
32 (17)	57
56 (27)	92
100 (42)	89

[A] Between brackets the mean measured concentration 1,2-dichloropropane is given

Mean growth rate inhibition (%) on Days 0-3

Nominal concentration (mg/l)[A]	Day 0 - 3
10 (5.5)	6.5
18 (8.9)	2.3
32 (17)	62
56 (27)	98
100 (42)	102

[A]Between brackets the mean measured concentration 1,2-dichloropropane is given

Although the variation in the measured concentrations between replicates was relatively high (see Table 2 of the report) a good concentration-response relationship was obtained after 3 days of exposure.

Using linear interpolation, with mean measured concentrations on a logarithmic scale (base = 10), the EC50.0-72h for biomass integral and growth rate were 15.8 and 15.1 mg/l, respectively.
The No Observed Effect Concentration (NOEC), based on biomass integral at test termination, was determined with Williams' Test (Williams, 1972). Based on mean measured concentrations this revealed a NOEC of 8.9 mg/l.

Conclusion: Based on this re-analysis, the 72 hr EC50 for 1,2-dichloropropane in Skeletonema costatum is 15.1-15.8 mg/l, with a 72 hr NOEC of 8.9 mg/l.
Reliability: (2) valid with restrictions
Reanalysis of data using accepted calculation methods.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (148)

Species: Phaeodactylum tricornutum (Algae)
Endpoint: biomass
Unit: mg/l **Analytical monitoring:** no data
EC50: = 50

Method: other: Algae, Assimilation Inhibition Test
Year: 1975
GLP: no data
Test substance: no data

Remark: The retardation of the 14C-assimilation was investigated. The test medium (seawater) did not follow standardized conditions, therefore, only a limited comparison is possible.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (138)

Species: Selenastrum capricornutum (Algae)
Endpoint: growth rate
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 1000

Method: other: Algae Inhibition Test
Year: 1987
GLP: no data
Test substance: other TS: purity = 99.9 %

Remark: The cell increase was tested at the end of days 2, 3, 4 and 5.
After 5 days there was no longer correlation between the nominal and the actual concentration due to "variable evaporation" from the closed vessels. They could not establish a correlation between the actual concentration and growth of the cell chains. The NOEC corresponds to the highest tested concentration.
In relation to the average number of algae (high standard deviation) for days 2, 4 and 5, there was no difference in the growth compared with the nominal concentration of 1000 mg 1,2-dichloropropane/l. On the other hand, day 3 showed a significant difference in the average cell number for 180, 560 and 1000 mg 1,2-dichloropropane/l (nominal).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: The algae was exposed for 5 days to 5 different 1,2-dichloropropane concentrations (nominal: 100, 180, 320, 560 and 1000 mg/l), static test, closed vessels, temperature: 22 - 26 degrees C, photoperiod: continuous exposure.
Reliability: (3) invalid
Invalid. Not reliable due to highly variable evaporation of Test Material from vessels.
21-DEC-2004 (152)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge, domestic
Unit: **Analytical monitoring:** no data

Method: other: OECD Guide-line 301 D
Year: 1981
GLP: no data
Test substance: other TS: purity = 65 %

Remark: After 28 days no significant inhibition of oxygen intake of domestic, activated sludge was established using Na-Benzoate with 3 mg 1,2-dichloropropane/l.
A mixture with 1,2-dichloropropane as the main component was tested. Other components of the mixture were:
1,3-dichloropropene 25%
2,3-dichloropropene 10%

1,1-dichloropropane trace
3,3-dichloropropene trace
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Invalid. Not reliable; other test material.
21-DEC-2004 (124)

Type: aquatic
Species: other bacteria: BASF-activated sludge
Exposure period: day(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 630
EC80 : = 1400
EC20 : = 290

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (132)

Type: aquatic
Species: other bacteria: BASF-activated sludge
Exposure period: day(s)
Unit: mg/l **Analytical monitoring:** no data
EC20 : = 1300

Method: other: not specified
GLP: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (153)

Type: field
Species: other bacteria: autochthone microorganisms
Exposure period: 16 hour(s)
Unit: mg/l **Analytical monitoring:** no data
MEC : = 1700

Method: other: Bioluminescence
Year: 1986
GLP: no data
Test substance: no data

Remark: The inhibitive effect of 2,3-dichloropropane was tested on autochthone microorganisms from water samples of pristine aquifer. The ATP concentration in water was determined with bioluminescence. The MEC value (minimum effect concentration) is the lowest value which results in a significant inhibition.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Incubation temperature: 10 degrees C, measure temperature: 25 degrees C, integration time: 10 seconds.
Reliability: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (154)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: Pimephales promelas (Fish, fresh water)
Endpoint: other: survival, growth
Exposure period: 28 day(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 6 - 11

Year: 1982
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: General
Prior to starting the Early Life Stage (ELS) test, the 96 hr LC50 was determined using 30 day old fish. This was followed by 6-10 day range-finding test using 24 hr old larvae. The objective of both tests was to identify the lowest concentration that caused abnormal behaviour (erratic swimming, lethargy, decreased feeding etc) in the test organisms. This concentration was used as the highest concentration for the ELS study.

Test organisms and housing
All organisms were reared in the laboratory performing the study. Exposure of eggs and larvae took place in glass tanks (nominal volume 500 ml, water depth 4.5 cm) under continuous flow conditions (90% of the test solution replaced every 75 min).

For the main ELS test, 30 eggs (2-8 hr old) were placed in 4 replicate tanks per exposure concentration and observed until hatching (ie 4-5 days post-spawn). Fifteen healthy larvae per tank were then selected at random, placed in each of 4 replicate chambers and survival followed for 28 days. Body weight was determined at the end of the test. The fish were fed shrimp nauplii throughout the study.

Test conditions
Filtered, UV-sterilised water was obtained from Lake Superior, and had the following characteristics: hardness 45 mg CaCO3/l; alkalinity 42 mg CaCO3/l; pH 7.4; dissolved oxygen 7 mg/l. Illumination was provided by cool white fluorescent lamps with a 16 hr light period. Water temperature was 25 degrees C. Exposure concentrations of 0, 6, 11, 25, 51 and 110 mg/l (obtained by diluting a stock saturated solution of PDC in water) were used.

Analytical
The concentration of PDC in the tanks was measured twice per week in alternate replicate tanks using GC (limit of detection 0.1 mg/l).

Statistics
Hatchability of embryos, normal larvae at hatch and survival and mean weight and length data were subject to ANOVA with an F test and Dunnett's test.

Remark: Inspection of the results from this study provides the following NOEC values (LOEC in brackets):

Hatchability: 110 mg/l (>110 mg/l)
Normal larvae at hatch: 25 mg/l (51 mg/l)
Survival to day 28: 11 mg/l (25 mg/l)
Weight at day 28: 6 mg/l (11 mg/l)

Result: Measured exposure concentrations were 0, 6, 11, 25, 51 and 110 mg/l.

Embryo hatchability was 96% - 98%, with no treatment-related differences apparent, however the percentage of normal larvae was decreased significantly in the 51 mg/l and 110 mg/l tanks (decreased 33% and 100%, respectively).

Body weight at day 28 was reduced significantly in larvae exposed to 11 mg/l and above, while larval survival was significantly decreased at 25 mg/l and above.

The authors estimate that the Maximum Acceptable Toxicant Concentration (MATC, defined as a hypothetical toxic threshold falling mid-way between the NOEC and LOEC) for PDC is 59 mg/l.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of this ELS test in Fathead minnows, a chronic NOEC of 6 mg/l was obtained for growth and a chronic NOEC of 11 mg/l obtained for survival.

Reliability: (2) valid with restrictions
Test procedure in accordance with generally accepted scientific methods and described in sufficient detail.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (136)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: reproduction rate
Exposure period: 21 day(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 8.3 measured/nominal
LOEC: = 15.8 measured/nominal

Method: EPA OTS 797.1330
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Test organism and conditions
Daphnia magna brood stocks were acclimated under static conditions (period not stated) and fed Selenastrum capricorneutum daily throughout the test. Culture medium was carbon-filtered dechlorinated tapwater (hardness 160-180 mg/l CaCO3). All glassware was solvent/acid washed prior to use. The test method was based upon EPA OTS 797.1330.

Ten daphnids per treatement level were housed inside a glass

exposure chamber, which was placed in a 600 ml glass beakers containing 500 ml of medium. The beakers were loosely covered to reduce volatilisation of PDC from the test solution. The test was conducted at 20 +/- 2 degrees C with a 16 hr light / 8 hr dark cycle but no aeration. Dissolved oxygen, conductivity, pH and temperature in each vessel were recorded at 24 hr intervals during the test.

The calculated nominal concentration of PDC in the test vessels was 0, 7.5, 12.0, 21.0, 36.0 and 60.0 mg/l. The medium inside the test vessels was replaced with fresh medium on average 42 times per day. Samples of test medium were removed from the replicate vessels on days 0, 7, 14 and 21 and analysed using GC (limit of detection 0.02 mg/l).

The number of live daphnids and occurrence of sub-lethal effects (immobilisation, abnormal behaviour, abnormal appearance) were recorded daily.

Statistical analysis
The data were analysed using ANOVA and Dunnett's test, and Probit, moving average and binomial techniques used to calculated the 24 hr and 48 hr LC50. The 21-day NOEC and LOEC were calculated by observing which concentration produced responses.

Result: Mean, measured concentrations of PDC in the test vessels were 0, 8.3, 15.8, 21.5, 39.5 and 72.9 mg/l.

Daphnids exposed to 72.9 mg PDC/l were unable to maintain their position in the water column immediately after being placed in the test vessels, while those exposed to 39.5 mg/l were immobilised from day 2. Sub-lethal effects (smaller size, lighter colour) were noted in daphnids exposed to 21.5 mg/l.

The 21 day NOEC for reproduction was 8.3 mg/l and the LOEC 15.8 mg/l.

The 21 day NOECs and LOECs for sub-lethal effects (immobilisation, size, colour) and death were 15.8 mg/l and the LOEC 21.5 mg/l, respectively.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the flow-through conditions used in this test, the 48 hr LC50 of PDC in Daphnia magna was 55.9 mg/l, while the 21 day NOEC and LOEC for reproduction were 8.3 mg/l and 15.8 mg/l, respectively.

Reliability: (2) valid with restrictions
GLP guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (143)

Species: Mysidopsis bahia (Crustacea)
Endpoint: other: parental mortality, number of young per female, adult growth
Exposure period: 28 day(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: >= 4.09

Method: EPA OTS 797.1950
Year: 1989

GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Test organism and conditions
Mysid cultures (<24 hr old) were maintained in natural sea water (salinity: 20 parts per thousand) at 25 degrees C for 10 days prior to starting the test.

Exposure of the test organisms took place in glass aquaria (vol approx 6.8 l). Fresh medium, containing PDC, was pumped into each aquarium and provided approx. 11.8 volume additions per day. The mysids were fed brine shrimp nauplii during the test.

The final nominal concentration of PDC in the vessels was 0, 0.6, 1.2, 2.3, 4.6 and 9.3 mg/l (each in duplicate). Water samples were collected from the chambers on study days 0, 7, 14, 21 and 28 and their PDC content analysed using GC-electron capture.

At the start of the test, 40 post-larval mysids per treatment were selected at random and evenly distributed between four
chambers housed within two replicate vessels per treatment. On test day 16, each female within a treatment replicate was paired with a male from the same treatment group, the pairs isolated within their treatment groups until study termination. The number of dead mysids, the time to release of broods, length of adults on day 15 and the number of off-spring produced were recorded. (All off-spring were maintained in the same test concentration as the parents until the end of the test.)

Salinity, temperature and dissolved oxygen were measured regularly during the test.

Statistical analysis
The data were analysed using ANOVA and Dunnett's test after verifying homogenity of the variances using Bartlett's test.

Remark: The NOEC for parental and larval mortality, number of off-spring per female and time to release of first brood, and adult growth was 4.09 mg/l.

Result: Analysed exposure concentrations
Mean analysed concentrations of PDC in the test vessels were 0.41, 0.97, 1.35, 2.48 and 4.09 mg/l, however mechanical problems with the diluter apparatus meant that individual analysed values on days 0-28 were variable (i.e. in a range 0.36-0.61, 0.51-1.83, 1.24-1.57, 1.89-3.20 and 2.96-4.99 mg/l for the 0.6, 1.2, 2.3, 4.6 and 9.3 mg/l exposure groups, respectively).

Mortality
Parental mortality varied from 22% in cultures exposed to 0.97 or 1.35 mg PDC/l to 28% in cultures exposed to 0.41 or 4.09 mg/l. Mortality in controls was 10%. There was no statistically significant difference between mortality in the control or treated groups. Overall survival of juveniles from
treated parents varied from 85% in the 4.09 mg/l group to 91% in the 0.41 mg/l group, with 85% survival in the

controls.

Number of off-spring and time to first brood release
The average number of off-spring per female varied from 6.8 in the 4.09 mg/l group to 10.6 in the 2.48 mg/l group, with 11.3 young/female in the controls (not significant). Mean time to first brood release was 15.5 or 16.0 days in the treated mysids versus 16.5 days in the controls. These differences were not statistically significant.

Adult growth
Mean length of adults after 15 days and 28 days exposure, and adult weight at termination, were unaffected by treatment.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the test, the 28 day NOEC for mortality, reproduction and growth in the mysid shrimp over 28 days was at least 4.09 mg/l, the highest concentration tested.
Reliability: (2) valid with restrictions
GLP guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (155)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to Soil Dwelling Organisms

Type: artificial soil
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: mortality
Exposure period: 14 day(s)
Unit: mg/kg soil dw
LC50: = 4240

Method: OECD Guide-line 207 "Earthworm, Acute Toxcity Test"
Year: 1981
GLP: no data
Test substance: other TS: purity = 98 %

Remark: A mixture of peat, clay, fine sand and calcium carbonate served as test medium. Ten adult animals weighing between 300 - 500 mg were exposed to 1,2-dichloropropane. The 95 % confidence level was 3830 - 4680 mg 1,2-dichloropropane/kg of dry ground mass.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Temperature: 20 degrees C, pH-value: 5.5 - 6.5, ground humidity: 35%
Reliability: (2) valid with restrictions
Guideline study
25-OCT-2004 (156)

Type: artificial soil

Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: other: growth
Exposure period: 56 day(s)
Unit: mg/kg soil dw
LC0: = 92300

Method: other: Earthworm, Toxicity Test
Year: 1990
GLP: no data
Test substance: no data

Remark: Test medium were organic dung, sand and deionized water. The animals which were exposed to 1,2-dichloropropane were < 7 days old and weighed < 10 mg. Concentrations up to 80.8 g
1,2-dichloropropane/kg did not cause significant changes in the average weight of the animals or in the reproduction rate (parameter was number of cocoons/worms).
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: uncovered Petri dish, temperature: 25 degrees C, ground humidity: 70 - 80 %
Reliability: (3) invalid
Invalid. Not reliable due to assumed loss of test material via evaporation over a long-term study.
21-DEC-2004 (157)

Type: filter paper
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: mortality
Exposure period: 48 hour(s)
Unit: mg/cm² filter paper
LC50: = .064

Method: OECD Guide-line 207 "Earthworm, Acute Toxcity Test"
Year: 1981
GLP: no data
Test substance: other TS: purity = 98 %

Remark: Weight of animals exposed to 1,2-dichloropropane was between 300-500 mg. The 95% confidence level was 0.059 - 0.07 mg 1,2-dichloropropane/cm2.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test condition: Temperature: 20 degrees
Incubation at dark
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (156)

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo: In vivo
Type: Distribution
Species: rat
No. of animals, males: 4
No. of animals, females: 4
Doses, males: 5, 50 or 100 ppm
Doses, females: 5, 50 or 100 ppm
Vehicle: other: air
Route of administration: inhalation
Exposure time: 6 hour(s)

Method: other: EPA test rule study
Year: 1989
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male (121-136 g) and female (106-124) F344 rats (7 wk old, n=4/sex) were exposed (head only) for 6 hr to 5, 50 or 100 ppm 14C-labeled PDC under dynamic flow conditions. The concentration of radioactivity in plasma and the concentration of PDC in whole blood were determined during and after exposure (cannulated jugular vein).

Chambers, atmosphere and analysis
The chamber was constructed of Teflon-lined plastic, and allowed the simultaneous exposure of 8 rats (4 male, 4 female; housed on two tiers) during exposure. It was designed to permit collection of blood samples during exposure. Vapors were generated by pumping the contents of SARAN bags filled with measured volumes of 14C-PDC and dry compressed air into the chambers. The concentration of PDC at one point in the upper and the lower tier was determined by GC/FID, with LSC to quantify the concentration of radio-label.

Analysis of blood
Aliquots of blood were pooled (by sex and time interval) and analysed by GC/MS for quantity of PDC present.

Other details
All other methods etc were as decribed in the preceeding record.

Result: The measured concentration of PDC in the chambers was 4.6/4.7 ppm, 52.4/56.8 ppm and 141.8/125.2 ppm for males/females, respectively, in the low, mid and high exposure groups, respectively. Mean end exposure body burdens were 0.4/0.3, 2.8/2.8 and 6.3/7.1 mg equivalents of PDC for males/females in the low, mid and high exposure groups, respectively.
The distribution of recovered radioactivity is summarized in Attachment 5.0b. In summary, urine (54-66% of recovered dose) and expired air (15-23% as carbon dioxide) were the principle routes of excretion with smaller amounts present in tissues and carcass (6-10%) and faeces (6-10%). Less than 4% of the recovered radioactivity was present in cage washings. Exhaled volatiles accounted for 2-3% of the dose in animals exposed to 5 ppm and 50 ppm, and 6-7% in the 100

ppm group (high dose group significantly different from mid and low dose groups). The pattern of excretion did not differ between males and females.

Analysis of tissues
Radioactivity was distributed among all the tissues examined and generally represented less than 0.18% of the recovered dose/g wet weight. The liver and kidneys contained the highest amount of radioactivity, accounting for 0.1-0.3% and 0.1-0.2% of the dose/g wet weight, respectively. There were no obvious differences in tissue distribution between the sexes or in distribution or concentration for the different exposure concentrations.

Timecourse for elimination
Urinary elimination of radiolabel was greatest over the first 24 hr post-dosing (47-62% of dose) relative to the following 24 hr (2-9%). Comparative figures for exhaled carbon dioxide were 13-20% and <3%, and 5-8% and 0.7-3.0% for faeces (at 0-24 and 24-48 hr, respectively). The majority of exhaled volatiles were also eliminated during the
24 hr following exposure, with <0.03% detected during the 24-48 hr time period.

Blood concentrations in both sexes were generally at a maximum 4 hr into the exposure (exception: 5 ppm females which peaked at 1 hr). In both sexes the peak blood PDC level was not proportional to dose indicating a dose-dependent non-linearlity in clearance. The concentration in blood was below the limit of detection (0.03 ug/g) 2 hr after exposure ended. Modelling (one-compartment open model with linear fit) indicated a post-exposure blood clearance half life for PDC of 30 min in males and 24 min in females.

In plasma, the highest concentration of 14C in both sexes was found at 4 hr in the exposure, and ranged from 2, 12-15 and 27-29 ug eq/g plasma present in the 5, 50 and 100 ppm groups respectively. Corresponding AUCs were 21-23, 130-134 and 288-320 ug g^-1, respectively. Comparison of the 5 ppm peak plasma 14C level and AUC with the mid- and high dose groups indicated that plasma 14C was less than proportional to dose.

Metabolites
Approx. 60-90% of the radioactivity present in the exhaled volatile fraction was unchanged PDC. HPLC analysis of urine (pooled from the 3 inhalation experiments) revealed the presence of three n-acetylcysteine conjugates of PDC (N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine and N-acetyl-S-(2-carboxyethyl)-L-cysteine) but no detectable parent compound. Attempts to identify four other HPLC peaks were unsuccessful.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 5.0b.doc

Toxicokinetics of PDC, from Timchalk et al., 1989

	% recovered radioactivity		
	5 ppm [a]	50 ppm [a]	100 ppm [a]
MALES			
Urine	65.0 ± 6.7	54.5 ± 6.0	58.8 ± 7.3
Expired CO_2	16.4 ± 0.1	23.1 ± 2.6 b,d	17.4 ± 3.0
Expired volatiles	1.7 ± 0.6	2.1 ± 0.5	6.3 ± 3.0 b,c
Faeces	7.2 ± 2.3	7.5 ± 1.0	7.0 ± 3.9
Tissues/carcass	7.9 ± 2.6	10.0 ± 1.1	7.9 ± 1.7
Cage wash	1.8 ± 1.1	2.7 ± 1.4	2.4 ± 2.9
Total	100.0	99.9	99.9
FEMALES			
Urine	61.4 ± 3.8	55.6 ± 2.9	63.7 ± 8.2
Expired CO_2	17.3 ± 1.8	19.4 ± 0.9 b,d	15.5 ± 3.8
Expired volatiles	1.7 ± 0.3	3.4 ± 0.6	6.7 ± 3.4 b,c
Faeces	9.7 ± 2.8	9.2 ± 2.6	6.3 ± 2.5
Tissues/carcass	7.3 ± 1.2	8.5 ± 0.8	5.8 ± 1.4
Cage wash	2.6 ± 1.1	3.8 ± 1.2	2.0 ± 1.1
Total	100.0	99.9	100.1

Values represent mean ± SD for 4 animals.

a = values for 5 and 50 ppm represent mean ± SD for 3 animals; those for the 100 ppm group represent mean ± SD for 4 animals.
b = statistically identified difference from the 5 ppm group by Tukey comparison; alpha = 0.05
c = statistically identified difference from the 50 ppm group by Tukey comparison; alpha = 0.05
d = statistically identified difference from the 100 ppm group by Tukey comparison; alpha = 0.05

Conclusion: Urine and exhaled carbon dioxide were the principle routes for elimination of PDC in male and female rats after 6 hr inhalation exposure to 5, 50 or 100 ppm. The majority of radioactivity was excreted within 24 hr, with little unchanged PDC present.
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (158)

In Vitro/in vivo: In vivo
Type: Distribution
Species: rat
No. of animals, males: 4
No. of animals, females: 4
Doses, males: 1 or 100 mg/kg
Doses, females: 1 or 100 mg/kg
Vehicle: other: corn oil
Route of administration: gavage
Exposure time: 48 hour(s)

Method: other: EPA test rule study
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female F344 rats (7 wk old; n=4/sex) were given a single oral treatment of 1 or 100 mg/kg bwt 14C-labelled PDC (50 or 500 uCi/kg bwt, respectively) in corn oil. A third group received 7 daily oral doses of 1 mg/kg bwt non-radiolabeled PDC, followed by a single oral dose of 1 mg/kg bwt 14C-labeled PDC on day 8. Food was withdrawn 16 hr prior to dosing, and returned 4 hr post-treatment. The animals were housed in glass metabolism cages, and urine, feces and expired carbon dioxide and volatile substances collected for up to 48 hr post-dosing. The concentration of 14C in plasma (indwelling jugular cannula) was determined repeatedly during post-dosing period. Samples of body tissues (blood, bone, brain, liver, kidneys, fat, gonads, lung, heart, skeletal muscle, spleen, skin and carcass) were analysed for radioactivity at 48 hr.

