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Environmental Health Criteria for Methylene Chloride

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METHYLENE CHLORIDE (SECOND EDITION)

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INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA
FOR
METHYLENE CHLORIDE

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ENVIRONMENTAL HEALTH CRITERIA FOR METHYLENE CHLORIDE

1. SUMMARY

1.1 Identity, physical an chemical properties, and analytical methods

Methylene chloride (dichloromethane) is a clear, highly volatile, non-flammable liquid with a penetrating ether-like odour. Pure dry methylene chloride is a very stable compound. Methylene chloride hydrolyses slowly in the presence of moisture, producing small quantities of hydrogen chloride. Commercial methylene chloride is normally inhibited with small quantities of stabilisers to prevent acidification and corrosion.

Analytical methods are available for the determination of methylene chloride in biological media and environmental samples. All methods involve gaschromatography in combination with a suitable detector. In this way, very low detection limits have been reached (e.g. in food: 7 ng/sample; water: 0.01 $\mu g/\ell$; air: 0.5 ppb; blood: 0.022 mg/ℓ).

1.2 Sources of human and environment exposure

World production of methylene chloride is estimated to be 570 kt/y. Most applications are based on the solvent capacity for grease, plastics and paint binding agents, in combination with its volatility and stability; it is also no-flammable. The worldwide usage pattern breaks down into aerosols (20-25%), paint remover (25%), process solvent in the pharmaceutical industry (35-40%), miscellaneous uses (e.g. polyurethane foam manufacturing) and metal cleaning (10-15%). The usage of methylene chloride shows some indication of a decrease, at least in Western Europe!

More than 99% of the atmospheric releases of methylene chloride result from its use as an end-product by various industries, and the use of paint removers and aerosol products at home.

1.3 Environmental transport, distribution and transformation

Due to its high volatility, most of the methylene chloride released to the environment will partition to the atmosphere, where it will degrade by reaction with photochemically produced hydroxy radicals with a half-life of 6 months.

Abiotic degradation in water is slow compared to evaporation. Methylene chloride has shown to disappear rapidly from soil and groundwater.

The aerobic and anaerobic degradation of methylene chloride has been proven by a variety of different test systems. Its complete biodegradation, especially by acclimated bacterial cultures under aerobic conditions, is rapid (e.g. 49-66% mineralisation in 50 h with acclimated municipal sludge). In bioreactors up to 10% degradation per h is achievable. There is no evidence that significant bioaccumulation or biomagnification of methylene chloride along the food chain will occur.

Methylene chloride is expected to have no significant impact on stratospheric ozone depletion. It will not contribute significantly to photochemical smog-formation.

1.4 Environmental levels and human exposure

Methylene chloride has been detected in ambient air of rural and remote areas, at concentrations of 0.07-0.29 $\mu g/m^3$. In suburban areas, the average concentration is < 2 $\mu g/m^3$ and in urban areas < 15 $\mu g/m^3$. In the vicinity of hazardous waste sites up to 43 $\mu g/m^3$ was found. Precipitation may also contain methylene chloride.

Methylene chloride enters the aquatic environment through waste water discharges from various industries, and methylene chloride has been found in surface water, ground water and sediments.

Exposure of members of the general public to methylene chloride will occur from its use in consumer products, such as paint removers, which can result in relatively high levels being found in indoor air. Occupational exposure during production arises primarily during filling and packaging (manufacturing is in closed systems). Because of its use in paint strippers, occupational exposure to methylene chloride occurs during formulation of paint-remover, original equipment manufacture, maintenance sector and commercial furniture refinishers. Methylene chloride is widely used as a process solvent in the manufacture of a variety of products, in particular in the industries mentioned above (section 1.2)

Biological monitoring of methylene chloride exposure can be based on measurement of the solvent itself in exhaled air or blood. However, as production of carbon monoxide with exposure for more than 3-4 h/day appears to be the limiting factor in regard to health risk, biological monitoring based upon either analysis of carbon monoxide in exhaled air or of CO-Hb in blood is to be preferred. However, this can only be applied in non-smoking subjects. Sampling should be done at about 0-2 h post-exposure, or after 16 h i.e. on the following morning.

Post-exposure CO-Hb levels at 2 h after exposure ceases are not expected to exceed 2-3%, and at 16 h 1%, in the case of an 8 h exposure to less than 350 mg/m^3 methylene chloride in non-smokers.

1.5 Kinetics and metabolism

Methylene chloride is rapidly absorbed though the alveoli of the lungs into the systemic circulation. It is also absorbed from the gastrointestinal tract and dermal exposure results in absorption but at a slower rate than the other exposures.

It is quite rapidly excreted, mostly via the lungs in the exhaled air. It can cross the blood-brain barrier, it can be transferred across the placenta, and small amounts can be excreted in urine or in milk.

At high concentrations, most of the absorbed methylene chloride is exhaled unchanged. The remainder is metabolised to carbon monoxide, carbon dioxide, and

inorganic chloride. Metabolism occurs by either or both of two pathways, whose relative contribution to the total metabolism is markedly dependent on the dose and on the animal species concerned.

One pathway involves oxidative metabolism mediated by cytochrome P-450 and leads to both carbon monoxide and carbon dioxide. This pathway appears to operate similarly in all rodents studied and in man. Whilst this is the predominant metabolic route at lower doses, saturation occurs at a relatively low dose (around 1800 mg/m³). Increasing the dose above the saturation level does not lead to extra metabolism by this route.

The other pathway involves a glutathione transferase, and leads via formaldehyde and formate to carbon dioxide. This route seems only to become important at doses above the saturation level of the 'preferred' oxidative pathway. In some species (e.g. the mouse) it becomes the major metabolic pathway at sufficiently high doses. In contrast, in other species (e.g. hamster, man) it seems to be used very little at any dose.

Species difference in GST metabolism correlate well with the observed species difference in carcinogenicity. The extent of metabolism by this pathway in relevant species has been used as the basis for a kinetic model to describe the metabolic behaviour of methylene chloride in various species.

1.6   Effects on organisms in the environment

Algae and aerobic bacteria show no inhibition of growth below 500 mg/ℓ. Bacteria have been identified which are able to grow in the presence of methylene chloride at much higher concentrations including saturated water (Section 4.2.4.1). Anaerobic bacteria are more sensitive; growth inhibition has been observed at 1 mg/ℓ in anaerobic biological sludge.

In soil 10 mg/kg strongly decreased the ATP content of the biomass including fungi and aerobic bacteria, and induced transient inhibitionof enzyme activity. The no effect level was 0.1 mg/kg. In earthworms methylene chloride is moderately toxic (100-1000 μg/cm²). In sediment no toxic effects were observed even at very high levels.

In higher plants no effects were found after exposure for 14 days to 100 mg/m³.

Adult fish seem to be relatively insensitive to methylene chloride even after prolonged exposure (14-d LC_{50} > 200 mg/ℓ). The effect of methylene chloride on *Daphnia* is difficult to assess given the large variation in the outcome of the studies performed. The lowest reported EC_{50} was 12.5 mg/ℓ.

In the aquatic environment, fish and amphibian embryos have been shown to be the most sensitive with effects on hatching from 5.5 mg/ℓ.

1.7 Effects on laboratory mammals and *in vitro* test systems

1.7.1 Single exposure

The acute toxicity of methylene chloride by inhalation and oral administration is low. The inhalation 6h-LC_{50} values for all species are between 40,200 and 52,000 mg/m^3. Oral LD_{50} values of 1410 - 3000 mg/kg were recorded. Acute effects after methylene chloride administration by various routes of exposure are primarily associated with the central nervous system (CNS) and the liver and these occured at high doses. CNS disturbances were found of 14,100 mg/m^3 and higher with slight changes in EEG at 1770 mg/m^3. Slight histological changes in the liver were found of 17,700 mg/m^3 and higher. Occasionally other organs are affected such as the kidney or respiratory system. Cardiac sensitization to adrenaline-induced arrhythmias has been reported and cardiovascular effects were reported but the effects were inconsistent.

1.7.2 Short- and long-term exposure

Prolonged exposure to high concentrations of methylene chloride ($\geq$ 17,700 mg/m^3) caused reversible CNS effects, slight eye irritation and mortality in several laboratory species. Body weight reduction was observed in rats at 3500 mg/m^3 and in mice from 17,700 mg/m^3. Slight effects on the liver were noted in dogs continuously exposed to 3500 mg/m^3 for up to 100 days. After intermittent exposure, effects on the liver were observed in rats at 3500 mg/m^3 and in mice at 14,100 mg/m^3.

Other target organs were the lungs and the kidneys. In mice, effects on the lungs were restricted to the Clara cells after exposure to 7100 mg/m^3 and higher for 10 days.

No evidence of irreversible neurological damage was seen in rats exposed by inhalation to concentrations up to 7100 mg/m^3 for 13 weeks.

Oral administration of methylene chloride to rats caused effects on the liver from about 200 mg/kg per day.

1.7.3 Skin and eye irritation

Methylene chloride is moderately irritant to the skin. Only corrosive effects could occur under hard conditions. Reversible irritating effects appeared when methylene chloride gets into the eyes.

1.7.4 Developmental and reproductive toxicity

Methylene chloride is not teratogenic in rats or mice at concentrations up to 16,250 mg/m^3. No evidence of an effect on the incidence of skeletal malformations or other developmental effects were observed in 3 animal studies. Small effects on either foetal or maternal body weights were reported at 4400 mg/m^3. A two-generation reproductive toxicity study in rats exposed to methylene chloride by inhalation at concentrations up to 1500 mg/m^3, 6 h/day, 5 days/week for 14 weeks did not show evidence of an

adverse effect on any reproductive parameter, neonatal survival or neonatal growth in either the F_0 or F_1 generation.

1.7.5 Mutagenicity and related end-points

Under appropriate exposure conditions, methylene chloride is mutagenic in prokaryotic microorganisms with or without metabolic acivation (*Salmonella* or *E. coli*). In eukaryotic systems it gives either negative or, in one case, weakly positive results. *In-vitro* gene mutation assays and tests for UDS in mammalian cells were uniformly negative. *In vitro* assays for chromosomal aberrations using different cell types gave positive results, whereas negative or equivocal results were obtained in tests for SCE induction.

The majority of the *in vivo* studies reported have provided no evidence of mutagenicity of methylene chloride (e.g. chromosome aberration assay, micronucleus test or UDS assay). A very marginal increase in frequencies of SCEs, chromosomal aberrations and micronuclei in mice has been reported following inhalation exposure to high concentrations of methylene chlrodie. The significance of these results is questionable due to methodological deficiencies in the statistical analysis.

There was no evidence of binding of methylene chloride to DNA or DNA damage in rats or mice given high doses of methylene chloride. These studies are potentially the most sensitive *in vivo* studies, the best of which are capable of detecting one alkylation in 10^6 nucleotides.

Within the limitations of the short-term tests currently available, there is no conclusive evidence that methylene chloride in genotoxic *in vivo*.

1.7.6 Chronic toxicity and carcinogenicity

Methylene chloride is carcinogenic in the mouse, causing both lung and liver tumours, following exposure to high concentrations (7100 and 14,100 mg/m^3) of methylene chloride. The incidence of both lung and liver tumours was increased in mice exposed to 7100 mg/m^3 methylene chloride for 26 weeks and maintained for a further 78 weeks. There was no substantial evidence of associated toxicity or hyperplasia in the target organs.

Syrian hamsters exposed to methylene chloride by inhalation at concentrations up to 12,400 mg/m^3 for 2 years showed no evidence of a carcinogenic effect related to exposure to methylene chloride.

Rats exposed to methylene chloride via various routes have shown increased incidences of tumours at certain sites. An excess of tumours in the region of the salivary gland was reported in female rats exposed to either 5300 or 12,400 mg/m^3 methylene chloride for 2 years. This excess was only evident when the tumours, which were all of mesenchymal origin, were grouped together for statistical analysis. As the tumours arose from a variety of different cells, the statistical approach adopted was inappropriate. Furthermore, it was reported that the rats in the study had been infected

with a common viral disease (sialodacryoadenitis) early in the study, an infection that affects primarily the salivary gland. It is likely that these tumours were not causally-related to exposure to methylene chloride but that the exposure had exacerbated the response of the infection in the region of the salivary gland. The response was not seen in a second study in which rats were exposed to either 3500, 7100 or 14,100 mg/m³ methylene chloride for their lifetime. A further inhalation study in rats exposed to methylene chloride at concentrations up to 1770 mg/m³ for their lifetime showed no evidence of carcinogenicity. Rats exposed to methylene chloride via their drinking water or by gavage similarly showed no substantive evidence of carcinogenicity.

