Appendix B
Section G

DICHLOROETHYLENES
HEALTH-BASED MAXIMUM CONTAMINANT LEVEL
SUPPORT DOCUMENT

Office of Science and Research

New Jersey Department of Environmental Protection

Prepared by
Lubow Jowa

EXECUTIVE SUMMARY

1,1-Dichloroethylene (1,1-DCE) is a chemical intermediate of polyvinylidene chloride copolymers, used in barrier coatings by the packaging industry. 1,2-Dichloroethylenes have a limited use as solvents and preservatives. The instability of dichloroethylenes and their limited solubility in water diminish the potential for human exposure by the drinking water route. Dichloroethylenes have an odor threshold of 2,000 mg/m^3 (1,1-dichloroethylene) and 1,100 mg/m^3 (1,2-dichloroethylene).

Dichloroethylenes at high exposure concentrations can depress the central nervous system, and produce narcosis that may result in death. Although toxic effects from chronic exposure to 1,2-dichloroethylenes are not known, 1,1-dichloroethylene has been shown to cause liver and kidney injury in animal studies. In bacterial systems with microsomal activation 1,1-dichloroethylene (1,1-DCE) has been shown to be mutagenic. Limited evidence from animal studies indicates that 1,1-DCE may be carcinogenic, but epidemiological studies of exposed human populations do not provide direct evidence of carcinogenicity. A health-based maximum contaminant level of 1 ug/L was derived to protect against possible liver toxicity and carcinogenicity. For cis- and trans-1,2-dichloroethylenes, a health-based maximum contaminant level of 10 ug/L is recommended based on the chronic toxicity of 1,1-dichloroethylene.

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BACKGROUND INFORMATION AND PROPERTIES

Chemical Properties

Chemical name: Dichloroethylenes (DCE)

Consist of 3 isomers: 1,1,-DCE; cis-1,2 DCE; trans-1,2-DCE.

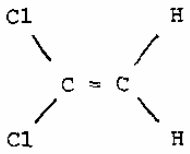
CAS# 75-35-4 540-59-0

Synonyms: 1,1-DCE: Vinylidene chloride, 1,1-Dichloroethene, VDC, DCE

1,2-DCE: Acetylene dichloride, 1,2-dichloroethene, syn-dichloroethylene, duoform

Chemical formula $C_2H_2Cl_2$

Chemical structure



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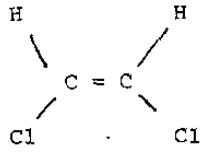

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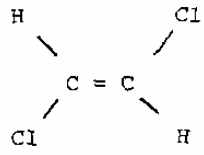

trans-1,2-DCE

	1,1-DCE	cis-1,2-DCE	trans-1,2-DCE
Molecular weight	96.95	96.95	96.95
Physical state	clear, colorless liquid	--	--
Melting point	-122.5 °C	--	--
Boiling point	31.7 °C	60 °C	42 °C
Vapor pressure	591 Torr at 20 °C	180 Torr (20 °C)	265 Torr (20 °C)
Specific gravity, density	1.2129 at 20 °C	same	same
Water solubility	400 mg/L at 20 °C	3500 mg/L	6300 mg/L
Conversions factors	1 ppm = 4 mg/m^3	--	--
Odor threshold, air	2,000 mg/m^3	--	1,100 mg/m^3

Production and Use

1,1-dichloroethylene (1,1-DCE) is primarily polymerized to polyvinylidene chloride, or used as a co-monomer with vinyl chloride to produce copolymers of the two monomers, for use in barrier coatings on paper and plastic films, or as binders for nonwoven fabrics, paints, and concrete. Approximately 120,000 metric tons was produced in 1975 (U.S.EPA, 1984).

1,2-dichloroethylenes (cis- and trans-) are used as solvents in the processing of rubber, fats, phenol, and camphor. They are most often produced and used as mixed isomers (cis- and trans-) and have been employed as coolants in refrigeration plants. No estimates of current production levels are available, however use is not widespread (U.S.EPA, 1984).