Test samples
The unlabelled material was 99.9% pure. The labelled material was 97% pure, had a specific activity of 17 mCi/mmol and was uniformly labelled on a single carbon atom.

Analytical methods
Total radioactivity in urine (plus distilled water cage rinse) and blood (plasma) was quantified by liquid scintillation counting (LSC). Feces were processed using a sample oxidiser, the released carbon dioxide trapped in 1-methoxy-2-propanol:monoethanolamine (7:3) and radioactivity determined by LSC; exhaled carbon dioxide was quantified in an analogous manner. Exhaled volatile compounds were trapped on activated charcoal, desorbed (hexane) and subject to LSC.

Major urinary metabolites were separated by reverse phase HPLC both before and after acid hydrolysis. Metabolite identification was by full-scan chemical ionization-GC/MS.

Kinetic analysis
The data were fitted to a one compartment open pharmacokinetic model with zero-order input rate, and half-lives calculated, using the SIMUSOLV computer programme (Mitchell and Gauthier Associates, Inc, Concord, MA).

Statistical analysis
ANOVA and Tukeys test were applied to the data.

Result: Recovery of radioactivity
Results for the recovery and excretion of radioactivity following oral administration of PDC are given in Attachment 5.0a.

Single dose:
In summary, urine (46-52%) and expired CO2 (23-36%) accounted for over two-thirds of the dose, with smaller amounts present in tissues and carcass (7-11%) and faeces

(7-8%). Less than 3% of the dose was present in cage washings. Exhaled volatiles accounted for 0.3-1.1% of the dose in animals given 1 mg/kg bwt, and 10-16% of the administered radioactivity in high dose animals. Overall, 100-107% of the radiolabel was recovered.

The proportion of the dose excreted as CO2 was significantly lower in rats given 100 mg PDC/kg bwt relative to that for rats given 1 mg/kg; conversely exhalation of radioactivity in the volatile fraction was significantly greater than in the low dose group. While the pattern of excretion was generally similar in males and females, statistical analysis indicated less of the dose was excreted as CO2 and more in the urine in females compared to males.

Multiple doses:
While the overall pattern of excretion and recovery of 14C-label was comparable to that seen in animals given a single treatment, there was a statistically significant decrease (approx. 10%) in percentage recovered in urine from the repeat dose animals. Elimination of 14C-CO2 was slightly but significantly increased in the repeat dose group for females.

Analysis of tissues
Radioactivity was distributed among all the tissues examined. The liver contained the highest amount (0.2-0.4% of the dose /g wet weight), with generally 0.1% or less present in the other organs. There were no obvious differences in tissue distribution between the sexes or the different dosing regimens.

Timecourse for elimination
Elimination was greatest over the first 24 hr post-dosing, with negligible amounts eliminated during the 24-48 hr period. In urine, 35-50% of the dose was recovered during the first 24 hr, with trace amounts (1-2%) excreted subsequently. Comparative figures for exhaled carbon dioxide were 21-33% and 2-3%, and 5-7% and 0.5-1.0% for faeces (at 0-24 and 24-48 hr, respectively).

In plasma, the highest concentration of 14C in both sexes was found at 4 hr post-dosing, with 0.3-0.4 ug eq/g plasma present in low dose animals and 24-28 ug eq/g plasma in animals given 100 mg/kg bwt. Corresponding AUCs were 4.2-5.4 ug g^-1 and 351-368 ug g^-1, respectively. These results suggest that levels in plasma were slightly less than dose-proportionate (perhaps indicating saturation of biotransformation at the higher dose).

There were no obvious differences in timecourse for elimination between the sexes or the different dosing regimens used in the study.

Metabolites
Approx. 82% of the radioactivity present in the exhaled volatile fraction was unchanged PDC. No unchanged PDC was present in urine. Three n-acetylcysteine conjugates were detected in urine, (N-acetyl-S-(2-hydroxypropyl)-L-cysteine, N-acetyl-S-(2-oxopropyl)-L-cysteine and

N-acetyl-S-(2-carboxyethyl)-L-cysteine). These accounted for 10%, 14% and 2% of the dose given to the 100 mg/kg bwt animals, respectively. Attempts to identify three other HPLC peaks were unsuccessful.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Attached doc.: Attachment 5.0a.doc

Toxicokinetics of PDC, from Timchalk et al., 1989

	Single oral dose		Multiple oral dose
	% dose recovered		
	1 mg/kg bwt	100 mg/kg bwt	1 mg/kg bwt
MALES			
Urine	45.6 ± 4.2 b	51.1 ± 2.7	36.8 ± 1.5 a,b
Expired CO_2	35.9 ± 3.0 b,c	27.2 ± 1.1 a,c	36.4 ± 2.8 a,b
Expired volatiles	0.3 ± 0.3	10.3 ± 1.3 a	0.2 ± 0.1
Faeces	7.7 ± 1.6	7.0 ± 1.4	6.4 ± 0.9
Tissues/carcass	10.6 ± 0.4	7.3 ± 0.4	10.5 ± 0.6
Cage wash	0.7 ± 0.4	2.0 ± 1.8	0.7 ± 0.4
Total	100.9	104.9	91.0
FEMALES			
Urine	51.7 ± 2.1 b	51.9 ± 3.2	43.8 ± 5.1 a,b
Expired CO_2	30.8 ± 0.9 b,c	23.2 ± 3.4 a,c	35.4 ± 0.8 a,b
Expired volatiles	1.13 ± 1.5	16.3 ± 8.3 a	0.1 ± 0.0
Faeces	7.9 ± 1.9	5.5 ± 2.6	6.3 ± 3.2
Tissues/carcass	7.7 ± 0.6	7.1 ± 0.7	8.5 ± 0.6
Cage wash	0.8 ± 0.2	2.6± 1.7	2.2 ± 1.8
Total	100.0	106.6	96.4

a = statistically significant difference from 1 mg/kg (single) group; ANOVA alpha = 0.05
b = statistically significant difference between single and multiple 1 mg/kg; ANOVA alpha = 0.05
c = identified sex difference between single 1 or 100 mg/kg; ANOVA alpha = 0.05
Values represent mean ± SD for 4 animals.

Conclusion: Urine and exhaled carbon dioxide were the principle routes for excretion of PDC in male and female rats after single or repeated oral administration. The pathway leading to CO2 is quantitatively less important at higher doses. The majority of radioactivity was excreted within 24 hr, with little or no unchanged PDC present.

Reliability: (1) valid without restriction
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (158)

In Vitro/in vivo: In vivo
Type: Metabolism
Species: rat
No. of animals, females: 2

Doses, females: 100 mg/kg
Vehicle: other: corn oil
Route of administration: gavage
Exposure time: 24 hour(s)

Method: other: EPA test rule study
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Two female F344 rats (12 wk old) were administered deuterated PDC (D6-PDC, 100 mg/kg bwt) to examine the mechanism of formation of urinary metabolites. After treatment the animals were housed in glass metabolism cages and urine collected for 24 hr. The test material contained an average of 5.9 deuterium atoms, with less than 1% unlabelled material present.

Analysis
Urine samples were derivatized twice (ethereal diazomethane and N,O-bis(trimethylsilyl)trifluoroacetamide) and analysed by GC-MS.

Result: Three mercapturic acids were identified as urinary metabolites of PDC:

Metabolite I
2-hydroxypropylmercapturate (containing 3 deuterium atoms);

Metabolite II
2-oxopropylmercapturate (containing 3 deuterium atoms);

Metabolite III
1-carboxyethylmercapturate (containing 4 deuterium atoms);

Based on the number of deuterium atoms present, the authors propose that PDC undergoes oxidation, either prior to or following conjugation with glutathione to give Metabolite II and Metabolite III. Enzymatic reduction of Metabolite II gives Metabolite I.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Conjugation with glutathione is an important pathway for the metabolism of PDC in vivo.
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (158)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: other: Carforth-Wistar
Sex: male/female
No. of Animals: 5

Value: = 2200 mg/kg bw

Year: 1969
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: The acute oral toxicity of PDC was determined in groups of non-fasted Carworth-Wistar rats (males and females, 4-5 wk old, non-fasted).

PDC was administered undiluted, and doses were arranged in a logarithmic series and differed by a factor of two.

Animals were onserved for 14 d post-treatment, and the LD50 calculated using the methods of Thompson (Bacteriol. Rev. (1947) 11, 115) and Weil (Biometrics (1952) 8, 249). The result is presented as the mean and SD.

Result: Acute oral LD50 = 1.9 +/- 0.2 ml/kg (mean and SD)

This is equivalent to 2200 mg/kg bw, based on a density of 1.155 g/ml [Source: MacKay et al (1993) Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Vol III, p479]

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: 1,2-Dichloropropane.
Reliability: (2) valid with restrictions
Early (pre-guideline) study. Methods and results briefly reported. Generally acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (159) (160)

Type: LD50
Species: rat
Vehicle: other: aqueous emulsion in Traganth
Doses: 2-20%
Value: = 2890 mg/kg bw

Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: Rats (strain, number and sex not specific) were given a single oral treatment with 2-20% PDC, as an aqueous emulsion in Traganth. Animals were observed for 7 d post-dosing, prior to necropsy (macroscopic examination). The LD50 was calculated using the method of Litchfield and Wilcoxon.

Result: Clinical signs were reported as apathy and orange-coloured urine.

The acute oral LD50 was 2.5 ml/kg (equivalent to 2890 mg/kg bwt, based on a density of 1.155 g/ml [Source: MacKay et al (1993) Fate of Organic Chemicals, Vol III, p479]).

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
4e (documentation insufficient for assessment)
Early (pre-guideline) study. Methods and results only briefly reported; supporting data.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (161)

Type: LD50
Species: rat
Value: = 1942 mg/kg bw

Method: other: Acute Oral Toxicity
Year: 1959
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (162)

Type: LD50
Species: rat
Value: ca. 460 mg/kg bw

Method: other: BASF-Test
Year: 1981
GLP: no
Test substance: other TS

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: Described as "1,2-dichloropropane raw OE". No information available on chemical composition, purity or presence of other acutely toxic substances.
Reliability: (3) invalid
3 (Invalid. Other test material.)
21-DEC-2004 (163)

Type: LD50
Species: rat
Value: ca. 1000 mg/kg bw

Method: other: BASF-Test
Year: 1978
GLP: no
Test substance: other TS

Source: Dow Europe
DOW Europe Horgen
A.K. Mallett Surrey
Test substance: Described as "1,2-dichloropropane raw". No information available on chemical composition, purity or presence of other acutely toxic substances.
Reliability: (3) invalid
3 (Invalid. Other test material.)
21-DEC-2004 (164)

Type: LD50
Species: mouse
Value: = 860 mg/kg bw

Method: other: Acute Oral Toxicity
Year: 1986
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (165)

Type: LD50
Species: mouse
Value: = 960 mg/kg bw

Method: other: Acute Oral Toxicity
Year: 1982
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (166)

Type: LD50
Species: guinea pig
Value: = 2000 mg/kg bw

Method: other: Acute Oral Toxicity
Year: 1989
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (167)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain: Sherman
Sex: male/female
No. of Animals: 6
Exposure time: 4 hour(s)
Value: = 2000 ppm

Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: Six male or female Sherman rats (approx. 100 - 150 g) were exposed to PDC vapor (nominal concentrations up to 2000 ppm) for 4 hr or 8 hr, then observed for a 14 day follow-up period.
The test atmosphere was generated by passing air (2.5 l/min) through a fritted glass disc immersed in liquid PDC. The resulting vapour-laden stream was mixed with fresh air to produce a series (log base 2) of exposure concentrations. The reported values are nominal (based on weight of material

evaporated) and not verified analytically.
Remark: Conversion factor: 1 ppm = 4.70 mg/l
Result: Results from a preliminary study, summarised in tabular form, indicate that there was 33-67% mortality following 4 hr exposure to 2000 ppm PDC (equivalent to 9.4 mg/l).

There were 3/6 deaths in the definitive study following an 8 hr exposure to this same concentration.

Thus the same extent of mortality was observed in rats exposed to PDC vapor for 4 hr or 8 hr. Since the longer exposure was not more hazardous than the shorter expsoure, it is concluded that these results most likely reflect the 4 hr acute toxicity of 1,2-dichloropropane in the rat.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: The 4 hr inhalation LC50 for PDC in the rat is 2000 ppm (9.4 mg/l).
Reliability: (2) valid with restrictions
Early (pre-guideline) study, generally well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (168) (160)

Type: LC50
Species: rat
Strain: Sprague-Dawley
Sex: no data
No. of Animals: 33
Doses: 2200 ppm
Exposure time: 7 hour(s)
Value: > 2200 ppm

GLP: no
Test substance: no data

Method: Thirty three adult rats (bwt 150 - 200 g) were exposed once to a 2200 ppm (nominal) PDC vapour for 7 hr.

The concentration of PDC in the exposure chamber was calculated from measurements of the weight of solvent volatilised and the rate of air flow through the chamber. This was compared with the analysed content of PDC in a sample of chamber air, quantified using thermal decomposition and estimation of inorganic chloride.

Groups of 3-5 animals taken for necropsy on days 0, 1, 2, 4, 7, 9 and 14 days post-exposure, and subject to macroscopic evaluation. Tissue sections were prepared from adrenals, heart, liver, kidney and subject to microscopic examination. Three unexposed rats served as controls.
Remark: 1 ppm = 4.70 mg/m3
Result: Two rats died shortly after exposure, while the remainder survived until scheduled necropsy. (Advanced autolysis precluded microscopic evaluation of tissues from the decedents.)

Slight visceral congestion and fatty liver were the main macroscopic changes present.

Microscopic examination of the liver revealed

marked-to-moderate, midzonal-to-diffuse, fine droplet fatty degeneration with centrilobular necrosis in all animals sacrified 24 hr post-exposure. Some necrotic liver cells were also present in 3/5 rats 48 hr post-treatment, and 1/3 rats at 4 days. Glycogen depletion was present 24-48 hr post-exposure, while deposition of hemosiderin in Kupffer cells was present from day 4 onwards. Livers of rats sacrificed 2 days after exposure to PDC showed some increase in occurrence of scattered mitotic figures.

Fine droplets of fat were observed in convoluted tubules and thick portions of the loop of Henle of 4/5 rats at day 1 post-exposure and 2/5 on day 2, with minimal fatty change in 3/5 rats at day 7.

The amount of fat in the adrenal cortex showed a slight-to-moderate decrease in animals necropsied immediately and 24 hr post-exposure.

Interstitial pneumonia was present occasionally in all groups, including controls.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the inhalation LC50 for PDC in the rat was >2200 ppm (7 hr exposure). Treatment-related changes appeared limited primarily to liver .
Reliability: (2) valid with restrictions
Early (pre-guideline) study, generally well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (169)

Type: LC50
Species: rat
Exposure time: 8 hour(s)
Value: = 14 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1959
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (162)

Type: other: IRT
Species: rat
Exposure time: minute(s)
Value: = ppm

Method: other: not specified
Year: 1978
GLP: no
Test substance: other TS

Remark: The exposure of 12 rats to a saturated atmosphere of 1,2-dichloropropane at 20 degrees C for 3 minutes caused no

lethality. All rats (groups of 6) died when they were exposed to 1,2-dichloropropane for 10 or 15 minutes.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: "1,2-dichloropropane crude"
Reliability: (3) invalid
Other Test Material
21-DEC-2004 (164)

Type: other: IRT
Species: rat
Exposure time: minute(s)
Value: = ppm

Method: other: not specified
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: The exposure of 12 rats to a saturated atmosphere of 1,2-dichloropropane at 20 degrees C for 3 minutes caused no lethality. Three rats died after exposure for 10 minutes .
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (161)

Type: other: LT0
Species: rat
Value: = 6.9 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LTO = time within which none of the tested animals died: > 7 hours
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: LC50
Species: mouse
Exposure time: 10 hour(s)
Value: = 2.256 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1968
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (171)

Type: other: LT50
Species: mouse
Exposure time: 8.3 hour(s)
Value: = 3.389 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1968
GLP: no data
Test substance: no data

Remark: LT50 = time within which 50% of the tested animals died
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (171)

Type: other
Species: mouse
Exposure time: 4 hour(s)
Value: = 4.6 mg/l

Method: other
Year: 1978
GLP: no data
Test substance: no data

Remark: Measured parameters were SGOT, SGPT, glucose-6-phosphatase and ornithine carbamoyltransferase enzymes in the serum of male rats following a single 4-hour inhalation exposure at a concentration of 4620 mg/m3. A significant increase in enzyme activities was observed for SGOT, SGPT and ornithine carbamoyltransferase at 24 and 48 hours.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (172)

Type: other: LT0
Species: mouse
Value: = 4.4 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LT0 = time within which none of the tested animals died: approx. 1 hour
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: other: LT100
Species: mouse
Value: = 4.4 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LT100 = time within which all of the tested animals died: approx. 4 hours
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: other: see remark
Species: mouse
Exposure time: 2 hour(s)
Value: = 6.5 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: Mortality: 3/10
Symptoms: fatty degeneration in liver and kidney as well as centrilobular necrosis of the liver.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: other: LT0
Species: rabbit
Value: = 6.9 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LTO = time within which none of the tested animals died: > 7 hours
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: other: LT0
Species: dog
Value: = 4.4 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LTO = time within which none of the tested animals died: > 7 hours

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: other: LT0
Species: guinea pig
Value: = 6.9 mg/l

Method: other: Acute Inhalation Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: LTO = time within which none of the tested animals died: > 7 hours
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (170)

Type: LC50
Species: guinea pig
Strain: no data
Sex: no data
No. of Animals: 33
Exposure time: 7 hour(s)
Value: > 2200 ppm

GLP: no
Test substance: no data

Method: Thirty three adult guinea pigs (bwt 600 - 800 g) were exposed to a 2200 ppm (nominal) PDC vapour for 7 hr.

The concentration of PDC in the exposure chamber was calculated from measurements of the weight of solvent volatilised and the rate of air flow through the chamber. This was compared with the analysed content of PDC in a sample of chamber air, quantified using thermal decomposition and estimation of inorganic chloride.

Groups of 2-5 animals taken for necropsy on days 0, 1, 2, 4, 7, 9, 11, 14, 16 and 21 after treatment, and subject to macroscopic evaluation. Tissue sections were prepared from adrenals, heart, liver, kidney and subject to microscopic examination. Three unexposed guinea pigs served as controls.
Remark: 1 ppm = 4.70 mg/m3
Result: There were no premature deaths during the study. At necropsy, many animals showed slight visceral congestion and fatty change in the liver, while the cut surface of the adrenal glands showed a hemorrhagic central portion.

Microscopic examination revealed small-to-moderate amounts of fat in the heart, liver and kidney of exposed animals sacrificed immediately after treatment.

Exposed animals showed a reduction in liver glycogen on day

0 and day 1 post-treatment, a normal amount at day 2 then a marked increase from day 4 onwards. Hepatocytes in affected animals were swollen with pale, vaculoated cytoplasm, especially in the centrilobular region.