An increased incidence of benign mammary tumours in rats exposed to methylene chloride has been reported in three studies, two following exposure by inhalation and the third by gavage. There are no reports of increases in mammary tumour incidence in hamsters or in mice receiving methylene chloride at comparable dose levels. The dependance of mammary tumours upon pituitary hormones in both male and female rats has been established unequivocally (Welsch & Nagasawa, 1977; Welsch 1985). In the rat, prolactin acts as both an "initiator" and "promoter" of mammary carcinogenesis. There is good evidence that increased prolactin levels increase the incidence of mammary tumours (e.g. the grafting of multiple pituitary glands into Sprague-Dawley rats increases the incidence of mammary tumours (Welsch et al., 1970), there is a positive correlation between elevated blood prolactin levels and mammary tumours in aged R-Amsterdam female rats (Kwa et al., 1974)). Treatments that induce hyperprolactinaemia in female rats which have received carcinogens induce a dramatic increase in tumour incidence. These treatments include adrenalectomy, pituitary homografts and high dietary fat (Welsch & Nagasawa, 1977).

The mechanism by which methylene chloride induces mammary adenomas in the rat is important for human hazard assessment. Female Sprague-Dawley rats receiving methylene chloride have a high blood level of prolactin (Breslin and Landry, 1986). In common with the response to other agents which act via hyperprolactinaemia, the methylene chloride-induced response is of benign neoplasms only. There is no evidence for the binding of methylene chloride to the DNA of other tissues and hence it seems unlikely that it will bind to mammary tissue when the primary site of metabolism is the liver. It seems most likely, therefore, that the increased incidence of mammary adenomas is the result of an indirect mechanism operating via hyperprolactinaemia.

In humans, there is conflicting evidence on whether or not mammary tumours are as responsive to prolactin as is the case in the rat (Sinha, 1981). The rat has elevated levels of prolactin when fed *ad libitum* in comparison to a restricted dietary regimen and this may explain why the mammary tumour incidence is so easily responsive to a variety of environmental and other effects. In the rat, however, prolactin is luteotrophic. An increase in the circulating levels of prolactin will lead to an increase in progesterone and exogenous oestrogen levels. It is the presence of all three factors that causes tubular-alveolar growth of the mammary glands which ultimately leads to tumour development. Prolactin is not luteotrophic in primates. It is unlikely, therefore, that this mechanism of tumour development is of relevance to man (Neumann, 1991).

The mechanism of production of mammary tumours in the rat involving hyperprolactinaemia will occur only at doses of methylene chloride which affect prolactin levels. There is no direct information on prolactin levels in rats receiving low doses of methylene chloride, but no increase in mammary adenomas has been observed following the administration of low doses in both inhalation and drinking water studies (i.e. below 250 mg/kg bodyweight).

The evidence on the mechanism of action of mammary tumour formation in the rat, taken together with the absence of these effects in mice or hamsters suggest that the findings are of little relevance to human hazard assessment.

1.8 Effects on humans

Methylene chloride will irritate the skin and eyes especially when evaporation is prevented. In these circumstances, prolonged contact may cause chemical burns. A case of serious pulmonary oedema has been reported after excessive inhalation. Fatalities due to accidental inhalation and skin contamination have been reported. The main toxic effects of methylene chloride are reversible CNS depression and CO-Hb formation. Liver and renal dysfunctions and effects on haematological parameters have also been reported following exposure to methylene chloride.

Neurophysiological and neurobehavioural disturbances have been observed in human volunteers exposed to methylene chloride at concentrations of 694 mg/m^3 for 1.5-3.0 h. No evidence of neurological effects was seen in men with for several years exposure to methylene chloride at concentrations ranging from 260 to 347 mg/m^3. Similarly, a group of retired airplane strippers with a long history of exposure to methylene chloride (22 years) at high but unspecified levels performed a battery of neurophysiological and psychological tests within the "normal" range, when compared with a control group who had a history of either no or only low exposure to methylene chloride.

An increased rate of spontaneous abortion in employees in Finnish pharmaceutical industries have been attributed to exposure to methylene chloride. A causal relationship was not established because of insufficiencies in the design of the study.

Several mortality studies in relevant cohorts show an inconsistent pattern in the causes of death. Excesses in mortality from specific diseases (eg pancreatic cancer, ischaemic heart disease) were not consistantly increased, but confined to single studies. These effects cannot be attributed to exposure to methylene chloride.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Formula:	CH_2Cl_2

Structure:

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      Cl
      |
   Cl-C-H
      |
      H
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Molecular mass:	84.93 (Weast et al., 1988)
Common name:	Methylene chloride
Synonyms:	DCM
	Dichloromethane
	Freon 30
	Methane dichloride
	Methylene bichloride
	Methylene dichloride
	Methylenum chloratum
Tradenames:	Aetothene MM
	Freon 30
	Narkotil
	Solaestim
	Solmethine
CAS name (9 CI):	Methane, dichloro-
CAS registry N°:	75-09-2
EC registry N°:	602-004-00-3
EINECS registry N°:	200-838-9
RTECS registry N°:	PA 8050000
Purity of technical product:	99.9% (analytical grade)
Impurities of technical product:	Mostly C_1- and C_2-chlorinated hydrocarbons (up to 200 mg/kg) (ECETOC, 1984)
Stabiliser:	Typically 0.005-0.2% (w/w) of methanol, ethanol, amylene (2-methyl-but-2-ene), cyclohexane or tertiary butylamine (ECSA, 1989)

2.2 Physical and chemical properties

Methylene chloride is a clear, colourless, highly volatile, non-flammable liquid with a penetrating ether-like odour. Pure dry methylene chloride is a very stable compound and will not produce corrosion. In the presence of water, it may undergo very slow hydrolysis to produce small quantities of hydrogen chloride which can lead to corrosion, e.g. to mild steel. This reaction is accelerated by elevated temperatures and the presence of alkali or metals. Methylene chloride hydrolyses very slowly in the presence of moisture. In the vapour phase under abnormal conditions (elevated temperatures, high UV light exposure, flame, sparks, red hot surfaces) methylene chloride may be decomposed to give small amounts of hydrogen chloride, carbon monoxide and phosgene (ECSA, 1989). Other physical and chemical properties are in Table 1.

Table 1. Physical and chemical properties

Parameter, units	Value	Reference
Boiling temperature, °C at 1,013 hPa	40	Weast et al., 1988
Melting temperature, °C at 1,013 hPa	-95.1	Weast et al., 1988
Relative density of liquid D_4^{20} (water at 4 °C = 1,000 kg/m³)	1.3266	Weast et al., 1988
Vapour pressure, hPa at 20°C	470	ECSA, 1989
Saturation concentration in air, kg/mℓ at 20°C	1.7	Calculated
Vapour density at 20°C (air = 1)	2.93	IPCS, 1984
Threshold odour concentration, mg/m³ (odour: ether-like)	743	Leonardos et al., 1969 as quoted in IPCS, 1984
	700-1060	DFG, 1981 as quoted in ECETOC, 1984
	880	Amoore and Hautula, 1983
	540-2,160	Ruth, 1986 as quoted in ATSDR, 1991
Solubility in water, g/kg at 20°C	20	Verschuuren, 1983
	13.0	Horvath, 1982
Solubility in alcohol, ether, acetone and benzene		Weast et al., 1988
Partition coefficients, at 20°C log P_{ow} (octanol/water)	1.25	Jow and Hansch as quoted in BUA, 1985
	1.3	Hansch et al., 1979 as quoted in ATSDR, 1991
log K_{oc} (octanol/sediment)	0.89	Banerjee et al., 1980 as quoted in BUA, 1986
	1.45	Koch et al., 1983
	0.94	Calculated
	1.05	Calculated
Henry's Law constant, Pa.m³/mol at 20°C	380	Smith et al., 1980 as quoted in BUA, 1986
Flash point, closed cup, °C	None	ECSA, 1989
Explosion limits in air*, %	13-22	ECSA, 1989
Auto-flammability, ignition temp., °C	605	ECSA, 1989

* This is with a high energy source; these conditions are unlikely to arise in normal operations.

Commercial methylene chloride is normally inhibited with small quantities of stabilisers (Section 2.1) to prevent acidification and corrosion. Applications in aggressive conditions, such as special metal cleaning operations may require more sophisticated stabiliser technology. Poorly stabilised methylene chloride can react violently with aluminium or other light metal.

2.3   Conversion factors

Conversion factor for methylene chloride concentrations in air, calculated at 20°C and 1,013 hPa are:

$1 \ mg/m^3 = 0.28 \ ppm$
$1 \ ppm = 3.53 \ mg/m^3$

and for carbon monoxide:

$1 \ mg/m^3 = 0.86 \ ppm$
$1 \ ppm = 1.16 \ mg/m^3$

2.4   Analytical methods

Details of sampling and methods of analysis used in biological media and environmental samples are in Tables 2 and 3.

Table 2. Analytical methods for determining methylene chloride in biological monitoring (as quoted in ATSDR, 1991)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Blood	Heat sample, collect headspace vapour	GC/FID	0.022 mg/ℓ	49.8±1.33	Di Vicenzo et al. (1971)
Urine	Heat sample, collect headspace vapour	GC/FID	No data	59±2.75	Di Vicenzo et al. (1971)
Breath	Heat sample, inject into gas sample, loop	GC/FID	0.2 ± 0.1 ppm	No data	Di Vicenzo et al. (1971)
Adipose tissue	Hydrolyse with acid, heat sample, collect headspace vapour	GC/FID	1.6 mg/kg*	No data	Engstrom and Bjurstrom (1977)
Human milk	Purge with helium, trap on sorbent trap, desorb thermally	GC/MS	No data	No data	Pellizzari et al. (1982)

*   Lowest reported concentration
FID = flame ionisation detector; GC = gas chromatography; MS = mass spectrometry

Table 3. Analytical methods for determining methylene chloride in environmental samples
(as quoted in ATSDR, 1991)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Adsorb on charcoal, desorb with carbon disulphide	GC/FID	25 ppb[a]	90-110[b]	APHA (1977)
Air	Adsorb on charcoal, desorb with carbon disulphide	GC/FID	2,900 ppb	95.3	NIOSH (1984)
Air	Adsorb on charcoal, desorb with benzyl alcohol	GC/ECD	$\approx$ 0.5 ppb	No data	Woodrow et al. (1988)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/HSD	No data	85	EPA (1989f)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/ELCD	0.01 μg/ℓ	97-100	EPA (1989g)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/MS	1.0 μg/ℓ	99	EPA (1989c)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	HRGC/MS	0.03-0.09 μg/ℓ	95-97	EPA (1989b)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	HRGC/ELCD	0.01-0.05 μg/ℓ	97$\pm$28	APHA (1989a)
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	HRGC/MS	0.02-0.2 μg/ℓ	95$\pm$5	APHA (1989b)

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Table 3. Analytical methods for determining methylene chloride in environmental samples (continued)
(as quoted in ATSDR, 1991)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Water	Purge with helium, trap on sorbent trap, desorb thermally	GC/MS	No data	99-105	Michael et al. (1988)
Waste water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/HSD	0.25 µg/ℓ	97.9±2.6	EPA (1982b)
Waste water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/MS	2.8 µg/ℓ	89±28	EPA (1982c)
Soil/solid waste	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/MS	5 µg/kg	D-221	EPA (1986a)
Soil/solid waste	Purge with inert gas, trap on sorbent trap, desorb thermally; or inject directly into GC	GC/HSD	No data	25-162	EPA (1986b)
Food	Equilibrate in heated sodium sulphate solution, collect headspace vapour	GC/ELCD	0.05 ppm	No data	Page & Charbonneau (1984)
Food	Isolate solvent by closed system vacuum distillation with toluene as carrier solvent	GC/ELCD	7 ng	94	Page & Charbonneau (1977)
Food	Isolate solvent by closed system vacuum distillation with toluene as carrier solvent	GC/ECD	7 ng	100	Page & Charbonneau (1977)
Food	Purge with nitrogen, trap on sorbent trap, elute with hexane	GC/ELCD	1.2 ppm[c]	84-96	Heikes (1987)
Food	Extract with acetone-water, back extract with isooctane	GC/ELCD	4 ppb	66	Daft (1987)

[a]   Lowest value for various compounds reported during collaborative testing of this method.
[b]   Estimated accuracy of the method when the personal sampling pump is calibrated with a charcoal tube in the line.
[c]   Lowest reported concentration.