Guidelines, Regulations, and Standards

The American Conference of Governmental Industrial Hygienists (ACGIH) adopted in 1980 a Time-Weighted-Average (TWA) of 10 ppm and a Short Term Exposure Limit (STEL) of 20 ppm (ACGIH, 1980) in workroom air.

The Office of Drinking Water, United States Environmental Protection Agency, developed Health Advisory levels for 1,1-DCE. The health advisories are based upon the identification of adverse health effects associated with the most sensitive and meaningful noncarcinogenic endpoint of toxicity (U.S.EPA, 1985a). The one-day, ten-day and longer term advisories for a 10-kg child are each 1,000 ug/L. The Lifetime Health Advisory, based on a 2-year (chronic) drinking water study in rats, was 70 ug/L (U.S.EPA, 1985a).

Recently, the U.S.EPA has issued a proposed recommended maximum contaminant level (RMCL) for 1,1-dichloroethylene of 7 ug/L based on the same two year study which was used for the Health Advisory. The RMCL incorporated an extra safety factor to protect against possible carcinogenic effects (U.S.EPA, 1985b).

The one-day, ten-day and longer term Health Advisories for cis-1,2-dichloroethylene (cis-1,2-DCE) is 4,000 ug/L, 1,000 ug/L and 1,000 ug/L, respectively (U.S.EPA, 1985e). As with 1,1-DCE, the Advisories are calculated for a 10-kg child. The Lifetime Health Advisory is the same as that of 1,1-DCE, 70 ug/L (U.S.EPA, 1985e).

The one-day, ten-day and longer term Health Advisories for trans-1,2-dichloroethylene (trans-1,2-DCE) is 2,720 ug/L, 1,000 ug/L and 1,000 ug/L, respectively. As with 1,1-DCE, the Lifetime Health Advisory for trans-1,2-DCE is 70 ug/L (U.S.EPA, 1985d).

ENVIRONMENTAL EXPOSURE

Fate and Transport

Annual emissions of 1,1-DCE are estimated to be 1.3 million pounds per year. Both the instability in air and the limited solubility in water is thought to limit the persistence of 1,1-DCE in the environment. Due to their slower decomposition and higher solubility in water the 1,2-DCEs are thought to persist longer (U.S.EPA, 1984).

Ambient Levels

Letkiewicz et al. (1983) estimated that 4,789,000 individuals are exposed to 1,1-DCE levels at or above 0.2 ug/L in drinking water (U.S.), while 52,000 are exposed to levels above 5 ug/L. No individuals appear to be exposed to levels above 10 ug/L. For the majority of Americans estimated daily intake from public drinking water supplies is thought to be less than 0.0057 ug per kg per day.

During the period of 1978 through 1981 the Office of Science and Research of New Jersey Department of Environmental Protection surveyed public drinking water supplies throughout the state for volatile organics. Levels of 1,1-and trans-1,2-DCE are shown in Table I.

In the initial round of A-280 testing results conducted by the Office of Science and Research, trans-1,2-DCE was found in 12/635 samples from 566 purveyors. The median concentration was 2 ppb and the range was from 0.2-10 ppb (N.J. DEP, 1986).

Brodzinsky and Singh (1982) calculated median air levels of 1,1-DCE for urban/suburban areas and source dominated areas to be 20 ng/m^3 and 14,000 ng/m^3, respectively. Data from rural settlings showed 0.0 ng/m^3.

METABOLISM AND PHARMACOKINETICS

Absorption

DCEs are nonionizable, low molecular weight and lipid soluble substances, they are expected to be readily absorbed by any route of administration. This has been demonstrated by oral, intravenous, and intraperitoneal routes (Reichert et al., 1979, Jones and Hathaway, 1978). The blood gas partition coefficient of 5-10 indicates equilibrium is reached quickly (Andersen et al., 1979).