Histopathological changes in adrenal tissue included thickening, vacuolation, hemorrhage increased occurence of mitotic figures and necrosis of the cortex during the first week post-treatment. These changes began to resolve during the second week post-exposure and adrenal tissue from two out of three guinea pigs sacrificed on day 21 appeared normal. Changes in the medulla included congestion, oedema, white cell infiltration and occasional necrotic cells up to day 7, but these tended to have resolved by day 9. Deposits of fat and hemosiderin were present in connective tissue surrounding the medulla at day 21.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the inhalation LC50 for PDC in the guinea pig was >2200 ppm (7 hr exposure). Treatment-related changes appeared limited to primarily to the adrenal gland.
Reliability: (2) valid with restrictions
Early (pre-guideline) study, generally well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (169)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Value: = 10100 mg/kg bw

Year: 1962
GLP: no
Test substance: no data

Method: PDC was applied to clipped skin of male albino rabbits (2.5 - 3.5 kg, n=4 per treatment) under occlusion for 24 hr. The animals were immobilised during expoure, then returned to their cages and observed for 14 days.
Result: An LD50 of 8.75 ml/kg bw was reported. This is equivalent to 10,100 mg/kg bw, based on a density of 1.155 g/ml [Source: MacKay et al (1993) Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Vol III, p479]
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the dermal LD50 for PDC in male rabbits was 8.75 ml/kg bw (10100 mg/kg bw).
Reliability: (2) valid with restrictions
Early (pre-guideline) study, generally well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (159)

Type: LD50
Species: rat
Value: > 2000 mg/kg bw

Method: other: BASF-Test
Year: 1981
GLP: no
Test substance: other TS

Remark: no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: "1,2-dichloropropane crude OE"
Reliability: (3) invalid
Other test material
25-OCT-2004 (173)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Route of admin.: i.p.
Value: = 1100 mg/kg bw

Method: other: Acute Intraperitoneal Toxicity
Year: 1989
GLP: no data
Test substance: other TS: purity = 97 %

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (174)

Type: LD50
Species: rat
Route of admin.: i.p.
Value: ca. 230 mg/kg bw

Method: other: BASF-test
Year: 1965
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: no additional information
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (161)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: = 700 - 2000 mg/kg bw

Method: other: BASF-test
Year: 1981
GLP: no
Test substance: other TS

Remark: no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Test substance: "1,2-dichloropropane crude OE"
Reliability: (3) invalid
Other test material
25-OCT-2004 (173)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: = 316 - 4640 mg/kg bw

Method: other: BASF-test
Year: 1978
GLP: no
Test substance: other TS

Remark: no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: "1,2-dichloropropane crude"
Reliability: (3) invalid
Other test material
25-OCT-2004 (164)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: undiluted
Exposure: Semiocclusive
Exposure Time: 4 hour(s)
No. of Animals: 3
Result: slightly irritating
EC classificat.: not irritating

Year: 1982
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: OECD Guideline 404. White Vienna rabbits (2 male, mean bwt 3.26 kg; 1 female bwt 2.89 kg) were used.

0.5 ml DCP was applied to a 2.5 cm x 2.5 cm piece of gauze which was held in contact with clipped rabbit skin (upper back or flank) under semi-occlusive conditions for 4 hr.

After removal of the patch, the application site was cleaned with lutrol/water (1:1) and skin reactions recorded at 24 hr, 48 hr, 72 hr and 8 d post-treatment.

Result: Individual reactions at 24 hr:
Redness 2, 2, 2
Oedema 1, 1, 1

Individual reactions at 48 hr:
Redness 2, 1, 1
Oedema 0, 0, 0

Individual reactions at 72 hr:
Redness 1, 1, 1

Oedema 0, 0, 0

Individual reactions at 8 d
Redness 1, 0, 0
Oedema 0, 0, 0
Flaking skin at application site in all animals

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Slightly irritating to skin.
Reliability: (2) valid with restrictions
Guideline study
Flag: Critical study for SIDS endpoint
25-OCT-2004 (175)

Species: rabbit
Result: not irritating

Method: other: Acute Dermal Irritation
Year: 1962
GLP: no data
Test substance: no data

Remark: Dermal application on shaved abdominal skin (nonocclusive); effect time: 24 hours
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (160)

Species: rabbit
Result: corrosive

Method: other: BASF-Test
Year: 1981
GLP: no
Test substance: other TS

Remark: "1,2-dichloropropane crude OE"
occlusive application; no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Other test material
25-OCT-2004 (173)

Species: rabbit
Result: slightly irritating

Method: other: BASF-Test
Year: 1982
GLP: no
Test substance: other TS

Remark: "1,2-dichloropropane crude OE"
Semiocclusive application; no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Other test material
25-OCT-2004 (176)

Species: rabbit

Result: highly irritating

Method: other: BASF-Test
Year: 1978
GLP: no
Test substance: other TS

Remark: "1,2-dichloropropane crude"
no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Other test material
25-OCT-2004 (164)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .05 ml
Exposure Time: unspecified
Result: irritating

Year: 1965
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Result: Slight redness and oedema with slight opacity were present 1 hr post-treatment, with marked redness and odema and slight opacity at 24 hr. All signs had resolved 8 d post-treatment.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Irritating to the eye.
Reliability: (2) valid with restrictions
Early (pre-guideline) study, generally well documented and acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (161)

Species: rabbit
Result: slightly irritating

Method: other: Eye Irritation
Year: 1962
GLP: no
Test substance: no data

Remark: Application of 0.5 ml undiluted 1,2-dichloropropane; irritation index 2 of 10 maximum
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (177) (160)

Species: rabbit
Result: irritating

Method: other: BASF-Test
Year: 1981
GLP: no

Test substance: other TS

Remark: "1,2-dichloropropane crude OE"
no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Other test material
25-OCT-2004 (178)

Species: rabbit
Result: irritating

Method: other: BASF-Test
Year: 1978
GLP: no
Test substance: other TS

Remark: "1,2-dichloropropane crude"
no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (3) invalid
Other test material
21-DEC-2004 (164)

Species: rabbit
Result: irritating

Method: other: BASF-Test
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (161)

5.3 Sensitization

Type: Mouse local lymphnode assay
Species: mouse
Vehicle: other: acetone olive oil
Result: not sensitizing

Method: other: OECD 429 (2002); U.S. EPA OPPTS 870.2600 (2003)
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Range-finding Test
Selection of the upper-dose level for the definitive study was based upon results from an irritation range-finding test where 80%, 60%, 40%, 20%, or 10% v/v PDC in acetone:olive oil (AOO) was applied to each ear of female mice (1 mouse /dose) on two consecutive days. No appreciable ear swelling or erythema were noted and 80% v/v was chosen as the highest dose.

Main study (LLNA)
Groups of six female BALB/c mice (approximately 18 g, 8 weeks old) received topical applications (25 ul/ear, total 50 ul/mouse) of 5%, 20% or 80% propylene dichloride (PDC) in AOO on three consecutive days. A positive control group was treated with 30% a-hexyl cinnamaldehyde (HCA), a recognized skin contact allergen, diluted using AOO.

On day 6, all mice received a 250 µl intravenous injection via the lateral tail vein containing 20 µCi of 3H-thymidine (specific activity 2Ci/mmol; Amersham code TRA310) diluted in phosphate buffered saline (PBS). Approximately five hours later, the mice were sacrificed and the auricular lymph nodes (located at bifurcation of the jugular veins) excised, combined for each mouse and placed in PBS.

A single cell suspension of lymph node cells was prepared by gentle mechanical disaggregation using a tissue homogenizer. The cells were washed using PBS and suspended in 5% trichloroacetic acid (TCA); suspended precipitates were centrifuged and the pellets reconstituted in 1 ml of 5% TCA prior to transfer to a scintillation vial containing 10 ml of Aquasol-2 scintillation cocktail. Tubes used for suspending the pellets were rinsed using two additional 2-ml aliquots of water and the rinses were added to the scintillation vials. The radioactivity in each precipitate (representing two lymph nodes from one animal) was measured using a B-scintillation counter and reported as disintegrations per minute (dpm) per mouse.

Interpretative criteria
In addition to the application of statistical methods, sensitization potential was further determined by the magnitude of any lymphocyte proliferative response in relation to vehicle controls. A stimulation Index (SI) of = or > 3 (i.e. 3-fold or greater proliferation than control animals) was considered indicative of a potential for dermal sensitization.

Statistical methods
Comparisons of dpm values for treated vs. control groups were done by Dunnett's t-test when ANOVA results suggested differences. The alpha level at which all tests were conducted was 0.05.

Result: PDC did not demonstrate any lymph node cell proliferation response, nor any LLNA results (dpm and SI) consistent with dermal sensitization as the lymph nodes draining the area of topical application did not demonstrate a proliferative response equal to or greater than the 3x threshold. SI values were consistently around 1.0 (equivalent to vehicle controls) at all doses tested:

	Proliferative response	
Control	A	1.0 +- 0.7
5%	B	1.0 +- 0.6
20%	C	1.3 +- 0.9
80%	D	0.8 +- 0.5

Proper conduct and responsiveness of the test was confirmed in animals treated with 30% HCA (positive control group)

where proliferation (SI) was 14-fold greater than that of vehicle controls.

Because the SI values for 5, 20, and 80% PDC were all below 3, an EC3 value could not be determined. On the basis of these results, PDC did not demonstrate any contact sensitization potential.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: 1,2 dichloropropane did not stimulate proliferation of lymphocytes in auricular lymph nodes from mice treated with up to 80% PDC in AOO on 3 consecutive days. It was concluded that PDC was not a sensitiser under the conditions of this assay.

Reliability: (1) valid without restriction
GLP guideline study.

21-DEC-2004 (179)

Type: Patch-Test
Species: human
Vehicle: petrolatum
Result: ambiguous

Year: 1989
GLP: no
Test substance: no data

Method: Subjects and symptoms
The test subjects were 10 workers (painters, metal workers) with exposure to mixed solvents, including preparations containing 10-40% 1,2-dichloropropane (analysis by GLC, no details presented). Reported symptoms included itchy erythematous, odematous lesions on the fingers and dorsa of the hands, with scaling and fissuring of the palms in 2 individuals. The patients were assessed during the period 1985-1988. 120 control subjects were included in the investigation (no further details provided).

Patch testing
Patch tests were carried out "according to internationally accepted methods" (no further details provided) using Porotest on Scanpor, with readings made according to ICDRG recommendations (no further details provided). PDC (1%, 2%, 5%, 10%, 20%) and other product constituents (resins, solvents, mineral oils, perchloroethylene, trichloroethylene) were tested in addition to the European standard series (Hermal-Trolab).
Comment: no information is provided on the origin or purity of the PDC used during the challenge phase of this study.

Statistical methods
None applied (observational study).

Result: Control subjects
No response to PDC was noted in 118 of the control subjects; slight erythema was present in the two remaining control individuals after challenge with 20% PDC in petrolatum. With the exception of a single positive reaction to methyl acrylate, no positive response was noted toward the other substances included in this study (no further details provided).

Test subjects
Skin reactions were elicited in all 10 subjects after patch testing with PDC, although not all responded for all tests. Responses were reported as follows:

1% PDC: 1 score + ; 1 score ++ ; 4 score - ; 4 not tested
2% PDC: 5 score + ; 2 score +++; 3 not tested
5% PDC: 4 score + ; 4 score ++ ; 2 score +++ ;
10% PDC: 1 score + ; 7 score ++ ; 2 score +++ ;
20% PDC: 4 score ++; 4 score +++; 2 not tested

A biopsy was performed on one subject (5% challenge site; skin response = score ++). Spongiosis, oedema and early vesiculation of the epidermis was present with perivascular lymphocytic infiltrate in the dermis.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: The authors conclude that 1,2 dichloropropane was responsible for skin reactions observed in this group of workers. Given the dearth of methodological and results detail presented in the publication, including no information on the origin or purity of the sample used during the challenge phase, and since the structure of PDC contains no obvious chemical groups with a potential to react with cellular components, this evidence is considered equivocal.

Reliability: (4) not assignable
Short case report, limited reporting of methods and results, no information on origin/purity of test sample, unknown reliability.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (180)

Type: Patch-Test
Species: human

Year: 1981
GLP: no
Test substance: other TS

Remark: Two female workers reported cases of recurrent dermatitis and were tested with 1% 1,2-dichloropropane and other substances present in their workplaces.

One individual had a reaction to several substances including PDC.

A second individual demonstrated low grade responses to chromate and PDC. This individual reported that initial symptoms were noted on her feet and one incident of a rash under a leather watch strap. This may indicate a reaction to chromates which are sometimes used in the tanning process of leathers.

The PDC used for the patch tests was of technical grade, which could comprise other components and/or impurities.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: No information available.
Reliability: (4) not assignable
Short case report, limited reporting of methods and results,

no information on origin/purity of test sample, unknown reliability.

25-OCT-2004 (181)

5.4 Repeated Dose Toxicity

Type: Sub-acute
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: gavage
Exposure period: 14 days
Frequency of treatment: Consecutive days
Post exposure period: One day
Doses: 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 500 mg/kg bw
LOAEL: = 1000 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Groups of 5 male and 5 female F344 rats (age 6 wk at start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d for 14 consecutive days, followed by one day of observation. The animals were group housed (5/sex/cage) and observed twice daily for mortality.

Necropsies were performed on all animals (macroscopic observations only, no histopathology).

The concentration of test article in the dosing solutions was verified using GC-FID.

Result: GC analysis of the dosing solutions demonstrated that the achieved concentration was 95 - 100% of target.

All rats given 2000 mg/kg bw died during the study, along with a single male from the 125 mg/kg bw/d group.

Final mean body weight was decreased 14-15% in animals given 1000 mg/kg bw/d relative to the controls.

The renal medullae were red in 4/5 males and 5/5 females given 2000 mg/kg bw/d but not in rats from the lower treatment groups.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the sub-acute NOEL for PDC in male and female rats was 500 mg/kg bw/d.
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint

21-DEC-2004 (182)

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: gavage

Exposure period: 13 wk
Frequency of treatment: 5 d/wk
Post exposure period: None
Doses: 0, 60, 125, 250, 500 or 1000 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 250 mg/kg bw
LOAEL: = 500 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Groups of 10 male and 10 female F344 rats (age 7-8 wk at start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 60, 125, 250, 500 or 1000 mg/kg bw/d 5 d/wk for 13 wk. The animals were group housed and observed daily for clinical signs and twice daily for mortality. Animals judged to be moribund were taken to necropsy. Each animal was given a detailed weekly examination, including palpation for tissue masses or swelling. Body weights were taken weekly.

Necropsies were performed on all surviving animals at the end of the treatment period. A comprehensive range of tissues were sampled and preserved, and those from the controls, 500 mg/kg and 1000 mg/kg groups subject to microscopic examination.

The concentration of test article in the dosing solutions was verified using GC-FID.

Result: GC analysis of the dosing solutions demonstrated that the achieved concentration was 95 - 100% of target.

All male and female rats given 1000 mg/kg bw/d and 5/10 males from the 500 mg/kg bw group died before necropsy. All animals from the other treatment groups survived until study termination. Final mean body weights were decreased 16% in male and 8% in females given 500 mg/kg bw/d.

The liver was the only organ to be affected by treatment, with centrilobular congestion present in 5/10 males and 2/10 females given 1000 mg/kg bw/d. Hepatic fatty change and centrilobular necrosis were observed in 2/10 females from the 1000 mg/kg bw/d group.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the sub-chronic NOEL for PDC in the rat was 250 mg/kg bw/d, based upon mortality and lower body weight in males, and lower body weight with no histopathological involvement in females, given 500 mg/kg bw/d.
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Chronic
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: gavage

Exposure period: 103 wk
Frequency of treatment: 5 d/wk
Doses: males 0, 62 or 125 mg/kg bw/d; females 0, 125 or 250 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 62 - 125 mg/kg bw
LOAEL: = 125 - 250 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Methods are described in detail in Section 5.7 (Carcinogenicity).

Samples of the following tissues were subject to histopathological evaluation:

Integumentary system
Respiratory system
Haematopoietic system
Circulatory system
Digestive system
Urinary system
Endocrine system
Reproductive system
Nervous system
Special sense organs
Musculoskeletal system
Body cavity
Adipose tissue
Any tissue appearing abnormal at necropsy.

Result: Body weight and clinical signs
Treated animals showed a dose-related reduction in body weight. Final body weights were approx. 5% lower than control for low dose animals, and 14% and 24% lower then control in the high dose male and female groups, respectively. No clinical signs are described.

Survival
The survival of high dose females (250 mg/kg bwt/d) was significantly ($P<0.001$) less than that of the low dose females and controls. Mortality and morbidity was especially marked at wk 94 of the study. Survival in males was comparable for all groups (78%, 84% and 82% alive at wk 103 for the control, 62 mg/kg bwt/d and 125 mg/kg bwt/d groups, respectively).

Non-tumor pathology
The incidence of heptic foci of clear change (22% versus 6% in controls) and liver necrosis (focal and centrilobular combined; 18% versus 2% in controls) were increased in high dose female rats only. The incidence of other lesions in the treated animals was similar or lower than that of the controls.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the chronic NOEL for PDC in male rats was 62 mg/kg bw/d (based upon a reduction in final body weight observed at 125 mg/kg bw/d). The NOEL in

females was 125 mg/kg bw/d (based upon lower body weight, lower survival and liver lesions present in the 250 mg/kg bw/d group).
Reliability: (1) valid without restriction
Comparable to guideline study, with restrictions.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Sub-acute
Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of administration: gavage
Exposure period: 14 days
Frequency of treatment: Consecutive days
Post exposure period: One day
Doses: 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 250 mg/kg bw
LOAEL: = 125 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Groups of 5 male and 5 female B6C3F1 mice (age 6 wk at start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 125, 250, 500, 1000 or 2000 mg/kg bw/d for 14 consecutive days, followed by one day of observation. The animals were group housed (5/sex/cage) and observed twice daily for mortality.

Necropsies were performed on all animals (macroscopic observations only, no histopathology included).

The concentration of test article in the dosing solutions was verified using GC-FID.
Result: GC analysis of the dosing solutions demonstrated that the achieved concentration was 95 - 100% of target.

All male mice receiving 1000 or 2000 mg/kg bw/d and 3/5 given 500 mg/kg bw/d died during the study. All females from the 2000 mg/kg bw/d group, and 4/5 from the 1000 mg/kg bw/d group also died pre-study termination.

Final mean body weight for the surviving mice was unaffected by treatment.

The renal medullae were red in all mice of both sexes from the 2000 mg/kg bw/d group, the majority of males given 500 mg/kg and the majority of females given 1000 mg/kg bw/d. This change was also present in single females from all other dose groups.

No other compound-related effects were observed at necropsy.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the sub-acute NOEL for PDC in male mice was 250 mg/kg bw/d. No NOEL was established for female mice (LOEL 125 mg/kg bw/d).
Reliability: (1) valid without restriction

Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Sub-chronic
Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of administration: gavage
Exposure period: 13 wk
Frequency of treatment: 5 d/wk
Post exposure period: None
Doses: 0, 30, 60, 125, 250 or 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: = 500 mg/kg bw
LOAEL: >= 500 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Groups of 10 male and 10 female B6C3F1 mice (age 9-10 wk at start of treatment) were administered PDC (99.4% pure) in corn oil by gavage at doses of 0, 30, 60, 125, 250 or 500 mg/kg bw/d 5 d/wk for 13 wk. The animals were group housed and observed daily for clinical signs and twice daily for mortality. Animals judged to be moribund were taken to necropsy. Each animal was given a detailed weekly examination, including palpation for tissue masses or swelling. Body weights were taken weekly.
Necropsies were performed on all surviving animals at the end of the treatment period. A comprehensive range of tissues were sampled and preserved, and those from the controls and the 500 mg/kg groups subject to microscopic examination.

The concentration of test article in the dosing solutions was verified using GC-FID.
Result: GC analysis of the dosing solutions demonstrated that the achieved concentration was 95 - 100% of target.

One male given 60 mg/kg bw/d died during the first week of the study, and a female from the 500 mg/kg bw/d group died during wk 12.

Body weights for all treated males were decreased 4-5% (ie no dose-relationship present). Body weights for females from the 250 mg/kg and 500 mg/kg groups were also decreased slightly by 3-4%. Since there were no histopathological changes noted, these minor effects on body weight are considered incidental and not related to treatment.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: Under the conditions of the study, the sub-chronic NOEL for PDC in the mouse was 500 mg/kg bw/d.
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Chronic

Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of administration: gavage
Exposure period: 103 wk
Frequency of treatment: 5 d/wk
Doses: 0, 125 or 250 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL: <= 125 mg/kg bw
LOAEL: = 125 mg/kg bw

Method: other: standard NTP methodology
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Methods are described in detail in Section 5.7 (Carcinogenicity).

Samples of the following tissues were subject to histopathological evaluation:

Integumentary system
Respiratory system
Haematopoietic system
Circulatory system
Digestive system
Urinary system
Endocrine system
Reproductive system
Nervous system
Special sense organs
Musculoskeletal system
Body cavity
Adipose tissue
Any tissue appearing abnormal at necropsy.

Result: Body weight and clinical signs
Mean body weights of treated and vehicle control animals were comparable, and no compound-related clinical signs were noted.

Survival
The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.035) less than that of the low dose females and controls, with 70%, 58% and 52% of the control, low and high dose animals surviving to termination. Survival in males was comparable for all groups (70%, 66% and 70% alive at wk 103 for the control, 125 mg/kg bwt/d and 250 mg/kg bwt/d groups, respectively). The report notes that the lowered survival in female mice was related to an increased incidence of reproductive tract infections in animals which died before the end of the study (45% of controls versus 64% of the low and high dose females that died during the study).

Non-tumor pathology
Hepatocytomegaly (6%, 10% and 30% for control, low dose and high dose animals, respectively) and hepatic focal necrosis (4%, 10% and 20%) were seen in male mice only.

Acanthosis of the surface epithelium of the forestomach

occurred at increased incidence in high dose males (0%, 0%, 4%) and both groups of females (0%, 10%, 8%).

Suppurative inflammation (affecting ovary, uterus or multiple organs, and a presumed consequence of reproductive tract infection) was found in 5/11 control, 9/14 low dose and 14/22 high dose females that died before the end of the study.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, the chronic LOAEL for PDC in mice was 125 mg/kg bw/d (based upon liver lesions in male mice and acanthosis of the stomach in females). The NOAEL was <125 mg/kg bwt/d.