ECD = electron capture detector; ELCD = electrolytic conductivity detector; FID = flame ionisation detector; GC = gas chromatography; HRGC = high resolution gas chromatography; HSD = halogen specific detector; MS = mass spectrometry.

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

3.1 Natural occurrence

Methylene chloride is not known to occur naturally in the environment.

3.2 Man-made sources

3.2.1 Production

Methylene chloride is produced almost exclusively by the Stauffer process. Methyl chloride is first produced by the reaction of methanol and hydrogen chloride, and is then reacted with chloride. Chloroform and, to a lesser extent, carbon tetrachloride are also produced. Historically the direct route to methylene chloride by chlorination of methane was also used; this also produced the other three chloromethanes; in varying proportions depending on the conditions used (CEC, 1986; ICI, pers. comm.).

World production of methylene chloride in 1980 was estimated to be 570 kt (Edwards et al., 1982); a similar figure is considered to apply currently (ECSA, 1992). US production was 229 kt in 1988, with demand at 207 kt (PTCN, 1991). The total amount produced in Western Europe ranged from 331.5 kt in 1986 to 254.2 kt in 1991 (ECSA, 1992).

3.2.2 Uses

The usage of methylene chloride in Western Europe shows some indication of a decrease from 200 kt/y from 1975 to 1985 (CEFIC, 1986) to 175 kt/y in 1989 (Dow Chemicals, Sweden, pers. comm.).

Most of the applications of methylene chloride are based on its considerable solvent capacity, especially for grease, plastics and various paint binding agents. Other important properties are its volatility and stability; it is also non-flammable. Among its uses are (CEFIC, 1983):

- a component of paint and varnish strippers, and adhesive formulations
- a solvent in aerosol formulations
- an extractant in food and pharmaceutical industries
- a process solvent in cellulose ester production and fibre and film forming
- a process solvent in polycarbonate production
- a blowing agent in flexible polyurethane foams
- the extraction of fats and paraffins
- plastics processing, and metal and textile treatment
- a vapour degreasing solvent in metal working industries

An estimated breakdown of usage worldwide is given in Table 4:

Table 4. Estimated Worldwide Usage Pattern for Methylene Chloride
(IARC, 1986)

Use Category	Percentage
Aerosols	20-25
Paint remover	25
Process solvent	35-40
(pharmaceutical industry, acetate film fibre)	
Miscellaneous	10-15
(polyurethane foam manufacturing, metal cleaning, nutrition industry)	

3.2.3 Consumer Applications

The main use in consumer products is in paint strippers, where methylene chloride is the main constituent, at 70-75%. The second important use is in hairspray aerosols, as a solvent and vapour pressure modifier. In the European Community (EC) it may be used in such products in concentrations of up to 35% w/w. It is also used in aerosol paints. Other categories of product are household cleaning products, lubricating, degreasing and automotive products, some of which may be in aerosol form.

3.2.4 Sources in the Environment

Most of the methylene chloride released to the environment results from its use as an end-product by various industries, and the use of paint removers and aerosol products in the home. Methylene chloride is mainly released to the environment in air and, to a lesser extent, in water and soil.

Methylene chloride is released to the atmosphere during its production, storage and transport, but more than 99% of the atmospheric releases result from industrial and consumer uses (EPA, 1985). It has been estimated that 85% of the total amount of methylene chloride produced in the USA is lost to the environment, of which 86% is released to the atmosphere (EPA, 1985). Using data reported to EPA for the 1988 Toxic Chemical Release Inventory, approximately 170 kt of the US production volume for 1988 (230 kt) was lost to the atmosphere; of this, 60 kt resulted from industrial methylene chloride emissions and 110 kt of the use of consumer products and other sources such as hazardous waste sites (TRI88, 1990).

Estimates of annual global emissions of 500 ktonnes have been reported for methylene chloride (WMO, 1991). The short atmospheric lifetime of methylene chloride (see 4.2.1) implies that emissions quantities given on a seasonal as well as on a regional basis are more relevant for comparison with atmospheric measurements. The total emission into the air in Western Europe was estimated to be 173 kt for 1989 and 180 kt in 1991.

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION

4.1 Transport and distribution between media

4.1.1 Water/air

Methylene chloride enters the hydrosphere either directly, via aqueous effluents, or indirectly from the atmosphere by dissolution in seawater and in rainwater. Due to its high volatility (Henry's law constant 380 Pa m^3/mol at 20°C, Table 1) and low liquid-film transfer coefficient (Kp=0.005 m/h) methylene chloride is rapidly transferred from the hydrosphere to the atmosphere.

Under laboratory conditions, the estimated half-life for volatilisation at 25 °C of methylene chloride from water is 18-25 min (when present at 1 mg/ℓ and stirred at 200 rpm). Removal of 90 percent of the methylene chloride required 60-80 min. When stirring was minimal (15 s every 5 min), the time required for 50% reduction in the concentration was about 90 min. The presence of 3% sodium chloride (as in seawater) decreased the evaporation rate by 10% (Dilling et al., 1975; Dilling, 1977).

Various factors have been shown to impact on the rate of volatilisation. For example, the half-life for volatilisation of methylene chloride from a depth of 1 m has been shown to be 3h (Lyman, 1982). The application of wind across the surface of the water caused an increase of 17% in volatilisation over a period of 20 min compared to the presence of still conditions (Dilling et al., 1975). A decrease in the water temperature decreases the rate of volatilisation; for example, over a period of 30 min, a 28% decrease in rate was seen at 1-2 °C compared to that at 25 °C (Dilling et al., 1975).

When measured under field conditions in experimental ponds, half-lives for methylene chloride of 26-28 h have been reported (Merlin et al., 1992). Its half-life for evaporation from the river Rhine has been estimated to be 33-38 days (Zoeteman et al., 1980). Further estimates of the half-life for its evaporation are between 3 h and 48 h depending on wind and mixing conditions (Halbartschlager et al., 1984). In a further study, methylene chloride was not detected at a point 4-8 km from the point of release into an estuarine bay (Helz and Hsu 1978) or at 25 km below its discharge point in a river basin (De Walle and Chain, 1978).

The atmospheric lifetime of methylene chloride of 5.8 months (Section 4.2.1) is longer than the intra-hemispheric mixing time of approximately 1 month. As a consequence, transport can occur to regions far removed from the emission source. The atmospheric lifetime is, however, fairly short relative to the inter-hemispheric transport time of 1-1.5 years, resulting in 1.8 times higher concentrations of methylene chloride (Table 6) and its degradation products in the northern hemisphere, where most of the emissions presently occur, than in the southern hemisphere (Singh et al., 1983).

Rain-out is considered to be a limited process for removal of methylene chloride from the troposphere. If it is assumed that its aqueous-phase concentration is in

equilibrium with the background concentration in the northern hemisphere of about 35-38 ppt (Cox et al., 1976; WMO/UNEP, 1991), the total amount of methylene chloride rained out in the northern hemisphere will be 700 t/y (assuming a rain fall of 2.5×10^{14} t/y containing 2.8 ppt at 10 °C). The same calculation performed at 20°C (Henry's constant is 1.57 times higher) would lead to an amount of 445 tons methylene chloride rained out annually in the northern hemisphere. For the southern hemisphere raincut quantities of 390 and 248 tons methylene chloride can be calculated. The half-life for removal by wet deposition is 550 years (Cupitt 1980, as quoted in ATSDR, 1991).

In 1978, it was estimated that 2.5% of releases at ground level may reach the stratosphere (Derwent and Eggleton, 1978).

4.1.2 Soil/air

Methylene chloride present in the soil is predicted to evaporate from the near-surface layer into the atmosphere because of its high vapour pressure (470 hPa at 20°C, Table 1).

4.1.3 Water/soil

The adsorption coefficient sediment/water for methylene chloride is 8.8 (log K_{oc} = 0.89-1.05) (Table 1).

The amount of adsorption of methylene chloride to dry granular bentonite clay added at a concentration of 375-750 mg/ℓ was found to be 10-22% within 10-30 min. In the presence of 500 mg/ℓ peat moss, about 40% of methylene chloride was absorbed after 10 min. Some adsorption by dry-powdered dolomitic limestone was observed, but not with silica sand (Dilling et al., 1975).

Methylene chloride has a low tendency to adsorb to soil (adsorption coefficient 0.25 for a soil containing 1% organic carbon, Giger et al., 1983). Therefore there is a potential for it to leach to ground-water.

4.2 Abiotic degradation

4.2.1 Atmosphere

The principal process by which methylene chloride is scavenged from the atmosphere is the reaction with hydroxyl radicals (·OH), naturally present in the troposphere. The removal rate of methylene chloride can be calculated from the rate constant for the initiating breakdown reaction with ·OH and the varying concentration of these radicals in the troposphere. Determination of the rate constant for the reaction of methylene chloride with hydroxyl radicals has been the subject of various investigations. WMO (1991) recommends the following value:

$$k_{OH} = 5.8 \times 10^{-12} \exp(-1100/T) \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$$

Other reactive species (e.g. ozone, oxygen atoms, chlorine atoms and nitrate radicals) are not thought to contribute significantly to the primary attack on methylene chloride (Table 5) . As methylene chloride does not absorb in the visible or near ultraviolet light region (> 290 nm), direct homogeneous gas-phase photolysis in the troposphere is of negligible importance.

Thus, the tropospheric lifetime of methylene chloride may be predicted from the hydroxyl radical concentration and the rate of reaction with methylene chloride. Using the method by Prather and Spivakovsky (1990, as quoted in WMO, 1991), i.e. by scaling the lifetime to that of the reference compound 1,1,1-trichloroethane at 277 °K a tropospheric lifetime of 5.8 months for the reaction of methylene chloride with hydroxyl radicals results (WMO, 1989).

Carbon dioxide and hydrogen chloride are the major breakdown products formed, with minor quantities of carbon monoxide and phosgene (Sanhueza and Heicklen, 1975; Rayez et al., 1987). The breakdown reaction can be described as follows:

$$CH_2Cl_2 + \cdot OH \longrightarrow \cdot CHCl_2 + H_2O$$

$$\cdot CHCl_2 + O_2 \longrightarrow \cdot CHCl_2O_2$$

$$\cdot CHCl_2O_2 + NO \longrightarrow \cdot CHCl_2O + NO_2$$

$$\cdot CHCl_2O \longrightarrow \cdot Cl + HCOCl \quad \text{or}$$

$$\cdot CHCl_2O + O2 \longrightarrow COCl_2 + HO_2 \quad \text{(minor reaction)}$$
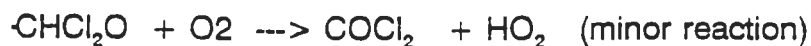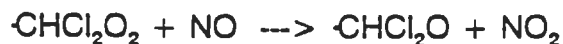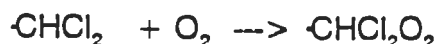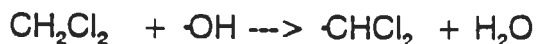
Formyl chloride may be taken up by cloud droplets, hydrolysed to formic acid and wet deposited as such, or dry deposited to the ocean or land surfaces and then hydrolysed. The overall lifetime for wet and/or dry deposition is unlikely to exceed a few months and may be much shorter. On the other hand, degradation in the troposphere by photolysis or reaction with ·OH may possibly be a more rapid

process. The reaction products would be carbon oxides (CO, CO_2) and HCl (Libuda et al., 1990).

Phosgene is known to hydrolyse slowly in gas phase, but rapidly once dissolved in liquid water, to give CO_2 and HCl.

HCl is removed from the troposphere by wet deposition (dissolution in atmospheric water droplets and subsequent rainout) or dry deposition (direct uptake by the oceans, land surfaces, vegetation etc.) with an average lifetime of about 1 week. The amount of chloride deposited in this manner is completely negligible compared to the natural atmospheric chloride flux of around 10,000 Mt/y primarily from sea-salt aerosols (WMO, 1990).

In the stratosphere methylene chloride will rapidly degrade by photolysis and reaction with chlorine radicals (Derwent et al., 1976).