Distribution

1,1-DCE distributes widely after inhalation exposure (Jaeger et al., 1977a). Administered (^{14}C)DCE was found to be associated with liver,

kidney, and lung in both fed and fasted animals (Jones and Hathawav, 1978). Substantial amounts of (^{14}C) label appeared in kidney and liver after 30 minutes. The intracellular location of (^{14}C)1,1-DCE was associated with the mitochondrial and microsomal fractions (Jaeger et al., 1977a).

Metabolism

1,1-DCE is metabolized to dichloroacetaldehyde and to monochloroacetic acid by hepatic cytochrome P-450 (Costa and Ivanetich, 1984). These intermediates are primarily conjugated with glutathione, ultimately leading to the formation of mercapturic acids (McKenna et al., 1978).

Isolated hepatocytes metabolized trans-1,1-DCE primarily to dichloroacetic acid and traces of dichloroacetaldehyde and 2,2-dichloroethanol, but not monochloroacetic acid (Costa and Ivanetich, 1984). Metabolism of cis-1,1-DCE in the same system resulted in the production of 2,2-dichloroethanol and smaller amounts of dichloroacetic acid and dichloroacetaldehyde.

Excretion

At low dose levels 1,1-DCE probably is actively metabolized and excreted by biliary and urinary routes. At higher concentrations, exhalation becomes an important route for elimination of DCE (Jones and Hathaway, 1978).

1,1-DCE is eliminated rapidly. Most of the total absorbed dose is excreted after the first 24 hours following exposure (Jones and Hathaway, 1978). No data are available on the excretion rates of 1,2-dichloroethylenes.

Human Exposure and Body Burden

Human exposure to dichloroethylenes can occur through drinking water, food, and air. The levels vary depending on the proximity to the sources of production and usage. There is little information on the levels of DCEs in foods, although human exposure can occur by contamination of food from polyvinylidene wrappings or aquatic organisms that bioconcentrate 1,1-DCE from water (U.S.EPA, 1985).

Table I
OSR Survey, 1978-1981

Compound	Frequencies of Detection (%)	Average Detected Value (ug/L)
1,1-DCE	2	41
trans-1,2-DCE	6	16

The U.S.EPA estimated that 3% of the total drinking water supplies in the U.S. contain 1,1-DCE (U.S.EPA, 1984) at an estimated mean concentration level of 0.3 ug/L. An estimated daily exposure to 1,1-DCE by drinking water was determined to be 0.6 ug per day. The estimated daily intake of 1,1-DCE from urban/suburban air was approximately 0.4 ug (U.S.EPA, 1984). Thus, drinking water is a significant known contributor to the human body burden of 1,1-DCE.

HEALTH EFFECTS

Overview

Exposure to high concentrations of 1,1-DCE causes depression of the central nervous system, and may ultimately result in death by respiratory depression. 1,1-DCE has been shown to produce liver and kidney injury which could be expected from prolonged human exposure. There is only limited evidence that 1,1-DCE is carcinogenic. Among several studies employing various routes of exposure only one showed a positive result. In several tests with metabolic activation, 1,1-DCE appeared to be mutagenic. Information on the toxicity of 1,2-DCEs is very limited.

Human

Acute. Dichloroethylenes, like all chemicals in the chlorinated ethylene series, possess anesthetic properties. Irish (1963) estimated that an air concentration of 4,000 ppm is sufficient to produce a state of stupor which could result in death.

Chronic. No studies have been performed to estimate mutagenic and reproductive hazards of 1,1-DCE or 1,2-DCEs in exposed human populations.

Evaluation of cancer risks among workers occupationally exposed to DCE has been inconclusive (U.S.EPA, 1985a).

Animal

Acute. Data on acute oral toxicity of the DCEs, as measured by the LD_{50}, was determined for various species and strains of animals. An oral LD_{50} for 1,1-DCE of 1,800 mg/kg was determined for male rats (Ponomarkov and Tomatis, 1980). For mouse and dog, the oral LD_{50} values were found to be 217 mg/kg and 5,750 mg/kg, respectively (Jones and Hathaway, 1978; NIOSH, 1978).