Reliability: (1) valid without restriction
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (182)

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: inhalation
Exposure period: 13 wk
Frequency of treatment: 6 hr/d, 5 d/wk
Doses: 0, 15, 50 or 150 ppm (0, 0.068, 0.225 or 0.675 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: = 15 ppm

Year: 1988
GLP: yes
Test substance: other TS: 99.4% purity

Method: Animals and treatments
Male and female F344 rats (n = 10 per group, age 7-8 wk at start of treatment) were exposed whole body to 0, 15, 50 or 150 ppm PDC vapor (0, 0.068, 0.225 or 0.675 mg/l) 6 hr/d, 5 d/wk for 13 wk. The test atmosphere was generated by passing heated air (50 degrees) though a J-tube containing a measured amount of PDC. The chamber volume was 4100 l (stainless steel and glass construction; 1 chamber per exposure group) and total airflow was 800 l/min (12 air changes/hr). The distribution of PDC within the chamber was determined 1-2 times/hr at 9 sampling points using a MIRAN 1A infrared spectrometer.

Observations
Animals were examined after each exposure period for clinical signs or indications of overt toxicity.

Haematology
Packed cell volume (PCV), red blood cell counts (RBC), haemoglobin (HGB), white blood cell counts (WBC), mean red cell volume (MCV), mean red cell haemoglobin (MCH), mean red cell haemoglobin concentration (MCHC), platelet counts (PLAT) and differential white cell counts were determined approx. 2 wk prior to study termination using blood collected by orbital sinus puncture.

Clinical chemistry
Total bilirubin (TBILI), serum glutamic pyruvic transaminase

(SGOT), serum glutamic oxaloacetatic transaminase (SGPT), alkaline phosphatase (AP), urea nitrogen (UN) and glucose (GLUC) were determined on blood (cervical vein) collected at necropsy. Red blood cell and plasma cholinesterase were quantified on blood collected by orbital sinus bleed apporx. 2 wk prior to sacrifice.

Urine analysis
Specific gravity (refractive index; American Optical Co), pH, glucose, ketones, bilirubin, occult blood and protein (Chemstrip 7, Bio-Dynamics) were determined approx. 2 wk prior to sacrifice.

Necropsy
Rats were sacrificed on the day after the last exposure following an overnight fast. The eyes and internal organs were subject to macroscopic examination, and the weights of the brain, heart, liver, kidneys, thymus and testes recorded. Approx. 50 tissues were sampled, preserved and processed for microscopic examination (haematoxylin and eosin).

Statistical methods
Clinical chemistry, haematology, urine analysis and organ weights were analysed using Bartlett's test for equality of variances, followed by parametric or non-parametric ANOVA with Dunnet's test or the Wilcoxon Rank-Sum test with Bonferroni's correction for multiple comparisons. The final interpretation of the results considered whether an orderly exposure-response relationship was apparent in the data since a high occurrence of Type I (false positive) errors would be anticipated due to the large number of statistical comparisons that were included in this study.

Result: IR analysis demonstrated that the mean concentration of PDC within the chamber (SD in brackets) was 0, 15(1), 50(3) or 151(3) ppm.

Clinical observations and body weight
One male rat from the 15 ppm group died on day 81 from haemorrhagic cystitis; this was considered a spontaneous event by the study pathologist. No other clinical or overt signs of toxicity were recorded in any of the treated animals during the 90 d exposure period.

Body weights for high dose animals were significantly decreased throughout the study (females decreased 7% at termination, males 10%), with a smaller (non-significant) decrease apparent in mid-dose animals from wk 2 onwards (4-8% decrease at termination).

Haematology and urine analysis
There were no toxicologically or statistically significant changes in haematological or urine parameters in any of the treatment groups.

Clinical chemistry
SGPT values from all treated females were decreased 25-31% relative to controls, while SGOT from females exposed to 15 or 50 ppm PDC were decreased 18-21% (no effect in high dose animals). Serum glucose was decreased 22% in mid dose males

only. None of these changes were considered toxicologically significant by the study authors.

Necropsy findings
Several slight but statistically significant effects in organ weights were noted in rats exposed to 50 or 150 ppm PDC for 13 wk i.e. relative brain weight increased 8% and relative heart weight increased 6% in mid dose males, absolute brain weight decreased 3% in high dose females. A qualitative reduction in the amount of abdominal adipose tissue was also noted in some high dose males. These changes were considered of negligible toxicologcial relevance by the study authors (secondary to lower bwt).

Histopathology
Histopathological effects were confined to the upper respiratory tract. Very sight or slight degeneration of the olfactory mucosa in the anterior portion of the nasal cavity was noted for all rats exposed to 50 or 150 ppm PDC (no effect at 15 ppm). Very slight or slight hyperplasia of the respiratory mucosa was also present in the majority of rats (both sexes) exposed to 50 or 150 ppm PDC, with very slight hyperplasia detected in around one quarter of the low dose group. This hyperplasia was focally restricted to the anterior portion of the nasal tissues and considered by the study pathologist to be an adaptive, protective response. Chronic inflammation of nasal tissue was present in all groups, including controls, but was slightly more prevalent in high dose rats of both sexes.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Minimal toxicological effects were recorded in male and female F344 rats following whole body exposure to 0, 15, 50 or 150 ppm PDC for 13 wk. Treatment related effects were limited to a minor reduction in body weight (NOAEL = 15 ppm), and very slight hyplasia of the nasal respiratory epithelium considered to be an adaptive/protective response by the study authors (NOAEL of 15 ppm).

Reliability: (1) valid without restriction
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (183)

Type: Sub-chronic
Species: mouse **Sex:**
Strain: B6C3F1
Route of administration: inhalation
Exposure period: 13 wk
Frequency of treatment: 6 hr/d, 5 d/wk
Doses: 0, 15, 50 or 150 ppm (0, 0.068, 0.225 or 0.675 mg/l)
Control Group: yes, concurrent vehicle
NOAEL: = 150 ppm

Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female B6C3F1 mice (n = 10 per group, age 7-8 wk at start of treatment) were exposed whole body to 0, 15, 50 or 150 ppm PDC vapor (0, 0.068, 0.225 or 0.675 mg/l) 6 hr/d, 5

d/wk for 13 wk.

See previous record for details of test atmosphere generation, in-life observations, haematology (orbital sinus puncture at termination).

Necropsy
Mice were sacrificed on the day following the last exposure (no overnight fast). See previous record for further details.

Statistical methods
See previous record.

Result: IR analysis demonstrated that the mean concentration of PDC within the chamber (SD in brackets) was 0, 15(1), 50(3) or 151(3) ppm.

Clinical observations and body weight
No clinical signs or evidence of overt toxicity were recorded in any of the treated animals, while body weights were indistinguishable from those of the controls.

Haematology
RBC and HGB were slightly but significantly decreased (approx. 5%) in low and high dose male mice (no effect at 50 ppm, all treated females indistinguishable from controls). PCV was statistically significantly increased in low dose animals (no effect in mid and high dose groups). The authors concluded these findings were of doubtful toxicological relevance given the lack of a clear dose-response relationship and an absence of histopathological involvement in bone marrow or spleen. All other heamatological parameters were comparable between the control and treated animals.

Necropsy findings
Body weight and organ weights (relative and absolute) were unaffected by treatment.

Histopathology
No treatment related histopathological changes were present.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: No adverse treatment related changes were noted in male and female B6C3F1 mice following whole body exposure to to 0, 15, 50 or 150 ppm PDC for 13 wk (NOAEL = 150 ppm).

Reliability: (1) valid without restriction
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (183)

Type: Sub-chronic
Species: rabbit **Sex:** male/female
Strain: New Zealand white
Route of administration: inhalation
Exposure period: 13 wk
Frequency of treatment: 6 hr/d, 5 d/wk
Doses: 0, 150, 500 or 1000 ppm (0, 0.675, 2.25 or 4.5 mg/l)
Control Group: yes, concurrent vehicle
LOAEL: = 150 ppm

Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female NZW (n = 7 per group, age approx. 7 mo at start of treatment) were exposed whole body to 0, 150, 500 or 1000 ppm PDC vapor (0, 0.675, 2.25 or 4.5 mg/l) 6 hr/d, 5 d/wk for 13 wk.

See previous record for details of test atmosphere generation

Observations
Animals were examined after each exposure period for clinical signs or indications of overt toxicity.

Haematology
Haematological assessments (see previous record) were conducted on blood collected by venipuncture 2 wk prior to study termination. Additional blood samples were collected at necropsy and the analyses extended to include nucleated red blood cells and reticulocyte count.

Clinical chemistry
See previous record for details of parameters assessed.

Necropsy
Rabbits were sacrificed on the day following the last exposure (no overnight fast). See previous record for further details.

Statistical methods
See previous record.

Result: IR analysis demonstrated that the mean concentration of PDC within the chamber (SD in brackets) was 0, 151(3), 502(7) or 1003(8) ppm.

Clinical observations and body weight
No clinical signs or evidence of overt toxicity were recorded in any of the treated animals, while body weights were indistinguishable from those of the controls.

Haematology
Analysis of blood samples collected 2 wk prior to study termination showed that RBC were significantly decreased in rabbits exposed to 150 ppm (10% decrease, males only), 500 ppm (both sexes, approx. 15-20%) or 1000 ppm (both sexes, approx. 20-25%) PDC vapor. HGB was decreased (both sexes) in mid (10-13%) and high (14-16%) dose rabbits. PCV was decreased (both sexes) in mid (11-15%) and high (17%) dose rabbits. MCV and MCH increased (both sexes) in a non-significant but apparently dose-related manner.

Essentially similar changes in RBC, HGB and PCV were present in blood samples collected at study termination. In addition, the number of nucleated erythrocytes was non-significantly increased in males exposed to 1000 ppm PDC, while the percentage of reticulocytes (regenerative response) was increased significantly in mid (approx.

2-fold) and high (3-4 fold) dose animals of both sexes. MCV and MCH were again increased in all treated animals.

Overall, these findings were consistent with regenerative macrocytic normochromic anemia.

Clinical chemistry
No treatment related changes were recorded.

Necropsy findings
Absolute liver weights from mid and high dose males were significantly increased by approx. 25-30%, and relative liver weight significantly increased by approx. 20%. Supplemental information presented in the study report demonstrates that absolute liver weights values from treated animals (107.9 - 122.0 g) were within the historical range for control male rabbits from the laboratory conducting this study (93.8 - 130.3 g), while the controls (93.8 g) were at the lower limit of the historical data. The authors conclude that these liver weight changes were not indicative of a treatment related effect. No other organ weight changes or gross lesions were present.

Histopathology
Bone marrow hyperplasia (regenerative response) was present in some rabbits exposed to 500 or 1000 ppm PDC vapor (NOAEL = 150 ppm), with a qualitative increase in haemosiderin-laden macrophages noted in bone marrow from high dose animals. Minimal degeneration of olfactory epithelium occurred in nasal tissue from all groups, including the controls, however the prevalence in high dose males (5/7 affected, versus 2/7 controls) was considered suggestive of a treatment-related effect by the study authors (NOAEL = 500 ppm). No other treatment related histopathological changes were observed.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Minimal toxicological effects were recorded in male and female NZW rabbits following whole body exposure to 0, 150, 500 or 1000 ppm PDC for 13 wk. Treatment related, toxicologically significant changes were limited to alterations in red cell parameters (decreased RBC, HGB, PCV) in male rabbits exposed to 150-1000 PDC for 13 wk (LOAEL = 150 ppm), and in females exposed to 500 or 1000 ppm over the same period of time (NOAEL = 150 ppm). The overall pattern of changes was consistent with a regenerative macrocytic normochromic anemia. Minimal degeneration of olfactory epithelium in high dose males (NOAEL = 500 ppm; females unaffected) was also observed.

Reliability: (1) valid without restriction
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (183)

Species: rat **Sex:** no data
Strain: no data
Route of administration: inhalation
Exposure period: 2 - 5 days
Frequency of treatment: 7 hours/day
Doses: 10400 mg/m3
Control Group: no data specified

Method: other: Repeated Dose Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: Mortality: 5/20
The histopathologic evaluation of 3 surviving animals showed visceral congestion, centrilobular fatty degeneration in the liver with atrophic and necrotic changes, hemosiderosis in the spleen and myelosis and bronchitis with pneumonia. In addition, lipoid atrophy was found in the adrenal cortex; 20 animals/exposure group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (170)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: 5 and 10 days
Frequency of treatment: daily
Doses: 100, 250, 500 and 1000 mg/kg body weight/day
Control Group: yes, concurrent vehicle
LOAEL: = 100 mg/kg bw

Method: other: Repeated Dose Toxicity
Year: 1989
GLP: no data
Test substance: other TS: purity = 99 %

Remark: Depending on dosage, animal body weight was reduced (no specific information) and sedation was detected. The highest dose was given for 5 days resulting in a significant (p <= 0.05) increase of sorbitol dehydrogenase transferase reactivity and alanine aminotransferase reactivity as well as urea content in the blood. After 10 days, only increase of urea content persisted. Doses given above 100 mg/kg, after days 5 and 10, the content of microsomal cytochrom P-450 in the liver decreased significantly (p <= 0.05). After 5 days using >= 250 mg/kg, the non-protein-sulfhydryl-content in the liver was significantly (p <= 0.05) decreased (dose-related). After 10 days of dosing, only the group with highest dose adminstered showed a significant (p <= 0.05) reduction in NPSH. After days 5 and 10 using >= 250mg/kg, the non-protein-sulfhydryl-content in the kidney was significantly (p <= 0.05) increased. After 5 days of
treatment, histopathological changes were found only in the liver. Jaundice was diagnosed, characterized by necrosis of the centrilobular hepatocytes, inflammatory cell infiltration and proliferation of fibroblasts. The changes appeared in all animals treated with 1000 mg/kg. In the group tested with 250 and 500 mg/kg , less than 50% of the animals showed changes (no further information). 5 days later symptoms persisted only in the two groups receiving highest doses but in a less intensive form. After days 5 and 10 of dosing, a hemolytic anemia was diagnosed in the

kidney; 6 - 8 animals/dosage and control group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (184)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Doses: 100, 250, 500 and 750 mg/kg body weight/day
Control Group: yes, concurrent vehicle
LOAEL: = 100 mg/kg bw

Method: other: Repeated Dose Toxicity
Year: 1989
GLP: no data
Test substance: other TS: purity = 99 %

Remark: The body weight gain was decreased significantly (p <= 0.05) at concentrations >= 100 mg/kg (dose related). All animals of the 750 mg/kg dosage group died or were killed moribund after the first 2 weeks of treatment. Mortality in the 500 mg/kg dosage group was approximately 60 %. In the 750 mg/kg dosage group the following histopathological changes appeared: light hepatitis, hemosiderosis in the spleen, vacuolization of medulla, lipidosis of the renal cortex, reduced sperm count and appearance of degenerated spermatogonia in the epididymis. Doses of 1,2-dichloropropane induce hemolytic anemia. Animals treated with 250 and 500 mg/kg, showed significantly (p <= 0.05) decreased hemoglobin and hematocrit in serum; histopathologic examination showed hemosiderosis and hyperplasia of the erythropoietic elements in the spleen for most animals in all dosage groups.
Only animals from the 500 mg/kg dosage group showed histopathologic changes in the liver (periportal vacuolization and fibroplasia). Relative weight of liver and spleen in dosage groups 250 and 500 mg/kg and relative weight of kidney in dosage group 500 mg/kg were significantly (p <= 0.05) increased; 15 - 16 animals/dosage and control group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (184)

Species: rat **Sex:** male
Strain: Wistar
Route of administration: i.p.
Exposure period: 4 weeks
Frequency of treatment: 5 days/week
Doses: 10, 25, 50, 100, 250 and 500 mg/kg body weight/day
Control Group: yes, concurrent vehicle
LOAEL: <= 10 mg/kg bw

Method: other: Repeated Dose Toxicity

Year: 1988
GLP: no data
Test substance: other TS: purity = 97 %

Remark: One animal from the 500 mg/kg group died after injection number 15. After a 5-day treatment of 500 mg/kg, activity of glutathione-S-transferase in the liver was significantly ($p < 0.025$) increased and the activity of the angiotensin converting enzyme in the striated border of the proximal kidney tubuli was significantly ($p < 0.025$) decreased. After a 4-week treatment the following biological changes in the liver were observed: content of reduced glutahione (GSH) as well as the activity of glutahione-S-transferase >= 50 mg/kg significantly ($p < 0.025$) increased; cytochrome P-450 activity >= 250 mg/kg and the activity of aminopyridindesmethylase >= 100 mg/kg significantly ($p < 0.025$ and $p < 0.05$) decreased. In the renal cortex, the GSH content >= 250 mg/kg and activity of glutathione-S-transferase in the 500 mg/kg dosage group was significantly ($p < 0.05$) increased. The cytochrome P-450 activity was significantly ($p < 0.05$) decreased in the highest dosage group; the angiotensin converting enzyme activity in the striated border of the proximal renal tubuli was significantly ($p < 0.025$) decreased >= 100 mg/kg (dose related). The histopathological analysis during the dissection indicated specifically regenerative, hyperplastic changes >= 10 mg/kg after a 4-week treatment. In the kidney, the 4-week treatment of 1,2-dichloropropane resulted in a necrosis of striated border in the highest dosage groups as well as mesangial glomerular nephritis (dose related) with mesangial and sub-epithelial granular sedimentation >= 50 mg/kg; 5-10 animals per dosage and control group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (185) (174) (186)

Species: rabbit **Sex:** no data
Strain: no data
Route of administration: inhalation
Exposure period: 2 - 5 days
Frequency of treatment: 7 hours/day
Doses: 10400 mg/m3
Control Group: no data specified

Method: other: Repeated Dose Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: Mortality: 2/3.
The histopathologic evaluation of 3 surviving animals showed visceral congestion, centrilobular fatty degeneration in the liver with atrophic and necrotic changes, hemosiderosis in spleen and myelosis and bronchitis with focal pneumonia; 3 animals/exposure group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable

Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (170)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of administration: gavage
Exposure period: 13 days
Frequency of treatment: daily
Post exposure period: no
Doses: 250, 500 and 1000 mg/kg body weight/day
Control Group: yes, concurrent vehicle
LOAEL: <= 250 mg/kg bw

Method: other: Repeated Dose Toxicity
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: All rabbits in the two high dose groups and one rabbit in the 250 mg/kg-dose group died or were killed moribund during the test period. The animals of the high dose group, before dying, showed lethargy and ataxy. All treated animals showed a decreased gain of body weight. Necrosis of the liver was detected in all dead animals per above, given 500 and 1000 mg/kg. Some of these animals suffered light anemia and dilation of renal tubuli was prevelant; two animals/dosage and control group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (187)

Species: dog **Sex:** no data
Strain: no data
Route of administration: inhalation
Exposure period: up to 128 exposures
Frequency of treatment: 7 hours/day, 5 days/week
Post exposure period: no
Doses: 4400 mg/m3
Control Group: no data specified

Method: other: Repeated Dose Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: Mortality: 4/9.
During dosing period, 3 dogs died between exposure 27 and 28 and 1 dog died after exposure 96. Fatty degeneration of the liver and the convoluted renal tubuli was detected in all animals that died. In addition, one dog was diagnosed with centrilobular congestion including atrophy and necrosis in the liver cells and 2 dogs were diagnosed with fatty degeneration of the heart and lipoid atrophy in the renal cortex. One dog dying after 28 exposures was observed with congestion, atrophy and focal necrosis in zona reticularis of the adrenal gland. Some of the surviving 5 dogs were killed after 55 single exposures and the rest after 128

exposures. These 5 dogs showed no histopathological differences compared with the control group; 9 dogs/exposure group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (170)

Species: guinea pig **Sex:** no data
Strain: no data
Route of administration: inhalation
Exposure period: 5 days
Frequency of treatment: 7 hours/day
Doses: 10400 mg/m3
Control Group: no data specified

Method: other: Repeated Dose Toxicity
Year: 1946
GLP: no data
Test substance: no data

Remark: Whole-body exposure; mortality 11/16. Fatty degeneration of the liver was detected during the dissection. Multilobular and centrilobular congestion with atrophy and necrosis of liver cells was detected in 3 animals. Necrotic liver foci with infiltrated neutophils was diagnosed in 1 animal. An increased build up of a fatty degeneration in the kidneys and necrosis in the adrenal glands was observed. In addition the animals were suffering with hemosiderosis in the spleen and congestion in the lung; 16 animals/exposure group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (170)

Species: other: rat, guinea pig and dog **Sex:** male/female
Strain: no data
Route of administration: inhalation
Exposure period: 128 to 140 hours
Frequency of treatment: 7 hours/day, 5 days/week
Post exposure period: no data
Doses: 400 ppm
Control Group: yes
NOAEL: =
LOAEL: =

Method: other
Year: 1948
GLP: no
Test substance: no data

Result: Rats, guinea pigs and dogs received from 128 to 140 seven-hour inhalation exposures. No ill effects were observed that could be attributed to the exposures except for decreased weight gain in the rats. Histological examination showed no changes specifically attributable to 1,2-dichloropropane.