Table 5. Primary tropospheric reactions of methylene chloride other than with ·OH

Methylene chloride + X -> products

X	k (at 298 K) (cm^3 molecule^{-1} s^{-1})	global average [X] (molecule cm^{-3})	lifetime (years)
·Cl	4.1 x 10^{-13} (IUPAC, 1992)	10^3 ?	77 ?
·NO$_3$	≤ 3.2 x 10^{-17} (CEC, 1990)	1.2 x 10^8	≥ 8.3
·O(^{3}P)	6.44 x 10^{-16} (Barassin & Cambourieu, 1973)	2.5 x 10^4	~ 2000
·O(^{1}D)	< 5 x 10^{-10} (estimated)	0.5	> 120

4.2.2 Water

Sunlight absorption of water results in the formation of hydroxyl radicals (·OH) and hydrated electrons (e$^-_{aq}$). The near surface concentrations of ·OH and e$^-_{aq}$ are 4.10^{-16} mol/ℓ and 5.10^{-17} mol/ℓ respectively, which theoretically corresponds to half-lives for methylene chloride of 400 and 33 days. In water systems with a depth of 2.5 m, these reactions are very limited and the ·OH reaction is dominant giving an overall lifetime of 68 years (Apeldoorn et al., 1988). No direct photolysis of methylene chloride was found after visible and UV irridiation for 5 days at 22°C (Chodola et al., 1989).

The half-life of 1 mg/ℓ aqueous solution of methylene chloride was found to be about 1.5 years when measured in sealed glass tubes in the dark at 25°C and pH 7 (Dilling et al., 1975). Similar results were obtained when the samples were exposed outdoors for one year to normal daylight and ambient temperature cycles(-20 to +40 °C) (Anonymous, 1988 cited in ECOLAS, 1991), no significant hydrolysis was found at 50°C and pH 4 or 9.2 after 7 days in the dark (Chodola et al., 1989). Extrapolation of hydrolysis data in either neutral or acidic conditions from 80-150°C to 25°C gives a

long half-life of about 680-704 years (Dilling et al., 1975; Radding et al., 1977 as quoted in BUA, 1986). As the activation energy for hydrolysis of methylene chloride varies with temperature, the extrapolation of rate data from 80-150°C may not be valid.

On the basis of these experiments it may be concluded that the hydrolysis and photolytically induced degradation of methylene chloride are not significant in aqueous systems.

Under acidic and basic conditions in the temperature range of 80-150 °C the hydrolysis of methylene chloride results in the formation of formaldehyde and HCl (Fells and Moelwyn-Hughes, 1958).

No reductive dehalogenation of methylene chloride in water was observed in the presence of sodium sulphide and haematein, a common iron porphyrin (Klečka and Gonsior, 1983).

4.2.3 Soil

As is the case in aqueous systems, hydrolysis is probably not an important process in the removal of methylene chloride (see 4.2.2).

In well documented cases of accidental spills it has been shown that methylene chloride disappears rapidly from ground-water, probably due to (bio)degradation (Baldauf, 1981; Leitfaden für die Beurteilung, 1983; both as quoted in BUA, 1986).

In a lysimeter experiment, a 90% decrease over 2.5 m soil column was obtained (Nellor et al., 1985).

In the report of a spillage, the concentrations of methylene chloride were up to 802 mg/m^3 and 26,900 mg/m^3 near the point of leakage. In both cases, methylene chloride could not be detected some hundred metres away from the points of contamination even in the direction of the ground-water flow (ECSA, 1989). In the neighbourhood of polluted areas an increase of bacterial activity has been found (Leitfaden für die Beurteilung und Behandlung von Grundwasserverunreinigung durch leichtflüchtige Chlorkohlenwasserstoffe, 1983 as quoted in BUA, 1986).).

4.2.4 Appraisal

Due to its high volatility, most of the methylene chloride released to the environment will partition to the atmosphere, where it will degrade by reaction with photochemically produced hydroxy radicals with a half-life of 6 months.

Abiotic degradation in water is slow compared to evaporation. Methylene chloride has shown to disappear rapidly from soil and groundwater.

4.3   Biotransformation

4.3.1 Aerobic

Negligible oxygen consumption was found over a 20-day period in a biochemical oxygen demand (BOD) test in the presence of methylene chloride (Klečka, 1982). However, complete degradation occurred during a static-culture flask test with 5 and 10 mg/ℓ methylene chloride after 7 days incubation; 6-25% was lost by volatilisation (Tabak et al., 1981).

Methylene chloride was considered as degradation resistant in a degradation test following the Japanese MITI standards (closed system oxygen consumption measurement, 28 days) (Kawasaki, 1980).

Methylene chloride (25 mg/ℓ) was almost completely destroyed by bacteria enriched from a primary sewage effluent within 24 h in a static closed system. The concentration of methylene chloride in a bio-film culture (flow velocity - 400 cm/day) was reduced from 24 mg/ℓ in the inlet to 1 mg/ℓ in the outlet (Rittmann and McCarty, 1980).

The concentration of methylene chloride was decreased from 50 to 4 mg/ℓ in 6 h in seed cultures from industrial waste-water and municipal activated sludge (Davis et al., 1981).

The concentration of methylene chloride added to the inflow of a continuous flow activated sludge reactor was reduced by over 99% from a starting concentration of 180 mg/ℓ for sludge residence times of 2-6 d; similar removal occured in the presence of benzene and ethylacetate. Only 5% of the methylene chloride was estimated to be removed by stripping (Stover and Kincannon, 1983).

Following 9-11 days of acclimation of municipal activated sludge with methylene chloride, degradation rates of 0.14, 2.3 and 7.4 mg/h per gram biomass were found with concentrations of 1, 10 and 100 mg/ℓ ^{14}C- methylene chloride, respectively. After 50 h, 49-66% mineralisation occurred. At 21 °C, the rate of biodegradation of methylene chloride was estimated to be about 12 times greater than the rate of volatilisation (Klečka, 1982).

In a further study with activated sludge acclimated for 6 weeks to methylene chloride, degradation rates of 20-28 mg/ℓ per h were reported for initial concentrations of 264-1300 mg/ℓ methylene chloride (Halbartschlager et al., 1984).

Removal rates of methylene chloride from well-run water treatment works ranging from 30-55% have been reported (Loehr, 1987). A conventional activated sludge plant was studied for its capacity to remove methylene chloride. The removal was estimated to be 96.2% by biodegradation (Namkung & Rittmann, 1987).

Certain strictly aerobic, facultative methylotrophic bacteria, like *Pseudomonas* DM1 and *Hyphomicrobium* DM2, both readily isolated from contaminated soil and waste

water treatment plants are capable of using methylene chloride as a sole carbon source for growth (Brunner et al., 1980; Stucki et al., 1981).

In *Hyphomicrobium* DM2, a glutathione(GSH) dependent, strongly inducible enzyme (a glutathione S-transferase) was found to be responsible for the degradation of methylene chloride. It converts methylene chloride to formaldehyde via the nucleophilic displacement of chloride and the formation of S-chloromethyl glutathione and S-hydroxymethyl glutathione. This enzymic dehalogenation in extracts of methylene chloride-grown cells amounts up to 1160 mg/g protein per h under alkaline (pH 8-9) conditions (Stucki et al., 1981; Leisinger, 1983).

Secondary substrate utilisation of methylene chloride was demonstrated by *Pseudomonas sp.* strain LP. This strain showed a preference towards degrading methylene chloride over acetate, whether it was the primary or secondary substrate (Lapat-Polasko et al., 1984).

Eight other bacteria (mainly *Pseudomonads*), capable of growing on methylene chloride as their only carbon source, were isolated from enriched cultures. Maximum degradation rates for methylene chloride up to 860 mg/ℓ/h were found for an initial saturated solution of 14,500 mg/ℓ in a pH controlled fermenter(flow rate 10 mℓ/h). Further increases in degradation rate were limited by the high salt concentration resulting from the neutralisation of the degradation products. In a fluidised bed reactor with bacteria immobilised on silica, a degradation rate of methylene chloride up to 1600 mg/ℓ/h was observed (Gälli and Leisinger, 1985; Stucki, 1990).

Ubiquitous soil- and water-dwelling nitrifying bacteria such as *Nitrosomonas europaea*, which depends for growth on the oxidation of ammonia, were able to degrade 1 mg/ℓ methylene chloride completely within 24 h in the presence of ammonia and by 67% in the absence of ammonia (Vannelli et al., 1990).

The removal of methylene chloride from aerobic soil was significantly increased following exposure to methane (Henson et al., 1988).

The biodegradation of methylene chloride in contaminated ground-water can be strongly inhibited in the presence of other contaminants such as 1,2 dichloroethane, xylene and ethylbenzene (Scholz-Muramatsu et al., 1988).

Aerobic biodegradation of methylene chloride was observed in a variety of surface soils including sand, a sandy loam and a sandy clay loam, as well as subsurface clay soil. Degradation occured over concentrations ranging from approximately 0.1 mg/ℓ to 5 mg/ℓ. The time required for 50% disappearance of the parent compound varied between 1.3 and 191.4 days.

4.3.2 Anaerobic

Methylene chloride is degraded at a concentration of 200 µg/ℓ in the aqueous phase of natural sediment. Degradation was observed to proceed via methyl chloride, although accumulation was not observed. 86-92% Conversion to CO_2 will occur after

a varying acclimation period using anaerobic digestion in waste water (Gossett, 1985 as quoted in Howard, 1990). The half-life of methylene chloride in an anaerobic water/sludge system is 11 days (Bayard et al., 1985).

Methylene chloride degradation was also observed under anaerobic conditions in the sandy loam soil (Davis & Madsen, 1991).

4.3.3 Bioaccumulation

The *n*-octanol/water partition coefficient for methylene chloride is 18 (log P_{ow}=1.25-1.3; Table 1). As a consequence, its bioaccumulation is not expected to be significant. Moreover, its high depuration and degradation rate will reduce the probability of bioaccumulation.

No experimental bioconcentration factor (BCF) for methylene chloride is available. Its theoretical BCFs range between 0.91 and 7.9 (Veith et al., 1980; Bayard et al., 1985; Lyman et al., 1982; Veith and Kosian, 1983).

There is no evidence of biomagnification of methylene chloride along the food chain.

4.3.4 Appraisal

The aerobic and anaerobic degradation of methylene chloride has been proven by a variety of different test systems. Its complete biodegradation, especially by acclimated bacterial cultures under aerobic conditions, is rapid (e.g. 49-66% mineralisation in 50 h with acclimated municipal sludge). In bioreactors up to 10% degradation per h is achievable. There is no evidence that significant bioaccumulation or biomagnification of methylene chloride along the food chain will occur.

4.4 Interaction with other physical, chemical or biological factors

Methylene chloride is expected to have no significant impact on stratospheric ozone depletion. At the current estimated total emission rate of 500 kt/year the calculated tropospheric chlorine loading due to methylene chloride is 35 ppt, i.e. approximately 1% of the total chlorine loading of 3600 ppt (WMO, 1991).

As methylene chloride has a low photochemical ozone creation potential in the troposphere (0.9) when compared with chemicals such as ethanol (27) or ethylene (100), it will not contribute significantly to photochemical smog-formation (Derwent and Jenkin, 1991).

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental Levels

Improved control of emissions over the last decade have led to lower environmental levels of methylene chloride. On the other hand, present analytical techniques have allowed a more detailed evaluation of the presence and fate of chemicals in the environment. This review has therefore been focused on publications after 1980.

5.1.1 Atmosphere

5.1.1.1 Ambient air (Table 6)

In ambient air of rural and remote areas, mean background levels of methylene chloride are 0.07-0.29 $\mu g/m^3$. The average concentrations in suburban and urban areas respectively are reported to be < 2 $\mu g/m^3$ and < 15 $\mu g/m^3$. In the vicinity of hazardous waste sites, up to 43 $\mu g/m^3$ have been found.

Table 6. Methylene chloride levels in ambient air.