Acute toxicity studies were carried out by Maltoni et al. (1985) on Swiss mice, Balb/c C3H, C57Bl, and Sprague-Dawley rats and Chinese hamsters. They concluded that the liver and kidney were the target organs of 1,1-DCE toxicity. Mice appeared to be more susceptible than rats or hamsters, and males more susceptible than females. Furthermore, the

variety of histopathologic changes did not vary with species or strain, however the same lesions were seen in these affected organs in all species.

For trans-1,2-DCE, an oral LD_{50} of 1.0 ml/kg (1,300 mg/kg) was determined for rats (Freundt et al., 1977).

Chronic. Continuous or repeated daily 90-day inhalation exposures of 0, 5, 15, 25, or 47 ppm 1,1-DCE were administered to rats, guinea pigs, dogs, rabbits and monkeys. Repeated exposures were found to produce no mortality or visible toxic signs. Continual exposure to 5 ppm for guinea pigs or 25 ppm for monkeys caused increased mortality. Hepatic toxicity was observed at 47 ppm but not at 25 ppm or lower (Prendergast et al., 1967).

A two-year chronic toxicity/oncogenicity study of rats given 0, 50, 100, and 200 ppm of 1,1-DCE in drinking water yielded no consistent dose related changes in any measured parameter (Rampy et al. 1977; Quast et al., 1983). The only pathological finding was a mid-zonal hepatocellular fatty change in the high dose group.

Quast et al. (1983) reported that four male and four female beagle dogs were administered 1,1-DCE in doses of 0, 6.25, 12.5, or 25 mg/kg daily for 97 days. The dose of 1,1-DCE was administered in a capsule in a vehicle of peanut oil. As compared with controls, the treated dogs had no differences in general appearance, of demeanor, body weight, food consumption, hematologic and clinical chemistry values, urinalysis, organ weight, and gross and microscopic appearance of tissues.

In a subchronic study conducted by the National Cancer Institute and National Toxicology Program (NCI/NTP, 1982), groups of 10 rats and 10 mice of both sexes were administered 1,1-DCE in corn oil by gavage 5 times per week at 0, 5, 15, 40, 100 or 250 mg/kg body weight for 13 weeks. After histopathologic evaluation, severe centrilobular necrosis was seen in three rats exposed to 250 mg/kg, which died during the first week. Hepatocellular cytomegaly and atrophy were seen in the 250 mg/kg dose group for both rats and mice. Minimal toxicity to the liver was seen at lower doses, particularly fatty metamorphosis.

A chronic study of the effects of 1,1-DCE was conducted by the National Cancer Institute and National Toxicology Program (NCI/NTP, 1982) using doses derived from the subchronic study which produced no apparent effects. Mice were treated with 2 and 10 mg/kg of 1,1-DCE in corn oil by gavage for 104 weeks. There were 50 animals for each dose group. Rats received 1 and 5 mg/kg per day, and were dosed in the same manner and same duration as the mice. Dose-dependent focal, multifocal, or diffuse necrosis of the liver was the most common pathologic change in dosed mice. In rats, a higher incidence of chronic inflamation of the kidney was observed at the 5 mg/kg dose.

Long-term carcinogenicity bioassays of 1,1-DCE were carried out at the Bologna Institute of Oncology (Maltoni, 1985) with male and female Sprague-Dawley rats, of different ages, Swiss mice, Balb/c mice, C3H mice, C57B1 mice and Chinese hamsters. Exposure to 1,1-DCE was primarily by inhalation, although in one experiment with rats, 1,1-DCE was administered by stomach tube. Hepatic changes consisted essentially of centrilobular necrosis, particularly in the 200 mg/kg dose group. Severe necrosis of the epithelial tubules from the kidney cortex was seen frequently in mice of all strains, particulary at the 200 mg/kg dose level. Excess mortality in mice exposed to 50, 100, and 200 ppm DCE was attributed to acute toxic effects of the monomer. In mice exposed to 10 and 25 ppm 1,1-DCE, there was no difference between exposed and controls in the incidence of inflammatory response and regressive changes; the survival rates were generally higher in comparison with the control groups.