There was a heavy mortality rate among mice exposed to 400 ppm of 1,2-dichloropropane. Hepatomas were found in 3 animals of the susceptible C3H strain, which were histologically similar to mice repeatedly exposed to carbon tetrachloride.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
21-DEC-2004 (188)

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA98, TA1537, TA100 and TA1535
Concentration: 0 (DMSO), 33, 100, 333, 1000 and 2000 ug/plate
Cytotoxic Concentration: > 2000 ug/plate
Metabolic activation: with and without
Result: negative

Method: other: liquid preincubation method
Year: 1986
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: PDC was dissolved in DMSO and incubated with the tester strains in suspension culture for 20 min prior to the addition of soft agar and plating-out. Exogenous metabolic activation was provided by liver S-9 preparations from Arochlor-1254 induced rats and hamsters. Each concentration was tested in triplicate, and the entire study run twice.
Result: There was no increase in number of revertants in any of the tester strains either in the absence or presence of rat or hamster S-9 fraction.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: PDC was not mutagenic to Salmonella typhimurium TA98, TA1537, TA100 or TA1535 in the presence or absence of S-9.
Reliability: (2) valid with restrictions
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA1537, TA100 and TA1535
Concentration: 0 (DMSO), 31.5, 100, 315, 1000 and 3150 nl/plate
Cytotoxic Concentration: >3150 nl/plate
Metabolic activation: with and without
Result: negative

Method: other: Ames et al. (1975) Mut Res 31, 347 - 364.
Year: 1979
GLP: no
Test substance: no data

Method: PDC (aqueous, 31.5 - 3150 nl/plate) was tested using a plate incorporation method in two series of experiments in the presence or absence of S9 from Arochlor 1254-treated rats. There were two plates per concentration. Benzo(a)pyrene and MNNG were used as positive control substances in the absence

of S9, and benzo(a)pyrene, 2-aminoanthracene and 3MC as positive controls in the presence of S9.

In a third series of tests, mutagenicity of PDC (3.15 - 3150 nl/plate; +S9) was evaluated in the presence of glutathione supplementation (8 mg/plate).

Result: A satisfactory response was obtained with the positive control substances.

No mutagenic repsonse was obtained with PDC, both in the absence or presence of S9. Glutathione supplementation was without effect.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: PDC was not mutagenic to Salmonella typhimurium TA 98, TA 1537, TA 100 or TA 1535 when tested using a plate incorporation method in the presence or absence of S9.

Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (189)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA1537, TA100 and TA1535
Concentration: vapour exposure: 0.3 - 10 ml PDC placed in a 20 l dessicator and incubated with poured plates for 4 hr.
Cytotoxic Concentration: greater than maximum tested
Metabolic activation: with and without
Result: negative

Method: other: Ames et al. (1975) Mut Res 31, 347 - 364.
GLP: no
Test substance: no data

Method: Poured plates, containing tester strain, cofactors and with or without S9 fraction from Arochlor 1254-induced rats, were placed in a 20 l dessicator along with 0.3 - 10 ml PDC. Dichloroethane (3 ml) was used as positive control in the presence and absence of S9.

A third series of plates were supplemented with 8 mg glutathione.

After 4 hr incubation at 37 degrees C the plates were removed from the dessicator and incubated for a further 3 days in the dark.

Result: Dichloroethane was not mutagenic in the absence of S9 mix, but a clear positive response was obtained in TA 100 and TA 1535 in the presence of S9.

No mutagenic repsonse was obtained with PDC, both in the absence or presence of S9.

Glutathione supplementation was without effect.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: PDC vapour was not mutagenic to Salmonella typhimurium TA 98, TA 1537, TA 100 or TA 1535 when tested in a closed system in the presence or absence of S9.

Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific

principles, acceptable for assessment.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (189)

Type: Ames test

Test substance: as prescribed by 1.1 - 1.4

Remark: IARC summarises results obtained for 12 studies in Salmonella typhimurium tester stains, with or without exogenous activation.

Positive results were reported with tester strains TA100 and TA1535 both in the absence or presence of S9, of which some were the results from Hawthorne et al. (1983) that were not a two-fold increase.

Negative results were reported for tester strains TA98, TA100, TA1535, TA1537, TA1538 and TA1978 both in the absence and presence of S9.

Overall, 4 out of 13 results were positive results in the absence of S9, and 4 out of 13 (31%) were positive in the presence of S9.

This information is presented in more detail in Attachment 5.5.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 5.5.doc

Summary of mutagenicity findings for 1,2-dichloropropane in *Salmonella typhimurium* tester strains (adapted from IARC, 1999)

Salmonella tester strain	Result		Dose* µg/ml	Reference
	Without S9	With S9		
TA100	+	+	5000	De Lorenzo et al. (1977) Cancer Res 37, 1915-1917
	-	-	565	Stolzenberg and Hine (1980) Environ Mutagen 2, 59-66
	+	+	2900	Principe et al. (1981) J Sci Fd Agric 32, 826-832
	(+)[1]	-	5000	Haworth et al. (1983) Environ Mutagen 5, 1-142
TA1535	+	+	5000	De Lorenzo et al. (1977) Cancer Res 37, 1915-1917
	+	+	2900	Principe et al. (1981) J Sci Fd Agric 32, 826-832
	(+)[2]	-	5000	Haworth et al. (1983) Environ Mutagen 5, 1-142
TA1537	-	-	5800	Principe et al. (1981) J Sci Fd Agric 32, 826-832
	-	-	1666	Haworth et al. (1983) Environ Mutagen 5, 1-142
TA1538	-	-	5800	Principe et al. (1981) J Sci Fd Agric 32, 826-832
TA98	-	-	5800	Principe et al. (1981) J Sci Fd Agric 32, 826-832
	-	-	5000	Haworth et al. (1983) Environ Mutagen 5, 1-142
TA1978	-	-	25000	De Lorenzo et al. (1977) Cancer Res 37, 1915-1917

+ = positive result
- = negative

(+) = weak positive ([1] Maximum increase in two independent tests 44-80% of background at 1500-3333 ug/plate; [2] Maximum increase in two independent tests 56-75% of background at 1000-3333 ug/plate)
* Either lowest effective dose (for positive study) or highest ineffective dose (for negative study)

Reliability: (2) valid with restrictions
Data from handbook or collection of data.
Flag: Critical study for SIDS endpoint
21-DEC-2004 (190)

Type: Mouse lymphoma assay
System of testing: L5178Y
Concentration: 62.5-1000 nl/ml; 62.5-1000 nl/ml; 100-1000 nl/ml;
Cytotoxic Concentration: >800 nl/ml (above limit of solubility in test media)
Metabolic activation: without
Result: negative

Method: other: TK+/- Test
Year: 1991
GLP: no data
Test substance: no data

Remark: 1,2-Dichloropropane was not very toxic in the absence of rat S9 (except when the solubility limit was visibly exceeded ie 1000 nl/ml) and was evaluated by the authors as nonmutagenic to L5178Y cells.

The authors comment that three trials were performed because weak mutagenic activity was suggested by a 1.5-fold increase in MF for the highest soluble dose of 750 nl/ml in the second trial. The third trial, however, yielded no response for doses up to 800 nl/ml and confirmed the lack of response obtained in trial 1.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment.
02-MAR-2005 (191)

Type: Mouse lymphoma assay
System of testing: L5178Y
Concentration: 3.13-100 nl/ml; 10-80 nl/ml
Cytotoxic Concentration: 80 nl/ml
Metabolic activation: with
Result: positive

Method: other: TK+/- Test
Year: 1988
GLP: no data
Test substance: no data

Remark: The mutagenic potential of PDC in the presence of male rat Arochlor 1254-induced S9 was investigated in two trials using concentration ranges of 0-100 nl/ml in the first and 0-80 nl/ml in the second.

When discussing these results, the authors comment that the first trial did not include a toxic treatment suitable for

analysis, but that the highest assayed dose of 50 nl/ml (65% relative total growth; RTG) induced a 2.3-fold increase in mutation frequency. The mutant colony count was clearly elevated. The next highest dose of 100 nl/ml was lethal.

A different batch of S9, which appeared to be more active, was used in the second trial. A dose-related increase in MF was obtained over the 10-80 nl/ml dose range, with 80 nl/ml being highly toxic (6% RTG) and causing a 10-fold increase in MF.

They concluded that S9 activation was clearly therefore essential to the mutagenic activity of 1,2-dichloropropane. The increase in mutant frequency was due primarily to the induction of small colony mutants.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment.

25-OCT-2004 (191)

Type: Chromosomal aberration test
System of testing: CHO cells
Concentration: -S9: 0 (DMSO), 1180, 1370 and 1580 ug/ml; +S9: 0 (DMSO), 460, 660 and 950 ug/ml
Metabolic activation: with and without
Result: positive

Method: other: standard NTP study design
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: In the absence of S9 CHO cells were incubated with serial dilutions of PDC (up to 1580 ug/ml) or vehicle (DMSO) for 8-10 hr at 37 degrees C. Cells were then washed, and fresh medium containing colcemid (0.1 ug/ml) added. After a further 2-3 hr of incubation, cells were harvested and stained with Giemsa, and 100 cells per dose scored 'blind' for chromosomal aberrations.

For tests in the presence of metabolic activation, cells were incubated with PDC (up to 950 ug/ml or vehicle) and rat S9 (Arochlor 1254-induced) for 2hr. Cells were then washed and incubated with fresh medium for a further 8-10 hr prior to processing as described above.

It is unclear if there was any independent repeat of the test.

Mitomycin C (0.125 ug/ml, no S9) and cyclophosphamide (50 ug/ml, plus S9) were used a positive controls.

No statistical analysis was applied to the results.

Result: Results are summarised in Attachment 5.5b.

The number of chromosomal aberrations/cell was increased 5 or >16 fold after incubation with 1370 or 1580 ug PDC/ml in the absence of S9. No clastogenic response was detected at 1180 ug/ml.

In the presence of S9, the number of aberrations/cell was increased 4 or >4 fold after incubation with 660 or 950 ug PDC/ml. No clastogenic effect was detected at 460 ug/ml.

A satisfactory response was obtained with the positive control substances.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 5.5b.doc

Cytogenetic effects of PDC in CHO cells, from NTP (1986)

Chromosome aberrations			
-S9		**+S9**	
Control (DMSO)	3	Control (DMSO)	>4
1180 ug/ml	3	460 ug/ml	4
1370 ug/ml	16	660 ug/ml	17
1580 ug/ml	>47	950 ug/ml	>16
Mitomycin c	>102	Cyclophosphamide	46

Conclusion: Under the conditions of the test, PDC increased the occurence of chromosomal aberrations in CHO cells both in the absence and in the presence of rat S9.
Reliability: (2) valid with restrictions
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (182)

Type: Sister chromatid exchange assay
System of testing: CHO cells
Concentration: 0 (DMSO), 112.7, 376.0 and 1127.0 ug/ml
Metabolic activation: with and without
Result: positive

Method: other: standard NTP study design
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: In the absence of S9 CHO cells were incubated with serial dilutions of PDC (up to 1127.0 ug/ml) or vehicle (DMSO) for 2hr at 37 degrees C, followed by addition of BrdU (10 uM) and incubation for a further 24 hr. Cells were then washed, fresh medium containing BrdU and colcemide (0.1 ug/ml) added and the incubation continued for another 2-3 hr. Samples were then fixed, stained with Giemsa, and fifty cells per dose from the top three dose levels (i.e. 112.7, 376.0 or 1127.0 ug PDC/ml) evaluated for SCEs. No further scoring was carried out if these results were clearly negative or positive. Scoring was carried out 'blind'.

For tests in the presence of metabolic activation, rat S9 (Arochlor 1254-induced) was added during the inital 2hr incubation with PDC or vehicle. Cells were then processed as described above.

Additional tests were performed to determine if PDC caused cell cycle delay, however no results are reported.

It is unclear if there was any independent repeat of the test.

Mitomycin C (0.01 ug/ml, no S9) and cyclophosphamide (1.5 ug/ml, plus S9) were used a positive controls.

No statistical analysis was applied to the results.

Result: Results are summarised in Attachment 5.5a.
The number of SCE/cell was increased 2 or 3.5 fold after incubation with 376 or 1127 ug PDC/ml in the absence of S9.

In the presence of S9, SCE/cell were increased 2 or 2.5 fold under these same exposure conditions.

A satisfactory response was obtained with the positive control substances.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Attached doc.: Attachment 5.5a.doc

Cytogenetic effects of PDC in CHO cells, from NTP (1986)

Sister Chromatid Exchanges			
-S9		**+S9**	
Control (DMSO)	10.1	Control (DMSO)	9.1
112.7 ug/ml	12.6	112.7 ug/ml	10.7
376.0 ug/ml	21.2	376.0 ug/ml	18.4
1127.0 ug/ml	36.2	1127.0 ug/ml	22.1
Mitomycin c	36.6	Cyclophosphamide	27.5

Conclusion: Under the conditions of the test, PDC increased the occurence of SCEs in CHO cells both in the absence and in the presence of rat S9.

Reliability: (2) valid with restrictions
Comparable to guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (182)

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA100, TA1537, TA98
Concentration: 31.5-3150 nl/plate in Standard plate test, 0.3-10 ml/20l desiccator
Metabolic activation: with and without
Result: negative

Method: other
Year: 1979
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: no additional information
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (192)

Type: Ames test

System of testing: Salmonella typhimurium TA 100, TA 1535
Concentration: 11500 ug/plate
Metabolic activation: with and without
Result: positive

Method: other: Ames Test
Year: 1975
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 1537, TA 1538
Concentration: 33 - 2000 ug/plate
Metabolic activation: with and without
Result: negative

Method: other: Ames Test
Year: 1975
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: Ames test
System of testing: Salmonella typhimurium TA 100, TA 1535
Concentration: 10000 - 50000 ug/plate
Metabolic activation: with and without
Result: positive

Method: other: Ames Test
Year: 1975
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (194)

Type: Ames test
System of testing: Salmonella typhimurium TA 100
Concentration: 113 - 11130 ug/plate
Metabolic activation: with and without
Result: negative

Method: other: Ames Test
Year: 1975
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (195)

Type: Escherichia coli reverse mutation assay
System of testing: Escherichia coli WP2s
Concentration: 7.05 - 7224 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: Prophage Lambda Induction Test
Year: 1990
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (196)

Type: DNA damage and repair assay
System of testing: Salmonella typhimurium TA 1535
Concentration: 476 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: Umu-Test
Year: 1985
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (197)

Type: Sister chromatid exchange assay
System of testing: V79 cells
Concentration: 11.3 - 113 ug/ml
Metabolic activation: with and without
Result: positive

Method: other: SCE-Test
Year: 1987
GLP: no data
Test substance: other TS: purity > 99 %

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (198)

Type: DNA damage and repair assay
System of testing: Escherichia coli PQ37

Concentration: <= 2700 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: SOS-Chromotest
Year: 1985
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (199)

Type: Bacterial gene mutation assay
System of testing: Streptomyces coelicolor
Concentration: 2315 - 115600 ug/plate
Metabolic activation: without
Result: negative

Method: other: Plate Incorporation Test
Year: 1978
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: Bacterial gene mutation assay
System of testing: Streptomyces coelicolor
Concentration: 115600 ug/plate
Metabolic activation: without
Result: negative

Method: other: Spot Test
Year: 1978
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: other: Gene mutation in Aspergillus nidulans
System of testing: Aspergillus nidulans haploid strain 35
Concentration: 115600 - 462400 ug/plate
Metabolic activation: without
Result: positive

Method: other: Plate Incorporation Test
Year: 1980
GLP: no data
Test substance: no data

Remark: 8-Azaguanine resistance
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: other: Gene mutation in Aspergillus nidulans
System of testing: Aspergillus nidulans haploid strain 35
Concentration: 346800 ug/plate
Metabolic activation: without
Result: positive

Method: other: Spot Test
Year: 1980
GLP: no data
Test substance: no data

Remark: 8-Azaguanine resistance
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (193)

Type: Unscheduled DNA synthesis
System of testing: Human lymphocytes
Concentration: 1130 - 113000 ug/ml
Metabolic activation: with and without
Result: negative

Method: other: DNA Damage and Repair/Unscheduled DNA-Synthesis
Year: 1983
GLP: no data
Test substance: no data

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (200)

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA100, TA1537, TA98
Concentration: 20-5000 µg/plate in Standard plate test, 3000-6000 µl/30l desiccator in the modified test
Metabolic activation: with and without
Result: positive

Method: other: Standard plate test and desiccator-Test (modified test)
Year: 1985
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: In the standard plate test only a light mutagen effect was found, in the desiccator-test the substance was clearly positive; no additional information.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to

determine reliability.
26-OCT-2004 (201)

Type: DNA damage and repair assay
System of testing: E. coli W3110/polA+, p3478/polA-
Concentration: 2-20 µl/plate
Metabolic activation: with and without
Result: negative

Method: other: according to Slater et al., J Bacteriol, 89, 1354-69
Year: 1971
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: no additional information
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (202)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA1537, TA100 and TA1535
Concentration: 10-10000 ug/plate; 100-1500 ug/plate
Metabolic activation: with and without
Result: ambiguous

Year: 1983
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: The mutagenic potential of 1,2-dichloropropane was investigated in two laboratories (Case Western Reserve, CWR; EG&G Mason, EGG) using a preincubation protocol. Hepatic S-9 was prepared from male SD rats (RL) and male Syrian hamster after induction with Arochlor 1254.
The report notes that results were interpreted in an ad hoc manner by each testing laboratory and by NTP personnel. The publication describes that a positive result was indicated by a "reproducible, dose-related increase, whether it be two-fold over background or not. "Statistical analysis was applied subsequently to data considered positive.

2-Aminoanthracene (all strains, plus rat and hamster S9), 4-nitro-o-phenylenediamine (TA98, -S9), sodium azide (TA100 and TA1535, -S9) and 9-aminoacridine (TA1537, -S9) were used as positive control.
Remark: Although the number of revertants was increased in TA1535 and TA100 following treatment with PDC in the absence of S9, it is clear that the magnitude of this effect was always less than two-fold background.

Maximal increase in TA1535 over control:
56% at 1000 ug/plate (lab CWR)
75% at 3333 ug/plate (lab EEG)

Maximal increase in TA100 over control:
44% at 3333 ug/plate (lab CWR)
80% at 1500 ug/plate (lab EEG)

The results were presented in the publication summary table as positive based on the author's definition (see above in Method) including results below an 2-fold increase.

Result: No mutagenic activity was reported by either laboratory in TA98 or TA1537 at dose levels up to 3,333 ug/plate in the presence or absence of either source of S9.

PDC was without effect on the number of revertants recorded by either laboratory when tested using TA98 or TA1537 in the presence of rat or hamster S9.

In the absence of S9, an apparent weak dose-response relationship was observed in TA1535:

	CWR	EGG
0 (DMSO)	16	25
100	--	24
333	--	31
750	--	37
1,000	20	39
1,500	--	33
1,667	26	--
3,333	28	--
6,667	18	--
10,000	10	--

In the absence of S9, an apparent weak dose-response relationship was observed in TA100:

	CWR	EGG
0 (DMSO)	172	123
100	---	107
333	---	141
750	---	154
1,000	197	161
1,500	---	222
1,667	219	---
3,333	247	---
6,667	221	---
10,000	232	---

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Test substance: Described as 'practical grade', purity not specified.
Reliability: (2) valid with restrictions
10-JAN-2006 (203)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse **Sex:** male
Strain: CD-1
Route of admin.: gavage
Exposure period: 48 hr
Doses: 0, 150, 300 or 600 mg/kg bwt/d
Result: negative

Method: EPA OPPTS 870.5395
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Range-finding Test:
Selection of the high-dose level for the definitive study was base upon results from a range-finding test where male and female mice (4/group) were administered up to 2000 mg/kg/day 1,2 dichloropropane by oral gavage in corn oil on two consecutive days. The animals were observed for 72 hr after the second dose, and decedents were subject to necropsy in an effort to determine the cause of death. Substantial drops in body temperature occurred 2 hrs after dosing in animals receiving 1000 mg/kg/day and higher doses and all mice at these doses died prior to the end of the observation period.

Micronucleus Test:
Groups of six male CD-1 mice (approximately 32g, 9 weeks old) were given PDC (0, 150, 300, and 600 mg/kg) by oral gavage in corn oil on two consecutive days. Clinical observations and body temperature were monitored prior to dosing, 2 and 5 hrs post dosing and prior to sacrifice. Only males were used in this assay since there was no substantial difference in toxicity between sexes in the range-finding test.
Cyclophosphamide (120 mg/kg bwt, gavage, approx. 24 hr before sacrifice) was used as positive control substance.

Animals (6/dose) were sacrificed 24 hours after the second treatment, and femoral bone marrow collected to evaluate the incidence of micronuclei (MN) in polychromatic erythrocytes (2000 PCE/animal). The proportion of PCE among erythrocytes in the bone marrow was estimated by examining 200 erythrocytes/animal.

Statistics
The raw data on the counts of MN-PCE for each animal were first transformed by adding one (1) to each count and then taking the natural log of the adjusted number. The transformed MN-PCE data and the data on percent PCE were analyzed separately by one-way ANOVA (Winer, B. J. (1971), Statistical Principles in Experimental Design (2nd Edition), McGraw-Hill, New York, New York). Pairwise comparisons of treated vs. control groups were done, if the dose effect was significant, by Dunnett's t-test, one-sided (upper) for MN-PCE and two-sided for the percent PCE (Winer 1971). Linear dose-related trend tests were performed only if any of the pairwise comparisons yielded significant differences. The alpha level at which all tests were conducted was 0.05.

Remark: Section 5.0 (Toxicokinetics) demonstrates widespread distribution of PDC within the body, confirming contact with the target tissue in this study.