Country	Location	Year of measurement	Concentration µg/m³	Reference
Netherlands	Delft, Vlaardingen	1980-1981	14.1 (max. annual mean)	Guicherit & Schulting (1985)
	Isle of Terschelling	1980-1981	1.4 (max. annual mean)	Guicherit & Schulting (1985)
	Mean conc. in the country	1980-1981	9	Guicherit & Schulting (1985)
Italy	Northern part, outdoor air	1983-1984	< 14	De Bortoli et al. (1986)
	indoor air	1983-1984	670	De Bortoli et al. (1986)
Germany	Urban area:			
	indoor air children's room	1988	44.9	Umwelt Bundesambt (1988)
	new houses (clean air region)		18.4	
	old houses (Frankfurt)			
	Frankfurt	1980	2.1-4.2	Arendt et al. (1982) in BUA (1986)
	Frankfurt Sindlenge	1982-1984	8-15	Hoechst (1982-84) in BUA (1986)
EEC	Indoor air	1982	N.D. - 4000	CEC (1982) in BUA (1986)
USA	Rural, suburban areas	-	0.18-2.1	Shah & Heyerdahl (1988) in ATSDR (1992)
	San Francisco Bay area	1984	3.2-9.1	Levaggi et al. (1988)
	Urban areas	1980	0.8-6.7	Shah & Heyerdahl (1988) in ATSDR (1992)
				Shikiya et al. (1984) in ATSDR (1992)
		1980-1981	1.35-6.76	Singh et al. (1982)
		1981	0.8-2.5	Harkov et al. (1984)
		1982	2.4-4.2	Harkov et al. (1984)
		1987	0.95-1.64	Pleil & McClenny (1990)
		1988	0.62-1.80	Pleil & McClenny (1990)
		1989	0.48-1.68	Pleil & McClenny (1990)
	Hazardous waste sites	1983-1984	0.3-43	Harkov et al. (1985)
Arctic	Spitzbergen	July 1982	0.26 ± 0.04	Hov et al. (1984)
		March 1983	0.29 ± 0.06	Hov et al. (1984)
Northern hemisphere	Eastern Pacific	1981	0.12-0.15	Singh et al. (1983)
Southern hemisphere	Eastern Pacific	1981	0.07	Singh et al. (1983)

5.1.1.2 Precipitation

Rain water sampled in Koblenz (Germany) in 1982/83 was found to contain up to 4 µg/ℓ methylene chloride (Hellman, 1984).

5.1.2 *Water* (Table 7)

Methylene chloride enters the aquatic environment primarily through waste water discharges. An estimated amount of 0.2% of the total methylene chloride production is released in waste water (Deguinze et al., 1984). The input from air rainout can be estimated for the northern and southern hemiphsere (Section 4.1.1).

Waste water from certain industries have been reported to contain methylene chloride at average concentrations in excess of 1000 µg/ℓ, these being coal mining, aluminium forming, photographic equipment and supplies, pharmaceutical manufacture, organic chemical/plastics manufacture, paint and ink formulation, rubber processing, foundries and laundries. The maximum concentration measured was 210 mg/ℓ in waste water from the paint and ink industry and the aluminium forming industry (EPA, 1981 as quoted in Howard et al., 1990).

In the US EPA STORET database on industrial effluents, 38.8% of the samples recorded containing methylene chloride with at a median concentration of 10.000 µg/ℓ (Staples et al., 1985).

Samples from the outfalls of 4 municipal treatment plants in Southern California with both primary and secondary treatment contained < 10 to 400 µg/ℓ methylene chloride (Young et al., 1983 as quoted in Howard et al., 1990). In 30 Canadian water treatment facilities, average concentrations of methylene chloride in summer and winter were found to be 10 µg/ℓ and 3 µg/ℓ respectively (max. 50 µg/ℓ) (Otson et al., 1982).

In leachate from industrial and municipal landfills, methylene chloride concentrations were reported to range from 0.01 to 184,000 µg/ℓ (Brown and Donnelly, 1988; Sabel and Clark, 1984; Sawhney, 1989 as quoted in ATSDR, 1992).

In surface water, levels of methylene chloride have been reported to vary from not detectable to up to 10µg/ℓ. From data recorded in the US EPA STORET database, 30% of the samples showed methylene chloride levels above the detection limits. A median concentration of 0.1 µg/ℓ was estimated (Staples et al., 1985).

Limited information concerning the contamination of sea water and estuaries by methylene chloride is available. It appears that methylene chloride can be found up to 2.6 µg/ℓ in coastal waters of the Baltic Sea. Levels up to 0.20 µg/ℓ have been found in North Sea coastal waters. Methylene chloride is generally not detected in open oceans. A mean concentration of 2.2 ng/ℓ methylene chloride has been reported in the South Pacific Ocean when using very sensitive analytical methods.

Table 7. Methylene chloride levels in water.

Country	Location	Year of measurement	Concentration µg/l	Reference
Ground water				
USA	Iowa 128 wells	1984-1985	1-5 (4 wells)	Kelley (1985)
Italy	Milan	1983	4.5	CEFIC (1986)
France	Val de la Marne 10m depth	1983	< 100	Penverne & Montiel (1985)
	40m depth	1983	< 100	Penverne & Montiel (1985)
Surface water				
Germany	Mosel	1983	1.5 - 2.0	Hellmann (1984)
	Neckar	1983	0.6 - 1.0	Hellmann (1984)
	Elbe	1983	0.7 - 2.1	Hellmann (1984)
	Weser	1982-1983	< 0.5	Hellmann (1984)
	Rhine different sites	1981	< 1	LWA (1981) in BUA (1986)
		1982	< 1	LWA (1982) in BUA (1986)
		1983	< 1	LWA (1983) in BUA (1986)
	Rhine at Koblenz	1983	5.35-171 (monthly mean)	Hellmann (1984)
	Rhine at the Wesel	1983	< 2.0	Hellmann (1984)
	Rhine at Duisburg	1984	1.5 (max.)	LWA (1984) in BUA (1986)
	Main at Frankfurt-Höchst	1982	10 (max.)	Hoechst (1982) in BUA (1986)
		1983	< 1	Hoechst (1983) in BUA (1986)
		1985	4.1 (annual mean)	Hoechst (1985) in BUA (1986)
		1986	0.1 (mean)	BUA (1986)
	Main	1985	± 0.2	Van de Graaf (1986)
USA	Susquehanna river, Columbia	1987	10 (mean)	Smith (1989)
	Lancaster	1987	4.7 (mean)	Smith (1989)
	Ohio river basin (11 stations, 4972 samples)	1980-1981	> 1 (238 samples) > 10 (19 samples)	Ohio River Valley Sanitation Commission (1982) in Howard et al. (1990)
Sea water & estuary	East Pacific Ocean (30 samples)	1981	0.002 (mean)	Singh et al. (1983)
	East Sea (German Coast)	1983	1.3 - 2.6	Hellmann (1984)
	North Sea (German Coast)	1983	0.06-0.20	Hellmann (1984)

5.1.3 Aquatic organisms

Concentrations of methylene chloride in fresh water organisms have been reported for oyster and clams. Levels ranging from 4.5 to 27 μg/kg (wet weight) could be detected (Ferrario et al., 1985).

No methylene chloride was detected in fish taken from the River Rhine in 1981 (Binnemann et al., 1983).

Levels of methylene chloride up to 700 μg/kg wet weight were found in marine bottom fish taken from Commencement Bay, USA (Nicola, 1987).

Data on biota collected in the US-EPA STORET show levels of 660 μg/kg in the 28% of the samples in which methylene chloride was detected (Staples et al., 1985).

5.1.4 Soil and Sediment

No data are available on the levels of methylene chloride in soil.

Background data on ground-water contamination by methylene chloride are limited. It is the sixth most frequently detected organic contaminant in ground water at hazardous waste disposal sites in the CERCLA database (178 sites) with a detection frequency of 19% (Plumb ,1987). In contaminated groundwater in Minnesota (USA) up to 250 μg/ℓ methylene chloride has been detected (Sabel and Clark, 1984). Levels up to 110 μg/ℓ methylene chloride were found in percolation water from a waste-disposal site in Germany. However methylene chloride was not found (< 1 μg/ℓ) in the groundwater below the site (Heil et al., 1989).

The levels of methylene chloride found in sediment from Lake Pontchartrain ranged from not detectable to 3.2 μg/kg wet weight (Ferrario et al., 1985).

Data recorded in the US EPA STORET database revealed a median concentration of 13 μg/kg methylene chloride in 20% of 338 sediment sampling data (Staples et al., 1985).

5.2 Human Exposure

5.2.1 General population

5.2.1.1 Ambient air (Table 6)

The ambient air levels of methylene chloride (Table 6) are much lower than the levels which may be encountered inside buildings in which products containing methylene chloride have been used (CEC, 1982 as quoted in BUA, 1986). In indoor air of residential houses, relatively high levels (up to 670 μg/m^3) of methylene chloride can be found during the winter (De Bortoli et al., 1986). In a TEAM study conducted in Los Angeles (CA) in 1987, the 24h average exposure of about 750 persons to methylene chloride in 6 urban areas was 6 μg/m^3.

5.2.1.2 Drinking water

Methylene chloride has been detected in drinking water supplies (estimations made before 1980) in numerous US cities (Dowty et al., 1975; Coleman et al., 1976; Kopfler et al., 1977; Kool et al., 1982; all as quoted in ATSDR, 1992), the mean concentrations reported being generally less than 1 $\mu g/\ell$.

Samples from 128 US drinking water wells showed that 3.1% of them had levels of 1-5 $\mu g/\ell$ methylene chloride (Kelley, 1985).

5.2.1.3 Foodstuff

Although methylene chloride is used in food processing (solvent extraction of coffee, spices, hops), little information is known on its residual levels in food. In the USA, residues of methylene chloride were found in decaffeinated coffee beans (0.32 to 0.42 mg/kg) whilst levels a major coffee processor reported 0.01 to 0.1 mg/kg (FDA, 1985 in Fed. Reg., 50, 9.51551 as quoted in ATSDR, 1992).

No methylene chloride was detected in ice-cream and yoghurt (Baner et al., 1981).

In 7 types of decaffeinated ground coffee the methylene chloride content ranged from <0.05 to 4.04 mg/kg; in 8 instant coffee samples <0.05 to 0.91 mg/kg was found (Page and Charbonneau, 1984).

5.2.1.4 Consumer exposure

Consumers are exposed to methylene chloride via the use of a number of formulated products such as aerosols or paint strippers. A US survey found that 78% of paint removers and 66% of aerosol spray paints sold as household products contained methylene chloride (EPA, 1987). Over 100 consumer products in Sweden contain methylene chloride. In Norway the number is around 140, including 45 paint removers (AKZO, pers. comm.).

There are no reported incidents of serious health effects arising from accidental over-exposure to methylene chloride in consumer products. Similarly, there are no reports of volatile substance abuse involving methylene chloride-based consumer products.

A large do-it-yourself consumer population uses paint strippers containing methylene chloride on furniture and woodwork. Formulations are available mainly in liquid form, but also, occasionally, in an aerosol. Exposures have been estimated on the basis of US investigations of household solvent products. The estimated levels ranged from less than 35 mg/m³ to a few short-term exposures of 14,100 to 21,200 mg/m³. The majority of the concentration estimates were below 1770 mg/m³ (EPA, 1990). A Danish study reported concentrations of methylene chloride in the breathing zone ranging from 740 to 7150 mg/m³ using liquid paint-strippers indoors (Miljøstyrelsen, 1988).

Methylene chloride exposure was estimated while using a number of formulations of paint stripper performed in a small room. Various ventilation conditions were evaluated and a worst possible case was simulated, with doors and windows closed. In one test, involving furniture stripping in a room with through ventilation, the operator exposure was measured at 289 mg/m^3 on a 2 h-TWA. Peaks of exposure were observed during application (460 mg/m^3) and during scraping off (710-1410 mg/m^3) (ICI, 1988).

The effect of the variation in the formulation has been investigated. During the paint strippings background concentrations in the room varied from 710-1410 mg/m^3 to less than 350 mg/m^3 depending on the formulation, although within 5-6 min of application the levels of methylene chloride fell to equilibrium concentrations around 71 mg/m^3 irrespective of the formulation used, the shortest time before reaching equilibrium being about 2-2.5 min (ICI, 1990).

Levels of exposure to methylene chloride during its use in personal care aerosols are well documented. Worker exposure levels in hairdressing salons is given in Table 8 (Section 5.2.2). Consumer exposures in salons are expected to be lower.

5.2.2 Occupational exposure

Production of methylene chloride is normally carried out in a closed system with a relatively small number of people being involved. Exposure arises primarily during filling and packing operations. Experience indicates that the application of sound and well recognised engineering control techniques will bring 8h-TWA exposures well below 350 mg/m^3 (NIOSH, 1980; HSE, 1987; ICI, 1984, 1992). A listing of occupational exposures against activities is given in Table 8.