Cis-1,2-Dichloroethylene. No information was located to assess the toxicity of cis-1,2-DCE.

Trans-1,2-Dichloroethylene. Wistar rats were exposed to trans-1,2-DCE at 0, 200, 1,000, or 2,000 ppm for eight hours per day, 5 day per week for 1, 2, 8, or 16 weeks. Exposure at 200 ppm produced a slight degeneration of liver lobules and lipid accumulation in Kupffer cells of one rat. Slight decreases in the numbers of erythrocytes were observed at 200 and 1,000 ppm dose levels (Freundt et al., 1977).

No data are available to evaluate the potential subchronic or chronic toxicity of trans-1,2-DCE after chronic exposure.

Behavioral and Central Nervous System

At high concentrations the dichloroethylenes possess anesthetic properties (Irish, 1963). The trans-1,2-DCE appears to be twice as potent as the cis-1,2-DCE in depressing the central nervous system (U.S.EPA, 1984).

Reproductive, Embryotoxic, and Teratogenic

The teratogenic potential of inhaled 1,1-DCE has been evaluated in rats and rabbits (Murray et al., 1979). No evidence was seen that concentrations less than necessary to produce maternal toxicity had any effect on fetal development.

Genetic

1,1-DCE was mutagenic in S. typhimurium strains only with metabolic activation (Simmon et al., 1977) and in E. coli (Greim et al., 1975). Other tests for mutagenicity and chromosomal aberration by 1,1-DCE proved negative (U.S.EPA, 1984). Both cis- and trans-1,2-DCE were negative in the E. Coli assay when tested in the same concentrations as 1,1-DCE (Greim et al., 1975).

Carcinogenicity

1,1-DCE has been classified by the EPA (U.S.EPA, 1985b) into Group C as a possible human carcinogen.

A large number of studies have been carried out to assess the carcinogenic potential of 1,1-DCE. These are summarized in Table II.

Sprague-Dawley male and female rats were exposed by drinking water to 0, 50, 100, and 200 ppm per day for 2 years (Quast et al., 1983). The time weighted-average of mg/kg body weight per day was calculated to be 7, 10, and 20 for males and 9, 14, and 30 for females. The only treatment related effect seen in this study was an increase in midzonal hepatocellular fatty change in the liver of males at 10 and 20 mg/kg while for females it occurred at all dose levels. Minimal hepatocellular swelling and fatty changes were detected.

Studies on the carcinogenic potential of 1,1-DCE were carried out at the Bologna Institute of Oncology (Maltoni et al., 1985). Sprague-Dawley rats, Swiss mice and Chinese hamsters were exposed to 1,1-DCE by inhalation for 4 hours daily, 4 to 5 days per week for 12 months. Rats (16 weeks old) were exposed to 1,1-DCE at 10, 25, 50, 100, and 150 ppm. Sixteen-week-old mice were exposed at 10 and 25 ppm. Twenty-eight-weeks old hamsters were exposed at 25 ppm. Rats were also exposed by gavage to 0.5, 5, 10, and 20 mg/kg per day 1,1-DCE dissolved in olive oil. Studies in rats were completed in 137 weeks for the inhalation study, and in 147 weeks for the ingestion study. The duration of studies in mice and hamsters was 121 and 157 weeks, respectively.

There was no significant tumor development ($p \leq .05$) in hamsters or rats. There was an increased incidence of mammary tumors in female rats, however it was not dose-related and the spontaneous occurrence of tumors was high in controls. Therefore, tumor induction by 1,1-DCE in hamster or rats was inconclusive.

In male Swiss mice exposed by inhalation to 1,1-DCE, there was a significant occurrence of kidney adenocarcinomas at 25 ppm. There was a higher incidence of lung and mammary adenocarcinomas, however the relevance to exposure to 1,1-DCE is not clear. This was thought to be treatment related since no tumors of this type were observed in controls. Maltoni et al. (1985) concluded that the toxic and carcinogenic effects of 1,1-DCE may depend on species, strain, and sex of tested animals.