Result: All animals survived until the end of the observation period. Incoordination was observed in one mouse from the high-dose group. A uniform drop in body temperature (approx. 2°C) occurred 2 hrs post-dosing in the high-dose animals.

There was no statistically significant increase in the frequencies of MN-PCE in groups treated with PDC when compared to the negative controls. In contrast, a significant increase in the frequency of MN-PCE was recorded

in the positive control group.

The mean proportion of PCE among bone marrow erythrocytes (200/animal) was unaffected by exposure to the test material while the positive control treatment significantly reduced this value.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Conclusion: 1,2 dichloropropane was negative for the induction of micronuclei in this test system under the experimental conditions used.
Reliability: (1) valid without restriction
GLP guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (204)

Type: Dominant lethal assay
Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: drinking water
Exposure period: 14 wk
Doses: 0, 0.024%, 0.10% or 0.24% (equivalent to 0, 28, 91 or 162 mg/kg bwt/d)
Result: negative

Method: other: 40 CFR 789.4700
Year: 1989
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
PDC was administered in drinking water (0, 0.024%, 0.10% or 0.24%) to groups of 30 male SD rats (age 4 wk) for at least 13 wk as part of the breeding phase of a reproduction study (reported in Section 5.8.3). Treatment then ceased, and 2 days later each male was co-housed with two naive females/wk for 2 wk.

The females were sacrificed by carbon dioxide inhalation approx. 14 days from the middle of their respective breeding period, and the numbers of corporea lutea, implantations and resorptions were recorded. No separate classification of early or late resorptions was performed. The uteri of apparently non-pregnant animals were stained with sodium sulphide solution (10%) and examined for evidence of early resorption sites.

A positive control group of 30 males received cyclophosphamide (100 mg/kg bwt in saline, by gavage) 48 hr prior to mating.

GC analysis showed that the test material was 99.9% pure. Stability testing demonstrated no degradation of aqueous solutions of PDC over 8 days. Based on these findings the experimental solutions were mixed and changed at least once per week, and analysed (GC) on at least 3 occasions prior to mating.

Statistics
Body weights were evaluated using Bartlett's test for equality of variances, followed by parametric or

non-parametric ANOVA. If results of the ANOVA were positive, a Dunnett's test or Wilcoxon Rank-Sum test was performed. Fertility indices were analysed by the Fisher exact probability test. The numbers of corporea lutea were analysed using non-parametric ANOVA followed by the Wilcoxon Rank-Sum test. Pre-implantation losses and resorption rates were analysed by the Wilcoxon test.

Interpretation of findings
Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological and pathological findings. This appears scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study.

Result:

General
Analysis of drinking water showed that the achieved concentration was 88%, 98% and 100% of nominal for the low, mid and high exposure groups, respectively (mean of 3 determinations).

In-life observations
There were no significant clinical effects noted in any treatment group during the in-life phase, however two animals from the low dose group died during the pre-breeding phase (test days 56 and 101; deaths ascribed to renal failure unrelated to treatment). Body weights for the high dose males were significantly decreased from day 8 of the study, while values for mid-dose animals were numerically (but not significantly) lower than control. Water consumption was decreased in a treatment-related manner (decreased by approx. 40-50%, 22% and 10% for the high, mid and low dose groups, respectively), and food intake lowered in high dose animals during the first week of the test. Seven of the 30 positive control group died, and one was sacrificed in a moribund state, during the breeding phase. Body weights and food and water consumption for these cyclophosphamide-treated animals were comparable to control values.

Received dose
Based upon body weight and water intake data, weekly average received doses were calculated as 0, 28.0, 90.7 and 162.1 mg/kg bwt/day for the 0%, 0.024%, 0.10% and 0.24% groups, respectively.

Mating and fertility indices
Mating performance and conception indices among treated males was comparable to control, ranging from 96.4% to 100%. These fertility parameters for cyclophosphamide-treated males were decreased significantly.

The number of corpora lutea from females mated with low and high dose was significantly increased during the first week of breeding, while the number of implantations for the second week of breeding was significantly lower in females mated with mid dose males. These differences appear

consistent with normal biological variabiliy rather than any treatment-related effect. The number of pre-implantation losses was significantly higher in the low and high dose groups during the first week of treatment, however the values were essentially identical to the rate of pre-implantation loss observed in controls during the second week and therefore appeared unrelated to treatment. Similarly, resorption rates among these same treatment groups were significantly higher than control, but values from the second week of mating were similar to controls. Further details are presented in Attachment 5.6a.

Litter sizes, number of corporea lutea and number of implantations in the positive control group were significantly lower than control values, with a 2-fold increase in pre-implantation loss during the second week of breeding, and a 10-fold increase in resorption rates during both phases of mating.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Attached doc.: Attachment 5.6a.doc

Pre-implantation losses and resorption rates, from Hanley et al., 1989

	PDC (%)				Cyclophosphamide (100 mg/kg bwt)
	0	0.024	0.10	0.24	
Week 1					
pre-implantation loss (%)	4.5 ± 6.6	12.2 ± 11.8 *	6.2 ± 8.4	11.9 ± 11.2 *	11.4 ± 12.9 *
Resorption rate (%)					
- fetuses	3.6 (28/783)	5.8 (45/780) *	4.3 (33/775)	7.6 (59/775) *	28.8 (172/597) *
- litters	48.3 (14/29)	85.5 (23/27) *	69.0 (20/29)	82.1 (23/28) *	91.3 (21/23) *
Week 2					
pre-implantation loss (%)	11.7 ± 1.5	11.5 ± 9.7	13.0 ± 9.5	12.1 ± 8.8	23.1 ± 14.1 *
Resorption rate (%)					
- fetuses	5.4 (47/871)	3.0 (24/796)	2.2 (18/818)	8.1 (74/909)	56.8 (188/331) *
- litters	79.3 (23/29)	53.6 (15/28)	50.0 (15/30)	76.7 (23/30)	100 (16/16) *

Values calculated using the male as the experimental unit, and presented as mean or mean ± SD, as appropriate.

* statistically different from control, alpha = 0.05.

Conclusion: PDC was not mutagenic at doses up to 0.24% in drinking water (162 mg/kg bwt/day) when administered to male SD rats for 14 wk.
Reliability: (1) valid without restriction
GLP guideline study.
Flag: Critical study for SIDS endpoint
25-OCT-2004 (205)

Type: Drosophila SLRL test
Species: Drosophila melanogaster **Sex:** no data
Strain: no data

Route of admin.: inhalation
Exposure period: 4 hours
Doses: 33840 ug/m3

Method: other: Sex-linked Recessive Lethal Test in Drosophila melanogaster
Year: 1984
GLP: no data
Test substance: no data

Result: negative
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (206)

Type: Somatic mutation assay
Species: rat **Sex:** no data
Strain: no data
Route of admin.: inhalation
Exposure period: 3 days
Doses: 2200 mg/m3

Method: other: Aneuploidy Test
Year: 1977
GLP: no data
Test substance: no data

Result: positive
The number of mononuclear and binuclear hepatocytes containing polyploid nuclei (8 and 16 times chromosomes/cell) increased compared to the control group.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.
26-OCT-2004 (207)

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: gavage
Exposure period: 103 wk
Frequency of treatment: 5 d/wk
Doses: males 0, 62 or 125 mg/kg bwt/d; females 0, 125 or 250 mg/kg bwt/d
Control Group: yes, concurrent vehicle

Method: other: standard NTP gavage study
Year: 1986
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female F344/N rats (4-6 wk old) were purchased from a commercial supplier, quarantined for 3 wk then randomly

assiged to one control and two treatment groups (n = 50/sex/group). Males were treated with 0 (corn oil), 62 or 125 mg PDC/kg bwt/d, 5 d/wk for 103 wk by gavage. Females received 0, 125 or 250 mg/kg bwt/d over the same period. The dosing volume was 3 ml/kg bwt/d (hence stock dosing solution concentrations were 21 mg/ml, 42 mg/ml and 83 mg/ml for the 62, 125 and 250 mg/kg bwt treatments). Dosing solutions were stored at 0-5 degrees C in dark glass bottles for up to 10 days.

Test sample, stability and achieved concentration
Reagent grade PDC was used, with a purity of 99.4% (GC analysis). Toluene (0.24%) was identified as an impurity (GC/MS). GC-FID analysis demonstrated that 5.7% PDC in corn oil was stable at 25 degrees C for 7 days (recovery = 100% +/- 4%). Duplicate aliquots of the dosing solutions were analysed by GC-FID on 15 occasions during the study. Overall mean recoveries were 95%, 99% and 100% for the 21, 42 and 83 mg/ml solutions, respectively.

Observations
All animals were observed twice daily for signs of morbidity or mortality. Body weights were recorded weekly for the first 13 wk, then monthly thereafter. Moribund animals and all animals that survived to the end of the study were killed and necropsied. Thirty-one major tissues were examined, sampled and processed for histopathological examination.

Histopathological findings
Tissue slides, animal data and summary records were sent to a quality assurance laboratory for independent verification of the diagnoses of the study pathologist. All tumor diagnoses, target tissues and tissues from a randomly-selected 10% of the animals were subject to this assessment. Slides from all target tissues, plus those where the study pathologist and independent pathologist disagreed, were sent for further independent evaluation by a panel of NTP pathologists. The reported findings therefore represent a
consensus from these various experts.

Statistical methods
Survival probabilities were estimated using Kaplan-Meir plots, and any treatment-related effect on survival analysed using the method of Cox. Analysis of tumor incidence data used Mantel and Haenszel contingency tables, and included pair-wise comparisons of low or high dose data versus control incidence plus an analysis of overall dose-response trends. Two methods were applied to animals dying before the end of the study. The first (life table analysis) assumed that all tumors of a given type were 'fatal' ie that they directly or indirectly were responsible for the death of the animal. Using this approach the proportion of tumor-bearing animals in the test and control groups were compared every time an animal died of a tumor of interest. The second method (incidental analysis) assume that all tumors observed before 103 wk were 'incidental', and the proportion of animals with tumors compared at 0-52 wk, 53-78 wk, 79-92 wk, wk 93-wk before terminal kill and the terminal kill. The

Fisher exact test for pairwise comparisons and the Cochoran-Armitage linear trend test for dose-response effects were applied to the tumor data.

Remark: Based on tumor findings, NTP concluded that there was no evidence for the carcinogenicity of PDC in male rats, while in females treated with 250 mg/kg bwt/d for 103 wk NTP concluded there was equivocal evidence of an effect based upon a marginal increase in the incidence of mammary adenocarcinomas concurrent with decreased survival and reduced body weight gain.

A historical incidence of 2% (3/150) was reported for the laboratory conducting this study, with an overall historical incidence of 1.2% (11/895)

Reduced survival and reduced body weight could indicate that treatments exceeded the Maximum Tolerated Dose in female rats.

Result: Body weight and clinical signs
Treated animals showed a dose-related reduction in body weight. Final body weights were approx. 5% lower than control for low dose animals, and 14% and 24% lower then control in the high dose male and female groups, respectively. (Female body weight was decreased by >20% from wk 76 of the study.) No clinical signs are described.

Survival
The survival of high dose females (250 mg/kg bwt/d) was significantly (P<0.001) below that of the low dose females and controls (32%, 86% and 74% survival to the end of the study). Mortality and morbidity were especially marked at wk 94 of the study. Survival in males was comparable for all groups (78%, 84% and 82% alive at wk 103 for the control, 62 mg/kg bwt/d and 125 mg/kg bwt/d groups, respectively).

Tumor pathology
Because of reduced survival in high dose female rats, statistical procedures that adjust for intercurrent mortality (life table and incidental tumor tests) were regarded as more meaningful than the 'unadjusted' analysis.

A quantitative increased tumor incidence in one or both treatment groups relative to control, or a positive trend in the absence of any statistically significant difference between the treated and control groups, was seen for the following tissues and tumor types:

* mammary gland
mammary gland hyperplasia was increased, and there was a positive trend for mammary adenocarcinoma (adjusted rates: 2,7%, 4.7%, 26.7%; significantly increased in high dose group), both in females only; the overall incidence of fibroadenomas showed a negative trend in females. Tumor incidence in the high dose group was strongly influenced by findings in 4 of 16 animals that survived to the end of the study. A historical incidence of 2% (3/150) was reported for the laboratory conducting this study, with an overall historical incidence of 1.2% (11/895).

* uterus

enometrial stromal polyps occurred with a significant positive trend, although the incidence in the individual treatment groups was not increased relative to control.

* thyroid
follicluar cell carcinoma were found in two low dose females (but not in control or high dose females) at study termination; historic range 0.2-0.7%.

* stomach or forestomach
a non-significant increase in squamous cell papillomas was found in two high dose females (none in control); historic range 0-0.3%.

* pancreas
islet cell carcinomas occurred with a positive trend in males, however the incidence of adenomas was greatest in the control group and the combined incidence (adenoma + carcinomas) was not different between the groups.

* pituitary
while the incidence of adenomas was significantly increased in low dose females, the survival-adjusted incidence was unremarkable; the incidence of pituitary carcinomas was greatest in control females; the incidence of combined (adenomas + carcinomas) was not increased significantly.

* adrenal glands
pheochromocytomas showed a negative trend in males, and there was no difference in the incidence in combined pheochromocytoma + malignant pheochromocytoma).

No tumors were present in liver, a tissue showing signs of non-neoplastic changes (see above).

Note: Significant increases were observed in virus antibody titers. The report notes that the relationship between these increases and occurrence of non-neoplastic- and neoplastic changes is unclear.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: NTP concluded that under the conditions of this study there was no evidence that PDC was a carcinogen in male rats treated by gavage at doses up to 125 mg/kd bwt/d or 250 mg/kg bwt/d, respectively, for up to 103 wk. There was equivocal evidence of an increase in mammary tumors in high dose females, but no other tissues were affected.

Reliability: (1) valid without restriction
Comparable to guideline study, with restrictions.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (182)

Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of administration: gavage
Exposure period: 103 wk
Frequency of treatment: 5 d/wk
Doses: 0, 125 or 250 mg/kg bwt/d
Control Group: yes, concurrent vehicle

Method: other: standard NTP gavage study

GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female B6C3F1 mice (4-6 wk old) were purchased from a commercial supplier, quarantined for 3 wk then randomly assiged to one control and two treatment groups (n = 50/sex/group). They were given 0, 125 or 250 mg PDC/kg bwt/d 5 d/wk for 103 wk by gavage. The dosing volume was 3 ml/kg bwt/d (hence stock dosing solution concentrations were 21 mg/ml, 42 mg/ml and 83 mg/ml for the 62, 125 and 250 mg/kg bwt treatments). Dosing solutions were stored at 0-5 degrees C in dark glass bottles for up to 10 days.

Test sample, stability and achieved concentration
Reagent grade PDC was used, with a purity of 99.4% (GC analysis). Toluene (0.24%) was identified as an impurity (GC/MS). GC-FID analysis demonstrated that 5.7% PDC in corn oil was stable at 25 degrees C for 7 days (recovery = 100% +/- 4%). Duplicate aliquots of the dosing solutions were analysed by GC-FID on 15 occasions during the study. Overall mean recoveries were 95%, 99% and 100% for the 21, 42 and 83 mg/ml solutions, respectively.

Observations
All animals were observed twice daily for signs of morbidity or mortality. Body weights were recorded weekly for the first 13wk, then monthly thereafter. Moribund animals and all animals that survived to the end of the study were killed and necropsied. Thirty-two major tissues were examined, sampled and processed for histopathological examination.

Histopathological findings
Tissue slides, animal data and summary records were sent to a quality assurance laboratory for independent verification of the diagnoses of the study pathologist. All tumor diagnoses, target tissues and tissues from a randomly-selected 10% of the animals were subject to this assessment. Slides from all target tissues, plus those where the study pathologist and independent pathologist disagreed, were sent for further independent evaluation by a panel of NTP pathologists. The reported findings therefore represent a
consensus from these various experts.
Statistical methods
Survival probabilities were estimated using Kaplan-Meir plots, and any treatment-related effect on survival analysed using the method of Cox. Analysis of tumor incidence data used Mantel and Haenszel contingency tables, and included pair-wise comparisons of low or high dose data versus control incidence plus an analysis of overall dose-response trends. Two methods were applied to animals dying before the end of the study. The first (life table analysis) assumed that all tumors of a given type were 'fatal' ie that they directly or indirectly were responsible for the death of the animal. Using this approach the proportion of tumor-bearing animals in the test and control groups were compared every time an animal died of a tumor of interest. The second method (incidental analysis) assume that all tumors observed

before 103 wk were 'incidental', and the proportion of animals with tumors compared at 0-52 wk, 53-78 wk, 79-92 wk, wk 93-wk before terminal kill and the terminal kill. The Fisher exact test for pairwise comparisons and the Cochoran-Armitage linear trend test for dose-response effects were applied to the tumor data.

Remark: The liver was the principal target for PDC toxicity in the mouse, with hepatocytomegaly and hepatic focal necrosis seen in male mice only. It was also the key site for tumor formation.

Hepatocellular adenoma is a common finding in control B6C3F1 mice. Historic control data for this lesion in NTP studies conducted to 1995 (corn oil gavage, 16 studies) returned an incidence of 267/813 or 33% in males, with a range of 14-58%; equivalent values for females were 111/809 = 14%, with a range of 2-28% (Source: Analytical Services Inc. (1995) Tumor Incidence in Control Animals by Route and Vehicle of Administrtaion: B6C3F1 Mice. prepared for NIEHS, 6 June 1995).

Comparison of this historic control information with findings from the NTP leads to the following conclusions:
* The control incidence of hepatocellular adenoma for male (20%) and female (3%) mice from this NTP study was markedly lower than the mean historic incidence (33% in males; 14% in females);
* The incidence of hepatocellular adenoma in high dose males (45%) was within the spontaneous range (14-58%);
* The incidence of hepatocellular adenoma in low- (17%) and high dose (19%) female mice was also within the spontaneous range (2-28%);
* Liver tumor incidence in both sexes appeared non-linear when related to received dose.

Result: Body weight and clinical signs
Mean body weights of treated and vehicle control animals were comparable, and no compound-related clinical signs were noted.

Survival
The survival of high dose females (250 mg/kg bwt/d) was significantly ($P<0.035$) less than that of the low dose females and controls, with 70%, 58% and 52% of the control, low and high dose animals surviving to termination. Survival in males was comparable for all groups (70%, 66% and 70% alive at wk 103 for the control, 125 mg/kg bwt/d and 250 mg/kg bwt/d groups, respectively). The report notes that the lowered survival in female mice was related to an increased incidence of reproductive tract infections in animals which died before the end of the study (45% of controls affected versus 64% of both the low and high dose females that died during the study).

Non-tumor pathology
Hepatocytomegaly (6%, 10% and 30% for control, low dose and high dose animals, respectively) and hepatic focal necrosis (4%, 10% and 20%) were seen in male mice only. Acanthosis of the surface epithelium of the forestomach occurred at increased incidence in high dose males (0%, 0%, 4%) and both groups of treated females (0%, 10%, 8%). Suppurative

inflammation (affecting ovary, uterus or multiple organs) was found in 5/11 control, 9/14 low dose and 14/22 high dose females that died before the end of the study.

Tumor pathology
Tumors were found in the following tissues, although the increase was not always statistically significant and/or dose-related:

* liver
There was a positive trend for liver adenomas in male (20%, 29%, 45%, adjusted for intercurrent mortality) and female (3%, 17%, 19%, adjusted) mice. Tumor incidences in high dose males (P=0.017, lifetable test) and both low (0.064, lifetable test) and high dose (P=0.047, lifetable test) females were increased significantly relative to control.

* thyroid
Two high dose females had follicular cell carcinomas, and 3 had follicular cell adenomas. The combined incidence of adenomas or carcinomas in high dose females (21% adjusted) was increased significantly (P=0.040, lifetable test) relative to the controls (3% adjusted), with a historical rate of 1%-3.8%. There were no tumors in the controls.

* forestomach
Squamous cell papillomas occurred at an incidence of 0%, 2% and 6% in control, low dose and high dose male mice, and at 0%, 4% and 4% in the equivalent female groups. Historical rates for this tumor are in the range 0-0.2% for male B6C3F1 mice and 0-0.3% for females. One high dose female had a squamous cell papilloma (2% incidence, historical range of 0-0.3%).

* lung
Alveolar/bronchiolar adenomas and alveolar/bronchiolar adenomas or carcinomas (combined) showed a significant negative trend in female mice.

* external surface
Subcutaneous fibromas or fibrosarcomas and fibromas or fibrosarcomas of the skin or subcutaneous tissue occurred with a significant negative trend in male mice.

Note: Significant increases were observed in virus antibody titers. The reports notes that the relationship between these increases and occurence of the non-neoplastic- and neoplastic changes is unclear.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: NTP concluded that under the conditions of this study PDC increased the incidence of hepatic adenomas in B6C3F1 mice treated with 125 mg/kd bwt/d or 250 mg/kg bwt/d by gavage for up to 103 wk.

Reliability: (1) valid without restriction
Comparable to guideline study, with restrictions.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (182)

5.8.1 Toxicity to Fertility

Type: Two generation study
Species: rat
Sex: male/female
Strain: Sprague-Dawley
Route of administration: drinking water
Exposure Period: 41 wk (f0 adults)
Frequency of treatment: daily
Premating Exposure Period
male: 10 - 14 wk
female: 10 - 14 wk
No. of generation studies: 2
Doses: 0.024%, 0.10%, 0.24%
Control Group: yes, concurrent vehicle
NOAEL Parental: = .024 %
NOAEL F1 Offspring: = .1 %
NOAEL F2 Offspring: = .1 %
other: reproduction NOEL : = .24 %

Method: EPA OTS 798.4700
Year: 1990
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female SD rats were purchased at 4 wk of age from a commercial supplier, stratified by weight and randomly assigned to treatment groups upon receipt. After two weeks acclimatization, PDC was administered in drinking water at concentrations of 0 (control), 0.024%, 0.10% or 0.24% (w/v).