Occupational exposures occur in the following industrial sectors:

(i) Formulation of paint-remover

Formulators are exposed while transferring methylene chloride from storage tanks, during mixing (blending) operations and packaging. The extent of exposure will depend on the control measures and work practices in force. Exposure (8h-TWA) range from a low of 0-18 mg/m^3 to over 1770 mg/m^3 (EPA, 1990).

(ii) Original equipment manufacture

Paint strippers are widely used in a number of industries: automotive, rubber products, furniture and fixtures, plastic, and electronic industries. Exposure to methylene chloride takes place during application, removal of the substrate soaked in methylene chloride and the disposal of the spent paint-remover. Typical exposures range from 18 mg/m^3 to about 1770 mg/m^3, 8h-TWA (IARC, 1986).

(iii) Maintenance sector

Maintenance workers are exposed to methylene chloride during application, stripping, cleaning and drying. Activities such as loading, cleaning, waste disposal and maintenance of dipping tanks presents occasional but very high exposures. Application of vapour retarders reduces exposures.

(iv) Commercial furniture refinishers

Exposure of commercial furniture refinishers to methylene chloride occurs when stripping involves either the dipping of furniture into a tank containing a mixture of solvents including methylene chloride (typically 65%) or coating it manually with a brush. Exposure levels are highly variable and greatly influenced by the size of the organisation, engineering controls in place and work practices. Some refinishers may operate on a part-time basis and from their homes. In some instances where the stripper was leaning over the tank or using a brush to scrub the surface coating, concentrations of > 7100 mg/m^3 have been recorded (NIOSH, 1992; HSE ,1992; McCammon et al., 1991). Better work stations and work practices have helped to reduce greatly exposures.

(v) Packing and use of aerosols

In the packaging of aerosol cans, exposure arises primarily during filling and packing. Levels observed are generally below 180 mg/m^3 (ECSA, 1989). Potential occupational exposure to methylene chloride as a result of aerosol products varies according to the use and the work undertaken.

In studies in salons in the Netherlands, peak concentrations of 21-106 mg/m^3 methylene chloride were measured, with an 8h TWA of 3.5-18 mg/m^3 (CEC Scientific Committee on Cosmetology). The same study measured a peak concentration arising from home use of a hairdressing aerosol containing 35% methylene chloride of 265 mg/m^3, equating to a TWA of 2.65 mg/m^3.

The use of paint spray aerosols involves much longer spray times leading to higher exposures. Exposure has been measured following simulated heavy use by consumers of paint aerosols containing 30% methylene chloride in a test room ventilated only after spraying (Stevenson et al., 1978). Peak methylene chloride concentrations of up to 3200 mg/m^3 were measured, equating to an 8h TWA of 35 mg/m^3.

Studies in the UK simulating consumer exposure during salon use showed figures well within the national Maximum Exposure Limit (350 mg/m^3 for an 8h TWA). The hairdresser had an exposure of 78 mg/m^3 (8h TWA) despite what is seen as exceptionally heavy use i.e. 10 s spray every 15 min for an 8 h period. The customer exposure was measured at 106-265 mg/m^3, 10 min TWA (ICI, pers. comm.).

(vi) Use as a process solvent

Methylene chloride is widely used as a process solvent in the manufacture of a variety of products. Most of the processes are carried out in closed systems, with the exception of triacetate fibre and film manufacture. Normally, exposure levels are low, but occasional high exposures (>350 mg/m^3; 10 min TWA) may occur such operations as filter changing, charging and discharging. Some industrial processes involve somewhat higher exposure levels; in particular, the manufacture of cellulose triacetate fibres and films can involve exposure up to 350 mg/m^3 8h-TWA even when good engineering controls are installed (ECSA, 1989; Zahm et al., 1987; Ott et al., 1983).

In the pharmaceutical industry, methylene chloride is used as a solvent and extraction medium. Sealed processes, high recovery rates and careful handling of discharges have helped to keep the exposures below around 106 mg/m^3 (Zahm et al, 1987; Astra, 1991; HSE, 1992).

Methylene chloride is also used as an extraction medium in the nutrition industry, again the processes are sealed and the exposure levels generally low.

Methylene chloride is used in the foam industry for clean process equipment, purging spray guns, and as an auxiliary blowing agent. It is also used as a releasing agent in the moulding of polyurethane products. Exposures ranging from a few mg/m^3 to short-term exposures of over 1770 mg/m^3 have been reported (Jernelov and Antonsson, 1987; Boeniger, 1991; HSE, 1992).

The use of methylene chloride as a solvent in adhesives can result in occupational exposures during the application of the adhesive to short-term levels in excess of 350 mg/m^3 (Fleeger & Lee, 1988; HSE, 1992). Processes involving the formulation of adhesives are likely to be well controlled.

Methylene chloride is also used as a solvent in the analysis of bitumen samples. This work is normally carried out in small laboratories and exposure levels will be high unless adequate control measures are used.

(vii) Metal degreasing

In the manufacture of metal products, cleaning (degreasing) is required before painting, plating, plastic coating, etc. The degree of exposure to methylene chloride will be influenced by many factors including the age of the equipment, type of engineering controls available, their maintenance, handling, and drying methods. In general, it is possible to reduce exposures to below 124 mg/m^3 (Swedish National Board of Occupational Safety & Health, pers. comm.).

Table 8. Occupational exposure to dichloromethane.

Industry (SIC)	Activity	Exposure range (TWA) mg/m³	Reference	Comments
Production	Production activities	219-374	HSE (1987)	Maintenance activity with RPE
	Process plant	0.35-388 18-88	ICI (1984, 1992) NIOSH (1980)	Communications to HSE (UK) Results obtained at one plant
Pharmaceuticals	N.A.	7.1-3749	Zahm et al. (1987)	NCI feasibility study
	Production work	0-18	HSE (1992)	Enclosed process
	N.A.	< 124	Astra (1991)	Personal communication
GRP Manufacture	Cleaning and mould preparation	187-6693	HSE (1992)	Intermittent exposure, RPE may be worn. May not be representative of the industry.
	Cleaning, mixing etc.	0-350	Post et al. (1991)	Small factory units
Packaged Products	Aerosol filling	95-628	ICI (UK) (1984)	
Aircraft	Paint stripping	35-81	HSE (1992)	RPE provided
	Paint stripping	35-289	Air Transport Association (USA)	Submission to OSHA in 1987. RPE provided
Printing	N.A.	3.5-558	Zahm et al. (1987)	NCI feasibility study
Hairdressing	Hairspray applications	3.5-67 < 35 3.5-7.1	Harris (1985) HSE (UK) Visit Reports Hoffman (1973)	Various types of products tested General ventilation
Decorative	Painting, maintenance	21-229	Chrostek & Levinee (1981)	See: IARC 41 (1986)
	Paint stripping	35-21,200	EPA (1990)	
	Used aerosol adhesives	< 0-494	Fleeger & Lee (1988)	Some work areas were congested
Rubber products	Fabrication	208-304	HSE (1992)	LEV

.../..

Table 8. Occupational exposure to dichloromethane (continued).

Industry (SIC)	Activity	Exposure Range (TWA) mg/m³	Reference	Comments
Triacetate fibre/film manufacturing	Production	180-350 237-3442 180-2440	ECSA (1989) Zahm et al. (1987) Ott et al. (1983)	NCI feasibility study Products contain acetone
Furniture	Paint stripping	25-3810	HSE (1992)	Many without adequate controls
	Paint stripping	201-1292	McCammon et al. (1991)	Variable degrees of control
	Washing/refinishing	53-780	McCammon et al. (1981)	Variable degrees of control
	Spraying adhesive	219-1490	HSE (1992)	Many without adequate controls
General Manufacturing Cleaning and Degreasing	Cleaning, degreasing etc.	180-2220 53-141 <0-460	Lee (1980) Ruhe et al. (1981) Ruhe et al. (1982)	See: IARC 41 (1986) See: IARC 41 (1986) See: IARC 41 (1986)
Foam Industry	Glue spraying	85-244	HSE (1992)	LEV
	Moulding	88-1090	HSE (1992)	High exposure due to insufficient/inadequate LEV
	N/A	<247	Jernelov & Antonsson (1987)	In Swedish
	N/A	7.1-251	Zahm et al. (1987)	NCI feasibility study
	Various jobs	18-580	Boeniger (1991)	High exposure experienced by sprayers
Motor vehicle Manufacture	Spray painting, stripping	7.1-247	HSE (1992)	LEV and RPE
Quarry	Laboratory work - mineral processing	71-1370	HSE (1992)	High exposures due to inadequate control
Metal Treatment		7.1-790	Zahm et al. (1987)	NCI feasibility study
Nutrition	Extraction	<0-106	Cohen et al. (1980)	See: IARC 41 (1986)

5.2.3 Occupational Exposure Limits

A listing of some national occupational exposure limits is given in Table 9.

Table 9. Occupational exposure limit values

Country	TWA (mg/m³, 20°C)[a]	STEL	TWA (ppm)	STEL	Remarks	Reference
Australia	350	-	100	-	Suspected carcinogen	ILO (1991)
Austria	360	1800[b]	100	500	Suspected of carcinogenic potential	DFG (1991)
Belgium	174	-	50	-	Suspected human carcinogen	ACGIH (1992)
Canada	175	-	50	-		*
Czechoslovakia	500	2500	-	-		ILO (1991)
Denmark	174	-	50	-	Adsorption through skin may be significant Suspected carcinogen	ILO (1991)
Finland	350	870	100	250		ILO (1991)
France	360	1800	100	500		ILO (1991)
Germany	360	1800[b]	100	500	Suspected of carcinogenic potential	DFG (1991)
Italy	174	-	50	-	Suspected human carcinogen	ACGIH (1992)
Japan	350	-	100	-		ILO (1991)
Netherlands	350	1750	100	500		Arbeidsinspectie (1991)
New Zealand	350	1740	100	500		*
Norway	125	-	35	-	Carcinogen	Arbeidstylsynet (1990)
Portugal	174	-	50	-		ILO (1991)
Singapore	174	-	50	-	Suspected carcinogen	*
Sweden	120	250[d]	35	70	Absorption through skin may be significant	AFS (1990)
Switzerland	360	1800	100	500	Classification for teratogenic effects not possible; biological monitoring required	ILO (1991)

Table 9. Occupational exposure limit values (continued)

Country	TWA (mg/m³, 20°C)[a]	STEL	TWA (ppm)	STEL	Remarks	Reference
UK	350	870[c]	100	250	Maximum exposure limit	
USA - ACGIH	174		50		Suspected human carcinogen	ACGIH (1992)
- OSHA	e		500			OSHA (1986)
- NIOSH	f		f		Potential human carcinogen	NIOSH (1986)

TWA, time-weighted average concentration (8h working period)
STEL, short-term exposure limit (15 min, unless specified)
[a] Official values; some countries use different conversion factors and/or other ambient temperature
[b] 30 min
[c] 10
[d] 15 min
[e] PEL (Permissible Exposure Limit) of 500 ppm (1737 mg/m³), ceiling concentration of 1000 ppm (3474 mg/m³), and a maximum peak, not to be exceeded for more than 5 min in 2 h period, of 2000 ppm (6948 mg/m³).
[f] Occupational exposure controlled to lowest feasible limit.

5.3 Human Monitoring Data

5.3.1 Body burden

Methylene chloride was detected in all 8 samples of human milk from 4 urban areas (Pellizzari et al., 1982).

(*Antoine, 1986) Whole blood specimens, 250 subjects, not detected to 25 µg/ℓ, 0.7 µg/ℓ average.

In saliva and tissues from people living in industrialised areas in Beckum, Germany no methylene chloride has been detected (Baner et al., 1981).

5.3.2 Occupational exposure studies

In a cohort of 14 furniture strippers exposed to methylene chloride at concentrations of 53 to 1290 mg/m³, post-exposure breath concentrations of methylene chloride ranged from 8.1 to 590 mg/m³ (McCammon et al., 1991).

Mother's milk in Soviet women manufacturing rubber articles contained a mean of 74 µg/kg mean in 17 of 28 samples approximately 5 h after start of work, the level declining after termination of work (Jensen, 1983).

A group of 7 non-smoking workers, who had previously been exposed to methylene chloride for several years, were exposed to a mean concentration of 635 mg/m³ methylene chloride (in addition, there was exposure to 154 mg/m³ (mean) chloroform). The pre-exposure average carbon monoxide level in alveolar air was 34 mg/m³, increasing to 58 mg/m³ during exposure; before the next exposure, the carbon monoxide level was 27 mg/m³ : these levels correspond to CO-Hb of 4.9%, 8.3% and

3.9%, respectively. The biological half-life of CO-Hb was 13 h (Ratney et al., 1974). Although methylene chloride does not accumulate following repeated exposure, these data clearly indicate that CO-Hb levels will be cumulative if the periods between exposure are insufficient to allow the CO-Hb levels to return to normal.