The NCI/NTP (1982) carcinogenicity bioassay was carried out on Fisher 344 rats and B6C3F1 mice at doses 1 and 5 mg/kg per day for rats, and 2 and 10 mg/kg for mice. The animals were treated for 5 days per week for a total of 104 weeks. There was some indication of increased tumor incidence in a number of organs for both rats and mice. However, the only statistically significant ($p \leq 0.05$) increased response was for lymphomas in the low dose group of female mice, as compared with matched controls

using Fisher's exact test. However, when the lymphoma response was tested for linear trend, it was negative. Therefore, the lymphoma response did not appear to be dose-related. In addition, the lymphoma incidence in the control group was low when compared with historical controls. The conclusion of the NCI/NTP report (1982) is that 1,1-DCE was not carcinogenic to F344 rats or B6C3F1 mice under the conditions of this assay. However, the highest dose administered was not adequately shown to be the maximum tolerated dose.

1,1-DCE was tested in a two-stage carcinogenesis model in female Ha: ICR and Swiss mice (Van Duuren et al., 1979). Application of 1,1-DCE dose (121 mg per mouse) to the shaved backs of mice resulted in no tumors. However when one application of DCE was followed by repeated application of phorbol myristate acetate, a significant increase (p 0.005) in skin papillomas was observed, indicating that 1,1-DCE was acting as a tumor initiator in mouse skin. The relevance of these results with regard to the assessment of health effects is not clear.

The National Toxicology Program has approved cis-1,2-DCE, trans-1,2-DCE, and a mixture of both of them for chronic toxicity testing.

Epidemiologic data regarding the carcinogenic potential of 1,1-DCE are inconclusive. Ott et al. (1976) studied 138 Dow Chemical Company workers exposed primarily to 1,1-DCE dating back to 1940. A summary of estimated cumulative exposure is shown in Table III, and the incidence of deaths in Table IV.

As indicated in the table, the size of the population having a long exposure to 1,1-DCE is small. It is also unclear whether those workers with the longest exposure were heavily exposed. Thus the U.S.EPA concludes (1985b) that for the purposes of detection of cancer, this study is inadequate.

QUANTITATIVE RISK ASSESSMENT

Studies Useful for Risk Assessment

There are eighteen chronic animal studies that provide information on the carcinogenicity/toxicity of 1,1-DCE. Eleven involve inhalation exposure, five are oral (four gavage, one drinking water). Only in Swiss mice inhaling 1,1-DCE was there a significant increase in tumors, specifically kidney adenocarcinomas, at 25 ppm for 12 months (Maltoni, 1985). This is the only study showing significant increases in tumors that may be treatment related. There is limited evidence to classify 1,1-DCE as a carcinogen. Therefore, an Acceptable Daily Intake (ADI) is derived on the basis of chronic toxicity using an additional safety factor to protect against possible carcinogenicity (U.S.EPA, 1985a).

Table II

Summary of Results from Carcinogenicity Studies with 1,1-DCE in Animals (U.S. EPA, 1984)

Route	Species	Dose	Study Duration	Carcinogenic Response	Reference
Inhalation	Swiss Mice	10 ppm 25 ppm for 12 months	98 weeks 98 weeks	negative positive	Maltoni, 1977; Maltoni et al., 1985
Inhalation	CD-1 Mice	55 ppm	52 weeks	negative	Lee et al., 1978
Inhalation	Sprague-Dawley Rats	10 ppm 25 ppm 50 ppm 100 ppm 150 ppm for 12 months	98 weeks 98 weeks 98 weeks 98 weeks 98 weeks	negative negative negative positive positive	Maltoni, 1977; Maltoni et al., 1985
Inhalation	Sprague-Dawley Rats	75 ppm 200 ppm for 12 months	lifetime	negative negative	Viola and Caputo, 1977
Inhalation	Rats (Wistar)	75 ppm 200 ppm for 12 months	lifetime	negative	Viola and Caputo, 1977
Inhalation	Rats (CD)	55 ppm	52 weeks	negative	Lee et al., 1978
Inhalation	Rats	25 ppm 75 ppm for 18 months	104 weeks	negative	Rampy et al., 1977
Inhalation	Chinese Hamsters	25 ppm	74 weeks	negative	Maltoni, 1977; Maltoni et al., 1985
Oral (gavage)	Rats (BDIV)	50 mg/kg/day	120 weeks	negative	Ponomarkov and Tomatis, 1980