Preparation of dosing solutions
The high dose exposure concentration was selected based upon the theoretical maximal solubility of PDC in water (ie 0.27 g/100 ml). Stability testing showed that >90% of the initial concentration of high dose solution was recovered after 21 days, therefore fresh solutions were prepared at weekly intervals. The lower exposure concentrations were prepared by dilution of the 0.24% solution. All dosing solutions were administered to the animals using sealed Tedlar gas and water sampling bags, fitted with a pressure-activated stainless steel nipple, in order to minimise losses by volatilization. All dosing solutions were analysed on at least 3 occasions per generation during the study. (Note: the analytical method used is not stated, however a limit of detection of 3.08 - 10.1 ug/ml is reported.)

Experimental design
The f0 generation comprised 30 male and 30 female rats per group, and treatment commenced at 6 wk of age. After approx. 10 wk treatment, f0 animals were mated (one male to one female) to produce the f1 litters. Following weaning (3 wk old), 30 males and 30 females from the f1 litters were randomly selected to be the parents of the next generation. Following approx. 12 wk treatment, the f1 adults were mated to produce the f2 litters. For the f1 mating, cohabitation of male and female littermates was avoided.

To reduce variation in pup growth, f1 and f2 litters with greater than 8 pups were reduced in size on PND 4 to 4 males and 4 female. Litters with 8 or fewer pups were not culled. Weaning of all litters occurred 3 weeks after delivery.

Further details of the experimental design are given in Attachment 5.8.1a.

Parental observations
Body weight and food and water consumption were recorded weekly in males and in females pre-parturition, and at 3 day intervals in females post-parturition. f0 and f1 adults were subject to a complete necropsy after the last litter from each generation had been weaned. Liver, kidney and a representative range of other tissues were weighed, sampled and preserved. Bone marrow, coagulating glands, epididymides, kidneys, ovaries, oviducts, pituitary, prostate, seminal vesicles, testes, uterus, vagina and any abnormal gross lesions from the control and high dose groups (f0 and f1) were processed and examined by light microscopy. Hematology parameters (hematocrit, hemoglobin concentration, red cell count, total white cell count, platelet count, red cell morphology) were determined in f0 and f1 animals using blood collected from 10 rats/sex/dose level at necropsy.

Litter observations
All litters were examined as soon as possible after delivery, and parturition date, litter size, weight and sex of each pup and number of live and dead pups on PND 0-21 recorded. Any physical abnormalities at birth or during lactation were recorded.

Weanling observations
10 pups/sex/dose level from the f0 and f1 generations were randomly selected for necropsy at weaning. Liver and kidney weights were recorded, and hematology parameters determined (same details as adults). Tissues were sampled and preserved, but not subject to histopathological assessment.

Statistics
Body weights, organ weights, litter size, hematology and gestation data were evaluated by Bartlett's test for equality of variances, followed by either parametric or non-parametric ANOVA. If the ANOVA was significant, a Dunnett's test or the Wilcoxon Rank-Sum test with Bonferroni's correction was performed. Descriptive statistics were reported for food and water consumption. Fertility indices were evaluated by the Fisher exact probability test and neonatal sex ratios analysed by the binomial distribution test. Survival indices and other neonatal incidence data were analyzed using the litter as the experimental unit.

Result: Analysis of dosing solutions and received dose
Mean exposure concentrations (determined on 3-4 occasions and presented as percent nominal with SD in parentheses) for the low, mid and high dose groups were as follows:
f0 males: 88.8 (6.1), 98.2 (7.3), 100.0 (8.2)
f0 females: 90.3 (6.9), 100.4 (4.3), 102.4 (8.4)
f1 males: 100.7 (29.0), 96.0 (0.9), 95.3 (2.2)

f1 females: 94.6 (21.8), 97.7 (2.6), 96.1 (3.1)

GENERAL
See Attachment 5.8.1 summary.doc for an overview of the main findings from this study.

PARENTAL GENERATIONS
Received dose
Based upon mean body weight and water consumption data, males of both generations from the low, mid and high dose groups received approx. 20 - 30, 70 - 130 and 130 - 250 mg/kg bwt/d. Equivalent female groups received 30 - 40, 110 - 140 and 190 - 270 mg/kg bwt/d. Female water consumption increased during lactation, with received doses of approx 60, 200 450-500 mg/kg bwt/d. Further details are presented in Attachment 5.8.1b.

In life observations
No treatment-related clinical signs were observed.

Food consumption
There were relatively minor and sporadic effects on food intake. f0 females from the high and low dose groups consumed 10% and 6% less than the controls, while f1 males from the high dose group showed an overall 8% reduction in food consumption (pre-mating and mating phases). Food intake data for the other groups were generally unremarkable.

Water consumption
A dose-related decrease in water consumption was apparent in animals from both the f0 and f1 generations, presumably reflecting reduced palatability in the mid and high dose groups. Overall, water consumption in high dose males and pregnant females was 50-60% of control, and 70% of control in lactating females. Water intake in mid dose males and mid dose pregnant females was 70 - 80% of control, and 75 - 85% of control consumption in mid dose lactating females. Results for the low dose animals were 90 - 104% of control.
NOTE: Water consumption typically increases from around gestation day 13 in order to compensate for increased plasma and extracellular fluid volumes during the late stages of pregnancy. This was not the case in this study, due to the unacceptable palatability of the drinking water. This would be expected to have an adverse influence on fetal development. It is also pertinent that water consumption in untreated (control) females increased in this study during lactation, whereas major reductions were apparent in treated animals during lactation. This would be expected to have impacted post-natal survival of the pups.

Parental body weight
Body weights for the high dose animals were significantly (alpha = 0.05) lower than control in f0 and f1 generations of both sexes. In terms of affecting reproductive outcomes, effects in females appeared particularly important. Thus body weights for high dose f0 and f1 females were 5% and 11% lower than control during the pre-mating period, with a 10 - 12% decrement present during gestation and an approx. 15% reduction during lactation. Gestation body weight gains were

decreased by approx. 20% in f0 and f1 females given 0.24% PDC, and by 7-13% in females given 0.1% PDC. Less consistent body weight decrements were noted in the mid dose animals, with negligible effects in the low dose generations.

Reproductive indices
There were no significant or obvious treatment-related differences in male or female reproductive performance, as assessed from mating- and conception indices, fertility or gestational period. Sporadic differences seen for some female parameters were not dose-related (ie present in low and/or mid but not high dose animals) or were within the range of historic control data. All females produced viable litters.

Hematology
Sporadic hematological changes noted in this study were not dose related and inconsistently expressed in males and females of the same generation and in same sex animals of different generations. Overall these effects appeared incidental and unrelated to treatment with PDC.

Necropsy observations
Increased relative kidney weight values in high dose animals (both sexes) appeared secondary to a lower terminal body weight. No gross pathological changes were noted in any of the parental animals.

Histology
Treatment-related histologic changes were limited to increased hepatocellular granularity (adaptive change) in males and females of both generations at all dose levels. Although no statistical analyses are reported, the incidence in high dose females (17% and 10% for f0 and f1, resectively) and high dose f1 males (13%) appears greater than control (0 - 2% for all sex/generation groups). The response in f1 high dose males (5% incidence) and mid and low dose animals of the other generations were less pronounced (2 - 8% incidence) and/or not dose related. All other tissues, including reproductive organs from both sexes, were unremarkable.

LITTER DATA
There were no significant treatment-related external observations or difference in sex ratio in either generation. The number of pups born alive was similar in the control and test groups from both phases of the study, however postnatal survival in high dose f1 litters was significantly lower than control while that of the high dose f2 litters was 10% lower than controls on PND 14 and 21; these effects appeared treatment-related. Bodyweights for high dose f0 neonates were significantly decreased, with day 21 values approx. 15% lower than control. Bodyweights of f1 litters were less severely affected (4 - 7% reduction), and attained significance only on lactation day 21.

WEANLING DATA
An increased hemoglobin concentration in high dose f1 males and an increased mean relative kidney weight in high dose f1 females appeared related to a lowered water intake and body

weight, respectively. All other hematological and gross necropsy observations were comparable to control in both the f1 and the f2 generations.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Attached doc.: Attachment 5.8.1 summary.doc

2-Generation reproduction study on PDC: Summary of Results, from Kirk et al. (1990)

Endpoint	0.024% PDC		0.1% PDC		0.24% PDC	
	F0	F1	F0	F1	F0	F1
Male Bwts	-	-	↓	-	↓	↓
Female Bwts (pre-breed)	-	-	-	-	↓	↓
Water Consumption (M + F)	↓	↓	↓	↓	↓	↓
Gestation Bwt	-	-	-	↓	↓	↓
Gestation Bwt Gain	-	Slight ↓	Slight ↓	↓	↓	↓
Gestation Water Consumption	-	-	↓	↓	↓	↓
Gestation Feed Consumption	-	Slight ↓	-	Slight ↓	-	↓
Lactation Bwt	-	-	↓	-	↓	↓
Lactation Bwt Gains	Slight ↓	-	↓	-	↓	-
Lactation Water Consumption	↓	-	↓	↓	↓	↓
Lactation Feed Consumption	-	-	↓	-	↓	-
	F1	F2	F1	F2	F1	F2
Litter Size	-	-	-	-	↓	-
Postnatal Survival	-	-	-	-	↓	↓
Neonatal Bwt	-	-	-	-	↓	↓

Attachment 5.8.1a.doc

Study design - 2-generation reproduction study, from Kirk et al., 1990

Weeks on study	**Generation**		
	f0	f1	f2
1 - 10	Treatment of f0 males and females prior to mating		
11 - 13	f0 mating period for f1 litters		
14 - 16		f1 born and litters culled on day 4 post-partum to 8 pups each	
17 - 19		f1 litters weaned on day 21 post-partum; offspring selected for 2nd generation adults; 10/sex/dose selected for necropsy; remaining pups sacrificed	
20	Necropsy of f0 adults	Pre-mating treatment period for f1 males and females begins	
32 - 34		f1 mating period for f2 litters	

35 - 37			f2 born and litters culled on day 4 post-partum to 8 pups each
38 - 40			f2 litters weaned on day 21 post-partum; 10/sex/dose selected for necropsy; remaining pups sacrificed
41		Necropsy of f1 adults	

Attachment 5.8.1b.doc

Received doses - 2-generation reproduction study, from Kirk et al., 1990

Group Phase		Received dose (mg/kg bwt/day) Treatment level		
		0.024%	**0.10%**	**0.24%**
f0 males	pre-mating	28	91	161
	post-mating	18	65	131
f0 females	pre-mating	33	108	189
	gestation	38	121	217
	lactation *	58	196	507
f1 males	pre-mating	33	128	250
	post-mating	19	69	137
f1 females	pre-mating	41	140	269
	gestation	38	126	239
	lactation *	56	200	450

* Note: greater exposure reflects increased water consumption during lactation

Conclusion: Propylene dichloride was not a reproductive toxin when tested over 2 generations in SD rats exposed to 0.024%, 0.1% and 0.24% in drinking water.

Decreased water consumption (presumably reflecting unacceptable
palatability of the test solution) and lowered body weight, and increased hepatocellular granularity (adaptive change), were present in parental animals from the 0.24% groups of both generations. Neonatal growth and survival were decreased in the 0.24% treatment groups, probably in response to decreased maternal water intake and lower growth. There was no effect on reproductive performance, live births or litter size in any of the test groups.

Thus the NOAEL for adults and neonatal effects was 0.1% PDC while the reproductive NOEL was 0.24% PDC, the limit of solubility.

Reliability: (1) valid without restriction
GLP guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (208)

5.8.2 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: GD 6 - 15 inclusive
Frequency of treatment: daily
Doses: 0 (corn oil), 10, 30 or 125 mg/kg bwt/d
Control Group: yes, concurrent vehicle
NOAEL Maternal Toxity: = 30 mg/kg bw
NOAEL Teratogenicity: = 125 mg/kg bw
NOAEL Fetotoxicity : = 30 mg/kg bw

Method: EPA OTS 798.4900
Year: 1995
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Pregnant female SD rats (approx. 14 wk old, n = 30) were randomised into groups and administered PDC by gavage at doses of 0 (corn oil), 10, 30 or 125 mg/kg bwt/d on GD 6 - 15 inclusive.

The concentration of PDC in the dosing solutions was verified using GC-FID.

Parental observations
Animals were observed daily in their cages, and also subject to a more intensive clinical examination 30 - 60 min post-dosing. This included observation of pupil size, respiration, movement (muscle tone, extensor thrust reflex, general behaviour, tremors, convulsions etc), condition of skin and haircoat (ie piloerection), salivation, lacrimation and any other abnormal events. Food and water intake was recorded every 2 - 4 days, and body weights on GD 0, 16 and 21. The dams were sacrified on GD 21, when liver, kidney, spleen and gravid uterine weights were recorded.

Fetal observations
The number of corpora lutea, the number and position of implantations and the number of live or dead fetuses were recorded. In addition, the sex and body weight of each fetus was recorded, and any gross external alterations recorded. At least one-half of each litter was examined immediately for visceral alterations, with subsequent evaluation of skeletal abnormalities using alizarin red-S.

Statistics
The data were analysed intially using Bartlett's test, parametric or non-parametric ANOVA, Dunnett's test and the Wilcoxon Rank-Sum test. Pregnancy rates were analysed using the Fischer exact probability test, and fetal sex ratios evaluated using a binomial distribution test.

Interpretation of findings
Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological

and pathological findings. This is scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study.

Result: Mean analysed concentrations of PDC were 5.0 (0.0), 15.0 (0.0) and 62.5 (2.0) mg/ml (SD in brackets).

Maternal observations
Clinical signs (ie decreased movement and muscle tone, increased lacrimation, decreased extensor reflex and increased salivation) were present in high dose animals on GD 6 and to a lesser extent on GD 7. Despite the transitory nature of these changes, they appeared indicative of an adverse effect in dams from the high dose group. No clinical effects were seen on other days in the high dose group, or on any day in the mid- or low dose animals.

Body weights were slightly (3-5%) but significantly lower in high dose dams throughout the study. Body weight gain was decreased significantly in high dose dams on GD 6-9, and although comparable to control during the mid- and latter stages of pregnancy the overall weight increase in the 125 mg/kg bwt/day group was approx. 30% lower than controls on GD 6-16 (that is, during the dosing period). Food consumption was reduced approx. 25% on GD 6-9, and water consumption increased by the same amount on GD 9-12 and 12-15.

There were no significant effects on absolute or relative organ weights, or on uterine weights or pregnancy parameters (including number of litters, corpora lutea per dam, implantations per dam, live fetuses per litter, resorptions, fetal bwt, etc).

Fetal observations
A low incidence of malformations was present in all groups, with no qualitative or quantitative increase in litters from treated dams. Overall there was no indication that PDC was a teratogen.

Fetal variations were present in both control and treated groups. The only treatment-related effect was a significant increase in the incidence of delayed ossification of the bones of the skull among fetuses from the high dose group. Interestingly, the occurrence of this observation was most common in high dose litters containing 16 or more pups. All other parameters were comparable to the controls.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, mild fetotoxicity (as evidenced by decreased ossification of the bones of the skull) was noted in litters from dams given 125 mg/kg bwt PDC/day. This effect was most common in the larger litters, and was co-incident with significant reductions in body weight gain and food consumption. It is concluded that the NOAEL for both maternal and fetal toxicity was 30 mg/kg bwt/day.

Reliability: (1) valid without restriction
GLP guideline study.

Flag: Critical study for SIDS endpoint

22-DEC-2004 (209)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of administration: gavage
Exposure period: GD 7 - 19 inclusive
Frequency of treatment: daily
Doses: 0 (corn oil), 15, 50 or 150 mg/kg bwt/ d
Control Group: yes, concurrent vehicle
NOAEL Maternal Toxity: = 50 mg/kg bw
NOAEL Teratogenicity: = 150 mg/kg bw
NOAEL Fetotoxicity : = 50 mg/kg bw

Method: EPA OTS 798.4900
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Artificially-inseminated pregnant female New Zealand rabbits (approx. 6.5 mo old, n = 18) were randomised into groups and administered PDC by gavage at doses of 0 (corn oil), 15, 50 or 150 mg/kg bwt/ d on GD 7 - 19 inclusive.

The concentration of PDC in the dosing solutions was verified using GC-FID.

Parental observations
Food and water intake was recorded every 2 - 4 days, and body weights on GD 0, 20 and 28. Blood samples were collected on GD 19 and subject to an extensive haematological examination. The dams were sacrified on GD 28, when liver, kidney, spleen and gravid uterine weights were recorded.

Fetal observations
The number of corpora lutea, the number and position of implantations and the number of live or dead fetuses were recorded. In addition, the sex and body weight of each fetus was recorded, and any gross external alterations recorded. All rabbit litters were examined immediately for visceral alterations, with subsequent evaluation of skeletal abnormalities using alizarin red-S.

Statistics
The data were analysed intially using Bartlett's test, parametric or non-parametric ANOVA, Dunnett's test and the Wilcoxon Rank-Sum test. Pregnancy rates were analysed using the Fischer exact probability test, and fetal sex ratios evaluated using a binomial distribution test.

Interpretation of findings
Final interpretation of the results considered statistical analyses along with other factors such as historical data, dose-response relationships and whether the findings were biologically significant in the light of other toxicological and pathological findings. This appears scientifically acceptable since a high level of Type I (false positive) errors would be anticipated as a consequence of the large number of statistical comparisons that were included in the study.

Result: Mean analysed concentrations of PDC were 14.8 (0.06), 49.4 (0.34) and 150.0 (1.94) mg/ml (SD in brackets).

Maternal observations
One rabbit from the high dose group died on GD 22 (ie after gavage treatment had ended) but no cause of death could be identified at necropsy. The remainder of the high dose dams exhibited intermittent anorexia (data not presented). There were no other significant changes in behaviour or demeanor among rabbits during the course of the study.

Body weight gain among the high dose dams was significantly lower than that of the controls (net loss of 165 g compared to a net gain of 49 g in the controls on GD 7-20), although absolute bwt appeared unaffected.

Haematological examinations demonstrated the clear effects in high dose dams (other groups unaffected), with red cell counts, haemoglobin concentration and haematocrit all decreased by 18-20% while platelet and white cell counts were increased 20-25%. The percentage of reticulocytes was approx. double in high dose animals when compared to the controls.

There were no significant effects on absolute or relative organ weights, or on uterine weights or pregnancy parameters (including number of litters, corpora lutea per dam, implantations per dam, live fetuses per litter, resorptions, fetal bwt, etc).

Fetal observations
There was no increase in the incidence of malformations in any of the treated groups when compared with the controls. Overall there was no indication that PDC was a teratogen.

Fetal variations were present in both control and treated groups. The only treatment-related effect was a significant increase in the incidence of delayed ossification of the bones of the skull among fetuses from the high dose group. All other parameters were comparable to the controls.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study PDC was not selectively toxic to the fetus, causing a slight delay in ossification of the fetal skull at doses causing systemic (haematological) changes in the dams. The NOAEL for maternal and fetal effects in the rabbit is 50 mg/kg bwt.

Reliability: (1) valid without restriction
GLP guideline study.

Flag: Critical study for SIDS endpoint

25-OCT-2004 (209)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

Endpoint: Neurotoxicity
Species: rat
Strain: Fischer 344 **Sex:** male/female

Route of administration: gavage
No. of animals: 15
Vehicle: other: corn oil
Exposure Period: 90 day(s)
Frequency of treatment: 5 d/wk for 13 wk
Doses: 0, 20, 65 or 200 mg/kg bwt
Control Group: yes, concurrent vehicle
Observation Period: 13 wk during treatment + 9 wk recovery period
Result: No gross or histopathologic changes in central or peripheral nervous system

Method: other: functional observation battery = EPA 798.6050; motor activity = EPA798.6200; neuropathology = EPA798.6400.
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals and treatments
Male and female F344 rats (approx. 8 wk old; n=15/sex) were administered 0 (control, corn oil, 1ml/kg bwt), 20, 65 or 200 mg PDC/kg bwt/d via gavage, 5 d/wk for 13 wk (equivalent to a total of 65 treatments). Fresh dosing solutions were prepared monthly, and the concentration of PDC confirmed using GC.

A dose of 200 mg/kg bwt/d was chosen for the high dose group based on the known acute CNS effects of PDC ie this level of exposure was expected to significantly challenge the animals but not cause frank systemic toxicity.

After 13wk treatment, 4 rats/sex/dose were randomly selected for terminal examinations. The remainder were allowed a 9 wk recovery period, after all were sacrificed and 5 rats/sex/dose were taken for necropsy.

Cage side observations were conducted twice daily. The animals were also subject to handling and observation at the time of dosing, and subjected to a detailed external examination each week.

Functional Observational Battery (FOB)
The animals were subjected to FOB evaluation before treatment commenced and at monthly intervals during the main study period. The observations were conducted by the same technician before the daily dosing. Endpoints included:
*Observations in-hand
- pupil size
- respiration
- movement
- condition of skin and coat
- salivation
- lacrimation
- urine staining
- faecal staining

* Observations in a clear plastic box
- locomotor behaviour
- responsiveness to touch
- responsiveness to sharp noise
- responsiveness to tail pinch
- visual placing

Grip strength
Hindlimb grip strength was measured before treatment commenced and at monthly intervals during the main study period. The test involved placing the rat's forelegs on a bench and the hindfeet on a horizontal screen attached to a strain gauge. The observer then smoothly but firmly pulled backward on the tail until the grip of the hind feet was broken. The strongest response from three trials was used for statistical analysis.