CO-Hb levels in a worker accidentally overcome by methylene chloride vapours were found to have increased to 19%. A further worker with a history of ischemic heart disease who had been exposed concurrently with the first patient had a CO-Hb level of 6% on the day following the exposure (Benzon et al., 1978).

Methylene chloride levels in alveolar air and blood were measured in 14 shoe-sole factory workers. The alveolar concentration, mean blood levels, and CO-Hb levels were, following exposure to 74 ± 28 mg/m^3 methylene chloride: 49 mg/m^3, 0.41 mg/ℓ, and 4.0%, respectively; upon exposure to 124 ± 42 mg/m^3 methylene chloride : 71 mg/m^3, 0.99 mg/ℓ, and 5.2%, respectively; and upon exposure to 339 ± 265 mg/m^3 methylene chloride : 229 mg/m^3, 3.07 mg/ℓ, and 6.5% respectively. In this factory, the methylene chloride exposure was highly variable; the data are too limited to allow valid extrapolation (Perbellini et al., 1977).

5.3.3 Biological Exposure Indices

Biological Exposure Indices (BEIs) are reference values intended for guidelines for the evaluation of potential health hazards in the practice of industrial hygiene. The BEIs for methylene chloride at the end of a working shift have been given as: CO-Hb level 5%, blood level of methylene chloride 1mg/ℓ.

5.3.4 Appraisal

Biological monitoring of methylene chloride exposure can be based on measurement of the solvent itself in exhaled air or blood. However, as production of carbon monoxide with exposure for more than 3-4 h/day appears to be the limiting factor in regard to health risk, biological monitoring based upon either analysis of carbon monoxide in exhaled air or of CO-Hb in blood is to be preferred. However, this can only be applied in non-smoking subjects. Sampling should be done at about 0-2 h post-exposure, or after 16 h i.e. on the following morning.

Post-exposure CO-Hb levels at 2 h after exposure ceases are not expected to exceed 2-3%, and at 16 h 1%, in the case of an 8 h exposure to less than 350 mg/m^3 methylene chloride in non-smokers.

6. KINETICS AND METABOLISM

6.1 Absorption

6.1.1 Inhalation Exposure

6.1.1.1 Human Studies

The principal route of human exposure to methylene chloride is inhalation. During absorption through the lungs, the concentration of methylene chloride in alveolar air approaches the concentration in inspired air until a steady state is achieved. After tissue and total body steady state is reached through the lungs and other routes, uptake is balanced by metabolism and elimination. Absorption is rapid, followed by a plateau of blood concentration in several h. At low levels of exposure, steady-state blood concentrations increase proportionally with exposure levels. However, at high exposure levels saturation occurs.

Evaluation of pulmonary uptake indicated that 70-75% of inhaled vapour was absorbed in human subjects exposed to 180, 350, 530 and 710 mg/m^3 of methylene chloride. Initial absorption was rapid as indicated by levels of methylene chloride in the blood of approximately 0.6 mg/ℓ in the first h of exposure to levels of 350-710 mg/m^3. At a level of 180 mg/m^3, the increase in blood methylene chloride concentration was 0.2 mg/ℓ for the first h. There was a direct correlation between the steady-state blood methylene chloride values and the exposure concentration, both during the exposure and for the first two h after the exposure in all groups. Steady-state blood levels appeared to be reached during the first h and remained constant until the end of exposure. Once exposure ceased, methylene chloride was rapidly cleared from the blood. Seven h after exposure, less than 0.1 mg/ℓ of methylene chloride was detected at the doses 180, 350 and 530 mg/m^3. Only 1 mg/ℓ was detected in the highest group (710 mg/m^3) 16 h after exposure. All other dose groups had returned to baseline concentrations (Di Vincenzo & Kaplan, 1981a,b).

In common with other lipophilic organic vapours, methylene chloride absorption appears to be influenced by factors other than the vapour concentration. Prior to reaching steady state, increased physical activity increases the amount of methylene chloride absorbed by the body, due to an increase in ventilation rate and cardiac output, since these factors increase blood flow through the lungs and promote absorption (Åstrand et al., 1975; Di Vincenzo et al., 1972).

Uptake also increases with the percent body fat since methylene chloride dissolves in fat to a greater extent than it dissolves in aqueous media. Therefore, obese subjects will absorb and retain more methylene chloride than lean subjects exposed to the same vapour concentration. Under controlled conditions, there was a 30% greater absorption and retention of methylene chloride by obese subjects exposed to 2650 mg/m^3 for 1 h as compared to lean subjects (Engström & Bjurström, 1977).

Åstrand et al. (1975) reported that the amount of methylene chloride taken up increased with physical workload, whereas the retention decreased. With 50-watt workload, the uptake was twice as high, whereas the retention decreased from 55% to 45%. When exposure was coupled with workload (physical exercise), the concentration in alveolar air was increased during the whole post-exposure period compared with exposure under rest conditions.

6.1.1.2 Animal Studies

Studies of the relationship between inhalation exposures of animals and their blood methylene chloride concentrations indicate that absorption is proportional to the magnitude and duration of the exposure over a methylene chloride concentration range of 350-28,200 mg/m³. This conclusion is based on the monitoring of blood methylene chloride concentrations following inhalation exposure in dogs and rats (Di Vincenzo et al., 1972; MacEwen et al., 1972; McKenna et al., 1982). As was the case with humans, blood methylene chloride levels reach a steady-state value which does not increae further as the duration of exposure increases (McKenna et al., 1982).

The data from studies of blood methylene chloride values during 6 h exposure of rats to between 180 and 5300 mg/m³ methylene chloride suggest that the steady-state blood/air concentration ratio increases as the exposure concentration increases. The ratio of the steady-state methylene chloride concentrations in the blood to the exposure concentration was 0.001, 0.005 and 0.007 at levels of 180, 1800 and 5300 mg/m³ respectively (McKenna et al., 1982). It is postulated that the increased ratio at steady state results from saturation of metabolic pathways as exposure increases rather than from an increased absorption coefficient.

Kim & Carlson (1986) conducted experiments to compare the effects of a 12 h exposure schedule to those of an 8 h schedule on the carboxyhaemoglobin (CO-Hb) formation resulting from methylene chloride inhalation. Rats and mice were exposed to 710, 1800, or 3500 mg/m³ methylene chloride 8 h/day for 5 days, or 12 h/day for 4 days. No significant difference in carboxyhaemoglobin levels was found. The peak blood methylene chloride level was found to be dependent upon the methylene chloride exposure concentration, but the half-life was independent of the duration of exposure or the concentration of methylene chloride.

6.1.2 Oral Exposure

No data are available on oral absorption of methylene chloride in humans.

Treatment of mice and rats with methylene chloride in water or in corn oil suggests that methylene chloride is easily absorbed from the gastrointestinal tract. Methylene chloride levels were measured in gut segments up to 40 min after rats were administered single oral doses in water. The amounts measured were similar at both doses (5ː or 200 mg/kg). Sixty percent of the administrated dose (200 mg/kg) was recovered from the upper gastrointestinal tract < 10 min after treatment (20% recovery after 40 min). The amount of methylene chloride in the lower gastrointestinal tract

accounted for <2% of the administered dose up to the 40-min test interval (Angelo et al., 1986b).

In mice administered oral doses of non-radioactive methylene chloride at 10 or 50 mg/kg in water, approximately 25% of the administered dose was detected in the upper gastrointestinal tract within <20 min. Similarly, after treatment with methylene chloride at 10, 50, or 1000 mg/kg in corn oil, approximately 55% of the administered dose was detected in the upper gut segment and remained there for 2 h (Angelo et al., 1986a). After oral administration, methylene chloride was detected in the expired air. 12,3% of a single dose of 1 mg/kg ^{14}C methylene chloride, and 72.1% of a single dose of 50 mg/kg, administered to the rat was eliminated in the breath unchanged within 48h (McKenna and Zempel, 1981). Mice excreted 40% of the administered dose (100 mg/kg) unchanged in expired air within 96 h (Yesair et al., 1977).

6.1.3 Dermal Exposure

No data are available on dermal absorption of methylene chloride in humans.

Methylene chloride can be absorbed though the skin of laboratory animals. Makisimov et al. (1977 as quoted in NIOSH, 1976) immersed two-thirds of the tail of 128 white rats and measured the methylene chloride concentration in various tissues (lung,liver, brain, kidney, heart and fat) by gas chromatography after 1-, 2-, 3- and 4-h exposures . Small increases were seen in most tissues after 1 or 2 h of exposure, and methylene chloride concentrations in fatty tissues increased markedly after 3 h of exposure. After 4 h of exposure , methylene chloride concentrations remained elevated in fatty tissues and were increased in all other tissues studied.

From the moment of application , dermal absorption of liquid methylene chloride in mice increased linearly with time at a rate of 0.1 mg/cm^3 (Tsuruta, 1975). Dermal permeability constants for rats were obtained with three concentrations of methylene chloride in air (106,000, 212,000 and 353,000 mg/m^3), for use in developing a pharmacokinetic model of dermal absorption of vapours. The mean permeability constant was 0.28 mg/cm^2/h. The total amount absorbed was determined to be 34.4, 57.5, and 99.4 mg, respectively, for the three concentrations tested (McDougal et al., 1986).

6.2   Distribution

6.2.1 Inhalation Exposure

6.2.1.1   Human Studies

Engström and Bjurström (1977) exposed 12 male subjects (6 slim and 6 obese) to 2650 mg/m^3 of methylene chloride for 1 h. The total uptake of methylene chloride of the slim group was 1,116 ± 34 mg (15.6 mg/kg) and of the obese group 1,445 ± 110 mg/kg. Estimation of methylene chloride in needle biopsies showed that the adipose tissues contained approximately 8 to 35% of the average total amount absorbed. The amount of methylene chloride absorbed was highly correlated with the degree of

obesity and body weight. In the slim subjects, the concentration in the adipose tissue during the 4-h period after exposure was approximately twice that in the obese subjects. However, despite a lower concentration, the total amount of methylene chloride calculated to be in the body fat was greater in obese subjects.

A survey of the levels of methylene chloride in certain tissues from pregnant or nursing women has been reported. The study was conducted following observations of disturbances in the pattern of pregnancy and lactation in female operatives in an industrial rubber article manufacturing facility. The survey was conducted in an unspecified number of women who had been exposed to several chemicals during their work for at least 3 years. The chemicals included gasoline, ethylene dichloride and methylene chloride. An estimate of the average workplace concentration of methylene chloride was reported to be 85.6 mg/m^3. A control group (number unspecified) was constituted from women working in the same facility but who had no direct contact with the chemicals. The tissues examined were the blood, the foetal membranes and the foetus, all tissue samples being obtained at the time of abortion of the foetus. The mean tissue concentrations of methylene chloride (54 observations) were reported to be 0.66 ± 0.21, 0.34 ± 0.10 and 1.15 ± 0.20 mg/kg for the blood, foetal membranes and foetus respectively, compared to 0.12 ± 0.07, 0.013 ± 0.01 and 0.016 ± 0.001 mg/kg in the controls. Methylene chloride was also detected in 17 out of 28 specimens of breast milk taken from exposed nursing women. An average concentration of 0.074 ± 0.04 μg/ℓ (n=40) was found in the breast milk 5 to 7 h after the start of the exposure; an insignificant quantity of methylene chloride was reported 17 h after cessation of exposure (Vosovaja et al., 1974).

6.2.1.2   Animal Studies

Distribution studies in rats demonstrate that methylene chloride (and/or its metabolites) is present in the liver, kidney, lungs, brain, muscle, and adipose tissues after inhalation exposures (Carlsson & Hultengren, 1975; McKenna et al., 1982). One h after exposure, the highest concentration of radioactive material was found in the white adipose tissue, followed by the liver. The concentration in the kidney, adrenal, and brain were less than half that in the liver. Radioactivity in the fat deposits declined rapidly during the first 2 h after exposure (Carlsson & Hultengren, 1975). Concentrations in the other tissues declined more slowly.