Table II (Continued)

Summary of Results from Carcinogenicity Studies with 1,1-DCE in Animals

Route	Species	Dose	Study Duration	Carcinogenic Response	Reference
Oral (gavage)	Rats (Sprague-Dawley)	0.32 mg/kg/day 3.2 mg/kg/day 6.4 mg/kg/day 13 mg/kg/day	136 weeks	negative negative negative negative	Maltoni, 1985
Oral (drinking Water)	Rats (Sprague-Dawley)	7-9 mg/kg/day 10-14 mg/kg/day 20-30 mg/kg/day	104 weeks	negative negative negative	Rampy et al., 1977 Quast, et al., 1983
Oral (Gavage)	Rats (F344)	1 mg/kg/day 5 mg/kg/day	104 weeks	negative	NTP, 1982
	Mice (B6C3F1)	2 mg/kg/day 10 mg/kg/day	104 weeks	negative	NTP, 1982
Subcutaneous	Swiss mice	121 mg	repeated	inactive as initiator of cancers in whole mice	Van Duuren, et al., 1979
		121 mg	single dose	active as initiator with phorbol myristate acetate	

TABLE III.

Estimated Cumulative Dose, Duration of Exposure and Date of First Exposure Among 138 Individuals Exposed to Vinylidene Chloride

Exposure measures	Total population
Estimated career dosage (TWA x months of exposure)	
500 ppm months	50
500-999 ppm months	28
1000-1999 ppm months	28
2000+ ppm months	32
Duration of exposure	
12 months	35
12-59 months	43
60-119 months	35
120+ months	25
Date of first exposure	
1940-1949	9
1950-1959	74
1960-1969	55

[a] Status as of January 1974.

SOURCE: Ott et al., 1976.

TABLE IV.

Observed and Expected Deaths Among
Vinylidene Chloride Employees by Cause
1945-1973

	Total cohort		Total cohort 15+ years after first exposure	
	Observed	Expected	Observed	Expected
All causes	5	7.5	2	2.6
Total malignancies	1	1.1	1	0.5
Digestive cancer		0.3		0.1
Respiratory cancer	1	0.3	1	0.2
All other		0.5		0.2
Cardiovascular disease	1	2.6	0	1.2
Pneumonia/influenza		0.1		0.0
Pulmonary emphysema/ asthma		0.1		0.0
Cirrhosis of liver	1	0.3	0	0.1
External causes		2.3	0	0.5
All other		1.0		0.3

SOURCE: Ott et al., 1976.

In many chronic toxicity studies of 1,1-DCE, mild toxic effects to the liver and kidney were reported. In the absence of stronger evidence for carcinogenicity, an ADI can be developed based on these effects.

The most appropriate studies for derivation of an ADI would be those in which exposure is through ingestion by drinking water or gavage. Studies that have identified toxic effects to liver after ingestion of 1,1-DCE are Quast et al. (1983) and NCI/NTP (1982). These are the most appropriate studies for risk assessment. Quast et al. (1983) found periportal hepatocellular hypertrophy in male rats at 20 mg/kg per day, and in females at all dose levels (9, 14, and 30 mg/kg per day). A lowest observed adverse effect level (LOAEL) of 9 mg/kg could be identified from this study. From the NCI/NTP study, necrosis of the liver (focal, multifocal or diffuse) was observed more frequently in dosed mice than in controls. A LOAEL of 2 mg/kg could be identified from this study. Since the NCI/NTP study employed doses of 1,1-DCE lower than the Quast study, a better estimate for a LOAEL could be derived from the NCI/NTP study (1982). The mouse appears to be more sensitive than the rat to the toxic effects of 1,1-DCE (Maltoni et al., 1985 and NCI/NTP, 1982). Therefore, the toxic effects to mouse liver (NCI/NTP, 1982) were selected as the study for the ADI development, because of the lower dose employed and the sensitivity of the mouse to 1,1-DCE.