Motor activity
Motor activity was evaluated before treatment commenced and at monthly intervals thereafter in a doughnut-shaped plexiglass alley over five 8 min sessions. An infrared photo beam crossed the alley in two locations to record movement.

Body weight and temperature
Body weights were recorded weekly and also on the days when the FOB and motor activity assessments were conducted. Body temperature was recorded using a thermistor on the last day of dosing concurrently with the FOB.

Necropsy
Four rats/sex/dose level were fasted overnight prior to necropsy. The animals were given heparin prior to anesthesia, then sacrificed by whole body perfusion and fixing with gluteraldehyde/formaldehyde solution. A macroscopic examination (limited in extent by the perfusion process) was performed prior to removal of the brain and selected nervous system tissues. The liver, kidneys and spleen (possible target tissues) were sampled and preserved.

Histopathology
The following nervous system tissues from control and high dose animals were subject to the microscopic evaluation:
- brain (6 levels)
- spinal cord (cervical and lumbar)
- Gasserian ganglia
- dorsal and ventral spinal nerve roots
- dorsal root ganglia (cervical and lumbar)
- sciatic, tibial and sural nerves
Special stains were used to examine neuronal bodies, axons and neurofibrials and myelin.

Recovery phase
11 rats/sex/dose level were retained for possible further examination, pending preliminary assessment of fidnings from the main study. The animals were observed for clinical signs twice daily and subject to a more detailed external examination each week. Body weights were recorded weekly, and body temperature recorded 1, 2, 4 and 8 wk after treatment ended. Five rats/sex/dose were taken for necropsy after a 9 wk recovery period, the remainder were euthantized without further examination.

Statistical analysis
The data were subject to extensive statistical evaluation, including Bartlett's test, parametric and non-parametric ANOVA, Dunnett's test, Wilcoxon Rank-Sum test, Bonferroni

correction, Outlier test, 2-way ANOVA. In view of the very large number of comparisons considered in this study, the final interpretation of the data considered results from statistical analyses along with other factors such as dose-response relationships and whether the results were meaningful in the light of other findings.

Result: Dosing solutions
Analysis of the dosing solutions demonstrated that the concentration of PDC was at or slightly above the target, varying from 100 to 110.5% of nominal. There was no appreciable loss due to volatilisation (<6% decrease) and the PDC was distributed in a homogeneous manner within the master batch of each solution.

General
All rats survived the 13 wk treatment period. Clinical signs included lacrimation and blinking in a dose-dependent manner on the first day, with decreased spontaneous motor activity (for up to 4 hr post-treatment in the high dose group). No effect on motor activity was noticeable in the low- and mid dose groups by day 3, or in the high dose animals by day 4. No other treatment-related clinical signs were present.

Body weight
A significant decrease in body weight of high dose males was apparent during the first week of treatment which persisted throughout the 13 wk dosing period (6-10% reduction overall). Body weights of mid dose males were also decreased consistently and, although the change was not always significant, this was also considered to be treatment related by the authors of the study report. Body weights of high dose females were also slightly decreased (equivocal, non-significant effect). There was no effect on the body weights of low dose males or mid and low dose females.

FOB
No differences were apparent between control and treated animals at any of the test intervals.

Hind limb grip strength
The only statistically significant effect noted was an increase in grip strength in high dose animals (both sexes) 1 month following the start of treatment. This finding was not replicated 2 or 3 months into the study, and was considered coincidental to treatment.

Motor activity
Data generated during the study did not reveal any significant differences between control and treated animals. Females tended to be more active than males at the 1- and 3 month evaluation points, however there was no [sex x treatment] interaction and this finding was considered incidental.

Body temperature
There was a slight but significant decrease in body temperature in high dose animals at the end of the main phase of the study (0.6 degree C reduction in females, 0.3 degree C reduction in males).

Observations at necropsy
There were no gross changes observed at necropsy that were considered related to treatment with PDC. Absolute brain weight was decreased by approx. 10% in high dose animals, probably reflecting the lower body weight noted above. Relative brain weight was marginally increased.

Histopathologic observations
A few incidental observations were identified however the incidence was similar in control and high dose animals, and the changes were considered unrelated to PDC treatment.

Recovery phase
Body weight decreases present in high dose males at the end of the main phase of the study were maintained throughout the 9 wk recovery phase (signifiant 8% decrease in high dose males at wk 22). Mid dose males and high dose females showed a non-significant 3-4% reduction in bwt over the same period.

Body temperature differences in high dose animals generally remained during the recovery period (significantly decreased by 0.6 - 1.0 degree C in females throughout recovery phase, 0.3-0.5 degree C reduction in males during wk 1-4 only).

No gross lesions were identified at necropsy.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: Under the conditions of the study, early transient clinical signs and minor decreases in body weight and body temperature were the only effects attributable to PDC. A NOAEL of 20 mg/kg bwt/d was established in males (reflecting bwt effects only) and a NOAEL of 65 mg/kg bwt in females. The NOAEL for gross, microscopic and functional effects on the central and peripheral nervous system was 200 mg/kg bwt (the highest dose tested) in both sexes.

Reliability: (1) valid without restriction
GLP guideline study.

Flag: Critical study for SIDS endpoint

22-DEC-2004 (210)

5.10 Exposure Experience

Type of experience: Human

Remark: An unconscious 71-year-old man was taken to the hospital approximately 1 hour after attempting suicide by ingesting approximately 180 ml of a cleaning agent (labelled as 90 % 1,2-dichloropropane and 10 % 1,1,1-trichloroethane). He died
after 48 hours never regaining consciousness. Upon arrival his liver and renal functions as well as coagulation were normal but 8 hours later, severe liver dysfunctions appeared. These dysfunctions were detected by a strong increase of transaminase activity in serum. After 48 hours aspartate aminotransferase activity was 5,912 U/l (upper normal value 19U/l), the alanine aminotransferase was 30,128
U/l (normal value 5-23 U/l) and prothrombin activity was lower than 10%. Further, the following were measured: a

bilirubin content of 2.3 mg/100 ml (normal value < 1mg/100ml), a creatinine content of 2.8mg/100ml (normal value 0.7-1.1 mg/100 ml), an increased activity of cholinesterase up to 2100 U/l, a fibrinogen content of 96 mg/100 ml (normal value 150-450 mg/100 ml) and 14000 blood platelets/ul. During the hospital stay, the patient was diagnosed with severe liver and renal dysfunction, abnormal coagulation (coagulopathy), metabolic acidosis, myocardial insufficiency and shock.

Estimated dose (180mL of 90% PDC) is 3400 mg/kg/day for a 60kg 71-year old.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (2) valid with restrictions
Short case report, limited reporting of methods and results. Includes an approximate dose and some available toxicological data.

20-OCT-2004 (211) (212)

Type of experience: Human

Remark: A 20-year-old girl was taken to a hospital with vomiting and abdominal pains. During the examination oliguria, epistaxis, hematocyturia, metrorrhagia as well as periorbital and conjunctival hemorrhages were found. The clinicochemical examination showed acute liver disease (increased activities of alanine and aspartate aminotransferase as well as an increased bilirubinemia and a decreased prothrombin level), severe kidney disease (hypercreatininemia and decreased urea value), hemolytic anemia and intravascular coagulation (increased fibrinolytic split products; number of thrombocytes 10,000/mm3). Further, complement factors C3 and C4 were not detectable. Three weeks after a blood transfusion and a hemofiltration, the liver, kidney and coagulation dysfunction were no longer detectable. Review of the patient's medical history presumed a connection between appearance of these symptoms and the abuse of "Trielina". The patient was sniffing "Trielina" for approximately 1 month, stopped for 10 months and then started again - the above-mentioned intoxication symptoms returned. The product contained 98% 1,2-dichloropropane and 2% trichloroethylene and dichloroethane based on GC analysis.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Short case report, limited reporting of methods and results, unknown reliability.

29-FEB-2004 (213)

Type of experience: Human

Remark: A unconscious 49-year-old man was taken to the hospital after attempting suicide by ingesting an unknown amount of 1,2-dichloropropane, as identified by GC/MS. The

patient was given artificial respiration and regained consciousness 3 days later. He was diagnosed with esophagitis. The following biochemical parameters were analyzed in serum at different times: alanine aminotransferase activity and the bilirubin content were increased for the first 2 weeks but normalized within approximately 1 month; Three days after arrival the prothrombin content severely decreased (20% of the starting value) and 9 days later it returned to normal.
One month after intoxication, hepatomegaly and splenic enlargement as well as ascites appeared. Liver biopsy revealed hepatocellular necrosis accompanied by an inflammatory reaction. Six months later another biopsy was taken; portal hypertension and portal fibrosis were found but there was no remaining evidence of hepatocyte necrosis.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Short case report, limited reporting of methods and results, unknown reliability.

20-OCT-2004 (214)

Type of experience: Human

Remark: A 46-year old man fell in a deep coma with pupil dilation and hypertension within 2 hours after ingesting approximately
50 ml of a cleaning agent by mistake; the man gained consciousness 24 hours after being given artificial respiration and osmotic diuresis. A little bit later delirium and tremor appeared. The man died 36 hours after intake, of irreversible shock with heart failure, acidosis and hepatic
cytolysis. Autopsy showed a centrilobular and mediolobular acute necrosis of the liver. Gas chromatography analysis of the cleaning agent demonstrated qualitatively the presence of 1,2-dichloropropane .

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Short case report (abstract only), limited reporting of methods and results,
no information on origin/purity of test sample, unknown reliability.

22-DEC-2004 (215)

Type of experience: Human

Remark: In a letter to the editor, a case report is described for a 73 yr old woman who was admitted to hospital with vomitting and somnolence. Three days earlier she had developed abdominal pains. The patient had been cleaning garments using a stain remover containing 1,2-dichloropropane (no analytical confirmation of composition). She reported having fallen asleep for 2 hr with her head about 40 cm away from the open glass of cleaning fluid.

Laboratory tests revealed decreased serum potassium, hyperglycemia and leukocytosis. Serum ASAT increased from 2114 U/l on the day of admission to 6300 U/l the following day, and serum ALAT from 1990 U/l to 5400 U/l; prothrombin

activity decreased from 31% of normal to 22% of normal over the same period.

Her condition had improved by day 5 (no details).

Hepatic biopsy on day 8 revealed centrilobular necrosis, characterised by pyknosis and 'cellular shadows'. Haemolytic anaemia (Hb 9.8 g/l; 3.01 x 10^6 ul red cells; HCT 30%) was present at day 10 and persisted for 10 days.

After 3 weeks, haematologic parameters were normal.

After 6 months, ASAT and ALAT were slightly elevated (55 and
75 U/l, respectively).

All tests were normal by 9 months.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Short case report, limited reporting of methods and results,
no information on origin/purity of test sample, unknown reliability.

29-FEB-2004 (216)

Type of experience: Human

Remark: In a letter to the editor, the authors report a 46 yr old individual who was admitted to hospital with symptomatic wide-complex tachiarrythmia, with subsequent diagnosis of hyperkalemia and oliguric acute renal failure and symptoms of hepatocellular necrosis, rhabdomyolysis, and a severe coagulopathy.

Symptoms were reported shortly after having worked for 6 hours in an outdoor environment with a commercial paint fixative reported to contain 35-40% 1,2-dichloropropane and toluene (33-38%). An accidental spill resulted in gross contamination of the front part of his body, trunk and abdomen. The individual delayed removal of his clothes and skin decontamination for 5 hours suggesting probable massive
dermal exposure with prolonged inhalation exposure also likely. He
reported only transient redness of the involved skin areas.

The patient responded favorably to treatment and became non-oliguric after two 10-hr sessions of dialysis over 2 d while coagulation values returned to normal over the same period. The patient was discharged after 7 d. Full renal and
hepatic function recovery was demonstrated after 2 weeks.

The authors summarize that this case represents a severe acute intoxication from 1,2-PDC via a percutaneous route of exposure, but acknowledge that additional mechanisms, which may
have played a contributing role, could not be excluded.
Reviewer's Comment:
Although the authors state that exposure is via dermal

contact, given the high volatility of PDC, it is likely that inhalation of volatilized material was a major contributor to exposure during the 5-hour period while he was wearing his "drenched" shirt.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Short case report, limited reporting of methods and results,
no information on origin/purity of test sample, unknown reliability.

25-OCT-2004 (217)

5.11 Additional Remarks

Type: Biochemical or cellular interactions

Remark: Inhalational exposure of 1,2-dichloropropane in concentration 10 mg/m3 for 3 months induced an increased lipid content in the cells of the adrenal gland cortex.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (218)

Type: Biochemical or cellular interactions

Remark: Test condition:
[14C]-marked 1,2-dichloropropane was dosed to female F344 rats via oral gavage in concentrations of 0.94; 7 and 255 mg/kg.

Results:
Radiolabel was exhaled as CO2 in concentration 27; 17 and 2 %. The liver was taken from the animals six hours after the application.
Radioactivity measurement was 83 dpm/mg in the low dose group, 470 dpm/mg in the middle dose group and 52 dpm/mg in the high dose group.
90 - 95 % of this radioactivity was analyzed in the isolated liver-DNA.
After the "acid depurinisation" of DNA, it was found that radioactive precursors of the nucleotide were present at biosynthesis and not during the covalent binding of radioactive 1,2-dichloropropane on DNA.

Maximal DNA-damage, given as the covalent binding index (CBI = mmol of substance bound per mol nucleotide/mmol substance applied per kg body weight), was < 2 for the low dose group, < 1 for the middle dose group and < 0.3 for the high dose group.

It can be assumed there is no strong (if existing) genotoxic risk in-vivo for 1,2-dichloropropane, as a large database already exists.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to

determine reliability.

26-OCT-2004 (219)

Type: Biochemical or cellular interactions

Remark: Test condition:
Two female F344 rats were inhalational exposed to radioactive [14C]-1,2-dichloropropane resulting in intake of 25 and 27 mg/kg.

Results:
The substance was exhaled for 7 and 7.5 hours as 18 % and 14 % CO2. At the end of the test, the animal livers were taken and DNA was isolated. Specific radioactivity in DNA was 350 dpm/mg. The separation of the DNA in natural nucleotides showed that the radioactivity is caused when the precursors were added to DNA during biosynthesis. The DNA-adducts can only be less than 3.1 % of the radioactivity in DNA. The covalent binding index CBI was given as < 0.7. This maximum possible CBI classifies 1,2-dichloropropane as 10000 times below the genotoxic potential of aflatoxin B1. A binding on DNA as an important mechanism of carcinogenic effect of 1,2-dichloropropane is improbable.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (220)

Type: Cytotoxicity

Remark: Rats and mice were exposed to 10 mg 1,2-dichloropropane/m3. Pulmonary arteries, veins and capillaries were histologically analyzed at different times. Vacuolization of endothelia cells and invagination of the karyolemma in the nucleus appeared after 5 days. Pinocytic rate was increased in cytoplasm of the endothelial cells after 13 days. Bladders between the capillaries were built after 50 days and a destruction of mitochondria and organelles followed. NADH dehyrogenase and glucose-6-phosphate dehydrogenase activity was significantly ($p < 0.01$) increased and after 15 and 30 days these activities returned to the control group range.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (221)

Type: Cytotoxicity

Remark: An increase of conglomeration in cytoplasm of fat cells as well as an increase of vacuolization and degranulation was caused after 7 days exposure to 1000 mg 1,2-dichloropropane/m3. An increase of functional activity of fat tissue cells was also found.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (222)

Type: Cytotoxicity

Method: In this study we have investigated the effects of PDC on intracellular glutathione (GSH) content in main target tissues of male Wistar rats, i.e. liver, kidney and blood, in order to establish if a correlation between PDC-induced GSH depletion and tissue damage exists.

Result: Administration of PDC (2 ml/kg body weight, orally) caused a dramatic loss of tissue GSH occurring 24 h after PDC intoxication, followed by a slow restoration approaching physiological levels after 96 h. GSH depletion was associated with a marked increase in serum GOT, GPT, 5'-nucleotidase, gamma-glutamyl transpeptidase, alkaline phosphatase, urea and creatinine, and a significant decrease of hemolysis.

When animals were pretreated with a GSH depleting agent, buthionine-sulfoximine (BSO; 0.5 mg/kg body weight; i.p.) 4 hours before PDC intoxication, an increase of overall mortality was found, significantly different from the group of animals treated only with PDC. On the contrary, the administration of a GSH precursor, N-acetylcysteine (NAC) i.p. (250 mg/kg b.w.) 2 and 16 hours after PDC intoxication prevented the dramatic loss of cellular GSH and reduced the extent of injury in target tissues, as demonstrated by laboratory indices. Furthermore, statistical analysis of the data revealed a correlation between:
1) depletion of liver GSH and increase in serum GOT, GPT, 5'-nucleotidase
2) depletion of kidney GSH and increase in serum urea and creatinine and
3) depletion of blood GSH and the occurrence of hemolysis.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Conclusion: The findings demonstrate that GSH plays a critical role in modulating the toxicity of PDC. They also highlight the protective role of NAC and suggest that this glutathione precursor could rationally be used in PDC poisoning in humans.

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

22-DEC-2004 (223)

Type: Distribution

Remark: Ninety-six hours after the administration of 0.88 mg [14C]1,2-dichloropropane/animal, Carworth Farm rats (6 animals/sex) were dissected and 0.5 % of the radioactivity was still present in the intestinal tract, 1.7 %(male) and 1.4 % (female) in the skin and 4.1 % (male) and 3.2 % (female) in the remainder of the body.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (224)

Type: Distribution

Remark: Partition coefficients for 1,2-dichloropropane were analyzed in vitro at 37 degrees C and resulted in:
blood (rat)/air 18.5 +- 0.5
blood (human being)/air 10.7 +- 0.5
blood (human being)/air 8.75 +- 0.50
fat tissue/air 499 +- 30
liver tissue/air 24.8 +- 2.4
muscle tissue/air 12.0 +- 1.1

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (115) (116)

Type: Excretion

Remark: Ninety-six hours after the administration of 0.88 mg [14C]1,2-dichloropropane/animal, Carworth Farm rats (6 animals/sex) were dissected and 51.1 % (male) and 54.4 % (female) of the radioactivity eliminated with urination, 6.8 % (male) and 4.9 % (female) was eliminated with faeces. After
administering the above-mentioned dosage to females (n = 5), within 96 hours, the exhalation was 19.3 % of radioactivity in the form of CO2 and 23.1 % as non-identified evaporable substances.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (224)

Type: Excretion

Remark: Urine and feces of F344 rats (4 animals/sex/concentration) were collected for 48 hours after inhalational exposure (head only) for 6 hours to 24, 235 and 470 mg [14C]1,2-dichloropropane/m3. 55 - 65 % of the recovered radioactivity was detected in urine and 6.3 - 9.7 % was detected in feces; 16 - 23 % of the radioactivity was exhaled as CO2.

Source: The 1,2-Dichloropropane ICCA/HPV Consortium

Reliability: (2) valid with restrictions
2e (meets generally accepted scientific methods, well-documented, and acceptable for assessment)

21-DEC-2004 (225)

Type: other: Biotransformation

Remark: Analysis with rat liver microsomes showed that the enzyme responsible for the dechlorination of 1,2-dichloropropane needs O2 and NADPH. Phenobarbital and benzpyrene can induce

this enzyme but not methylcholanthrene.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

22-DEC-2004 (226)

Type: other: Biotransformation

Remark: Various in vitro tests for oxidation of 1,2-dichlororpopane in human liver microsomes showed that during this oxidation the most important enzyme probably is P-450 II E1 isozyme.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
Not assignable; Insufficient detail in the IUCLID entry to determine reliability.

26-OCT-2004 (227)

Type: other: Resorption

Remark: The highest levels of 1,2-dichloropropane in blood were detected 30 -60 minutes after the administration of 55 - 440 mg 1,2-dichloropropane/kg body weight in male Wistar rats (5 animals/dose group). The half-life of 1,2-dichloropropane in blood was 3.1 - 5.0 hours after the administration of 55 - 220 mg/kg. After the administration of 440 mg/kg, the maximal blood level was reached after only 2 hours. The half-life for 1,2-dichloropropane in blood was then 13.6 hours.
Source: The 1,2-Dichloropropane ICCA/HPV Consortium
Reliability: (4) not assignable
26-OCT-2004 (211)

Remark: In addition to N-acetyl-S-(2-hydroxypropyl)cysteine, in the study on metabolism of 1,2-dichloropropane, two other metabolites were found in urine of Sprague-Dawley rats. They were identified as N-acetyl-S-(2,3-dihydroxypropyl)cysteine and beta-chlorolacate. The presumption would be that metabolism of 1,2-dichloropropane to N-acetyl-S-(2-hydroxypropyl)cysteine follows a dechlorination and oxidation step to 1-chloro-2-hydroxypropane. Further dechlorination produces N-acetyl-S-(2-hydroxypropyl)cysteine. Analysis of urine showed two substances beta-chlorolactate and S-(2,3-dihydroxypropyl)cysteine, which could have originated from 1-chloro-2-hydroxypropane.
Source: Dow Europe
DOW Europe Horgen
A.K. Mallett Surrey

25-OCT-2004 (228)

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