In the absence of data on the chronic toxicity of 1,2-DCEs, ADIs, derived from 1,1-DCE were thought to apply to 1,2-DCEs as well, although without an additional safety factor.

Calculation of the Health-Based Maximum Contaminant Level

1,2-Dichloroethylene

2 mg/kg = LOAEL (NCI/NTP, 1982)

$$ADI = \frac{2\ mg/kg/day \times 1.0 \times 70\ kg \times (5/7)}{100 \times 10} = 0.10\ mg/day$$

$$MCL = \frac{0.10\ mg/day\ (.2)}{2\ L/day}$$

MCL = 10 ug/L

1,1-Dichloroethylene

$$ADI = \frac{2\ mg/kg/day \times 1.0 \times 70\ kg \times 5/7}{100 \times 10} = \frac{0.140\ mg/day}{10a}$$

ADI = 0.010 mg/kg

$$MCL = \frac{0.010 \text{ mg/day } (0.2)}{2 \text{ L/day}}$$

$$MCL = 0.001 \text{ mg/L} = 1.0 \text{ ug/L}$$

where:	2 mg/kg/day	=	LOAEL
	1.0	=	ratio of administered dose absorbed
	70 kg	=	mass of protected individuals
	100	=	uncertainty factor appropriate for use with animal data with no comparable human data
	10	=	uncertainty factor appropriate for use in conversion of a LOAEL to NOAEL
	2 L	=	water consumption per day
	0.2	=	contribution from drinking water alone
	10a	=	safety factor to protect against possible carcinogenicity
	5/7	=	days of exposure per week

Assumptions and Uncertainty

Derivation of the health-based MCL is based on the assumption that 1,1-DCE is probably not a human carcinogen. There is no evidence at this time that it is a human carcinogen. Furthermore, 1,1-DCE has been found not to be carcinogenic in most animal studies. Chronic studies in animals have reported liver and kidney injury. Liver toxicity in mice (NCI/NTP, 1982) was used for derivation of a health-based MCL. It is assumed that the human is more sensitive to 1,1-DCE liver injury than the mouse.

Since 1,1-DCE has been classified as a possible human carcinogen by the U.S.EPA (1985b), a possible procedure for handling these compounds is to use either an extra safety factor of 10 or to use a 10^{-5} risk factor derived from a carcinogenesis study. Application of the extra factor of 10 to the MCL would result in a health-based MCL of 1.0 ug/L.; calculation of a 10^{-5} risk level from the Maltoni et al.(1985) Swiss mice experiment would result in a health-based MCL of 0.30 ug/L (U.S.EPA, 1985b). Selection of 1.0 ug/l for 1,1-dichloroethylene health-based MCL appears to be most appropriate.

There are no suitable studies available on (cis-/trans-)1,2-DCE that could be used to calculate an ADI. The available data indicates that the cis-/trans- forms appear to be less toxic than 1,1-DCE. Therefore, the ADI level derived for 1,1-DCE, based only on chronic toxicity and not on possible carcinogenic effects, would probably assure a safe level for 1,2-DCE as well.

Conclusions

A health-based maximum contaminant level of 1 ug/L was derived for

1,1-dichloroethylene to protect against possible liver toxicity and carcinogenicity. A level of 10 ug/L is recommended for cis- and trans-1,2 dichloroethylenes, and is based on the chronic toxicity of 1,1-dichloroethylene, with no adjustment for possible carcinogenic effects.

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