On the other hand, after 5 days of exposure to 710 mg/m^3 for 6 h/day, the concentration of methylene chloride in the perirenal fat was 6-7 fold greater than that in the blood and liver (Savolainen et al., 1977). It has been suggested that methylene chloride first saturates the blood and extravascular fluid compartment before entering the fatty deposits (Di Vincenzo et al., 1972). Thus, concentrations of methylene chloride will rise slowly in adipose tissues and longer exposures to methylene chloride will be required before adipose tissue levels equal these in the blood. The animal data are therefore consistent with the human adipose tissue data discussed above.

Exposure of pregnant rats to methylene chloride may lead to exposure of the foetus to both methylene chloride and carbon monoxide (Anders & Sunram, 1982).

6.2.2 Oral Exposure

No studies were located regarding distribution of methylene chloride in humans following oral exposure.

In animals, radioactivity from labelled methylene chloride was detected in the liver, kidney, lung, brain, epididymal fat, muscle, and testes after exposure of rats to a single gavage doses of 1 or 50 mg/kg methylene chloride. The tissue samples were taken 48 h after dosing. At that time, the lowest concentration of radioactivity was found in the fat. The highest concentrations were in the liver and kidney. This was true for both doses (McKenna & Zemple, 1981).

Similar results were observed in rats administered doses of 50-1,000 mg/kg methylene chloride for 14 days. At each dose tested, and in each tissue, the label was rapidly cleared during the 240 min after each exposure (Angelo et al., 1986b).

These data suggest that methylene chloride and/or its metabolites do not bioaccumulate in any tissues.

6.2.3 Dermal Exposure

No information was found regarding distribution in humans or animals following dermal exposure to methylene chloride.

6.3 Metabolism

Extensive studies have been carried out on the metabolism of methylene chloride in relevant species in order to understand the basis for the carcinogenic response of the liver and lung in the mouse, to understand the clear species difference in this response and to establish their relevance to human carcinogenic hazard assessment. These studies are described in Section 8.8.

6.4 Elimination and Excretion

6.4.1 Inhalation Exposure

Methylene chloride is removed from the body primarily in expired air and urine. In four human subjects exposed to 350 mg/m^3 methylene chloride for 2 h, an average of 22.6 µg methylene chloride was excreted in the urine within 24 h after the exposure; in 7 subjects exposed to 710 mg/m^3 methylene chloride for 2 h, the corresponding value was 81.5 µg (Di Vincenzo et al., 1972). These data show that the amount excreted in the urine is insignificant. Methylene chloride excretion in the expired air was most evident in the first 30 min after exposure. Initial post exposure concentrations of methylene chloride in expired breath following 2 and 4 h exposure periods were about 71 mg/m^3 and dropped to about 18 mg/m^3 at the end of 30 min. Small amounts of methylene chloride remained in the expired air at 2.5 h.

A detailed study of the relationship between the measurements of methylene chloride in expired air or blood, carbon monoxide in expired air, and CO-Hb in blood has been undertaken by Di Vincenzo & Kaplan (1981a,b). At the end of exposure of non-smoking, sedentary volunteers for 7.5 h to methylene chloride vapour concentrations of 180-710 mg/m³, the mean concentration of the solvent in alveolar air and in blood, and the percent CO-Hb saturation were measured, as shown in Table 10.

Table 10. Methylene Chloride in Expired Air and Blood, and Carboxyhaemoglobin (CO-Hb)
Levels of Human Volunteers Following 7.5 h Exposure
(Di Vincenzo & Kaplan, 1981a)

Methylene chloride exposure (mg/m³)	Methylene choride - expired air (mg/m³)	Methylene chloride - blood (mg/100 ml)	CO-Hb levels
180	53	0.03	1.9%
350	124	0.08	3.4%
530	194	0.12	5.3%
710	282	0.18	6.8%

By 7 h post-exposure to any concentration, the expired air contained less than 3.5 mg/m³ methylene chloride; at 16 h, only negligible levels were detected (Di Vincenzo & Kaplan, 1981a). These data suggest that, due to its rapid elimination, measurements of methylene chloride in expired air are unsuitable for use as a marker of occupational exposure.

Di Vincenzo & Kaplan (1981b) reported similar results : exercise was accompanied by increased pulmonary excretion of carbon monoxide during exposure which undoubtedly contributed to the lower than expected CO-Hb values encountered during heavy work loads.

Engström & Bjurström (1977) found that, during the first 2 h after exposure, the concentration in alveolar air tended to be lower and declined more rapidly in obese subjects than in slim ones. After this, the concentration dropped more slowly in the obese group. During the late phase of elimination, the obese subjects tended to have a higher concentration in expired air.

In rats, methylene chloride was excreted in the expired air, urine, and faeces following a single 6 h exposure to 180, 1800, or 53,000 mg/m³ methylene chloride (McKenna et al., 1982). Exhaled air accounted for 58-79% of the radioactive dose. At the 180 mg/m³ exposure only 5% of the exhaled label was found as methylene chloride. The remainder was exhaled as CO and CO_2. As the exposures increased, so did the exhalation of non-metabolised methylene chloride. Methylene chloride accounted for 30% of the label from the 1800 mg/m³ dose and 55% of the label for the 53,000 mg/m³ dose. A combination of exhaled methylene chloride, CO_2, and CO accounted for 58%, 71%, and 79% of the inhaled methylene chloride dose for the 180, 1800 and 53,000

mg/m^3 doses, respectively. Urinary excretion accounted for 7.2-8.9% of the dose and 1.9-2.3% of the dose was in the faeces.

6.4.2 Oral Exposure

Expired air accounted for 78-90% of the excreted dose in rats in the 48 h period following a 1 or 50 mg/kg methylene chloride dose in aqueous solution (McKenna & Zemple, 1981). The radiolabel was present in the exhaled air as CO and CO_2, as well as in expired methylene chloride. The amount of methylene chloride in the expired air increased from 12% to 72% as the dose was increased from 1 to 50 mg/kg. Radiolabel in the urine accounted for 2-5% of the dose under the above exposure conditions, while 1% or less of the dose was found in the faeces. These data indicate that the lungs are the major organ of methylene chloride excretion even under oral exposure conditions.

6.4.3 Dermal Exposure

No information was found regarding excretion and elimination in humans or animals following dermal exposure to methylene chloride.

6.5 Appraisal

Methylene chloride is rapidly absorbed though the alveoli of the lungs into the systemic circulation. It is also absorbed from the gastrointestinal tract and dermal exposure results in absorption but at a slower rate than the other exposures.

It is quite rapidly excreted, mostly via the lungs in the exhaled air. It can cross the blood-brain barrier, it can be transferred across the placenta, and small amounts can be excreted in urine or in milk.

At high concentrations, most of the absorbed methylene chloride is exhaled unchanged. The remainder is metabolised to carbon monoxide, carbon dioxide, and inorganic chloride. Metabolism occurs by either or both of two pathways, whose relative contribution to the total metabolism is markedly dependent on the dose and on the animal species concerned.

One pathway involves oxidative metabolism mediated by cytochrome P-450 and leads to both carbon monoxide and carbon dioxide. This pathway appears to operate similarly in all rodents studied and in man. Whilst this is the predominant metabolic route at lower doses, saturation occurs at a relatively low dose (around 1800 mg/m^3). Increasing the dose above the saturation level does not lead to extra metabolism by this route.

The other pathway involves a glutathione transferase, and leads via formaldehyde and formate to carbon dioxide. This route seems only to become important at doses above the saturation level of the 'preferred' oxidative pathway. In some species (e.g. the mouse) it becomes the major metabolic pathway at sufficiently high doses. In contrast, in other species (e.g. hamster, man) it seems to be used very little at any dose.

Species difference in GST metabolism correlate well with the observed species difference in carcinogenicity. The extent of metabolism by this pathway in relevant species has been used as the basis for a kinetic model to describe the metabolic behaviour of methylene chloride in various species.

7. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

7.1 Microorganisms

7.1.1 Bacteria

7.1.1.1 Aerobic Bacteria

No inhibition of growth was observed at 19.6-19,600 mg/ℓ methylene chloride in *Bacillus subtilis, Pseudomonas cepacia* and *Aeromonas hydrophylia* (Schubert 1979). Inhibition of bioluminescence of *Photobacterium phosphoreum* by 50% occurred after 15 min exposure to 2,880 mg/ℓ methylene chloride (Hermens et al., 1985).

In a standard growth 16 h inhibition test with *Pseudomonas putida* a threshold of 500 mg/ℓ for methylene chloride was determined (Bringmann and Kühn, 1977b). The glycolysis of *Pseudomonas putida* was inhibited after 16 h exposure to 1,000 mg/ℓ (Bringmann and Meinck, 1964).

With *Escherichia coli* a minimal inhibitory concentration of 1049 mg/ℓ methylene chloride was found. For *M. smegmatis* this concentration was 1468 mg/ℓ (Nendza & Seydel, 1988).

For heterotrophs, 50% inhibition of oxygen consumption occured at 320 mg/ℓ after 24 h (Blum and Speece, 1991).

In other bacteria (*Acinetobacter, Alcaligenes, Flavobacterium, Pseudomonas cepacia, Aeromonas hydrophila*) stimulation of growth was observed at 200 mg/ℓ (Davis et al., 1981).

The IC_{50} for inhibition of multiplication of *Escherichia coli* was 37.2 mg/ℓ (Nendza & Seydel, 1988).

In the OECD activated sludge, respiration inhibition test (method 209) using sealed vessels the EC_{50} value for methylene chloride was higher than 1000 mg/ℓ after 30 min (Volskay & Grady, 1988).

Concentrations up to 1,000 mg/ℓ had no effect on oxygen consumption or glucose metabolism of activated sludge acclimated to methylene chloride for 3 days (Klečka, 1982).

In methylene chloride utilising bacteria, like *Hyphomicrobium*, up to 1700 mg/ℓ did not interfere with growth (Stucki et al., 1981).

For methanogens the 48h IC_{50} for inhibition of gas production was 7.2 mg/ℓ methylene chloride and for *Nitrosomonas* the IC_{50} for reduction of ammonia was 1.2 mg/ℓ after 24 h (Blum and Speece, 1991).

7.1.1.2   Anaerobic Bacteria

Anaerobic bacteria are more sensitive. Methanogenesis of mixed rumen microflora was inhibited from 136 mg/ℓ (Bauchop, 1967). At 93 mg/ℓ methylene chloride the growth of a mixed bacterial population from an anaerobic digester was inhibited by 50% (Thiel, 1969). Addition of methylene chloride to anaerobic sludge from an operating municipal digester showed after 48 h a 20% inhibition of gas production at 3 mg/ℓ and 50% at 50 mg/ℓ (*Hayes & Balley, 1977). Addition of methylene chloride to the feed of a mixed anaerobic culture, developed in the laboratory from seed from a sewage treatment plant, decreased the gas production to such an extend that at 3.3 mg/ℓ that it had virtually ceased after 5 days compared with 15 days in controls (Vargas & Ahler, 1987). In another study with anaerobic biological sludge a concentration of 1 mg/ℓ methylene chloride appeared to be toxic (*Surfleet, 1974).

7.1.2. Protozoa

The bacteriovorous ciliated protozoan *Uronema parduczi* Chatton-Lwoff was not affected after 20 h exposure to 16,000 mg/ℓ (EC_5 inhibition cell proliferation) (Bringmann and Kühn, 1980). Also, no effects were observed in *Microregma heterostoma* after 28h exposure to 1000 mg/ℓ methylene chloride (Bringmann & Meinck, 1964).

7.1.3 Algae (Table 11)

In several freshwater green algae (*Selenastrum capricornutum, Scenedesmus subspicatus, Scenedesmus quadricauda, Chlorella vulgaris, Chlamydomonas angulosa*) photosynthesis (chlorophyll a content, CO_2 uptake) and cell number, were only affected by methylene chloride from 1450 mg/ℓ (Bringmann and Kühn, 1978; Hutchinson et al., 1978; Kühn, 1979; UBA, 1986; EPA, 1980). The threshold (7d EC_3) for effects in blue-green algae (*Microcystis aeruginosa*) was 550 mg/ℓ (Bringmann and Kühn, 1978).

In the marine diatom *Skeletonema costatum* methylene chloride exposure had no effect on chlorophyll a content or cell number at 662 mg/ℓ (Selenka and Bauer, 1978; EPA, 1980).

Table 12. Acute aquatic toxicity - fresh water

Organism	Description	T (°C)	pH/Dissolved oxygen (mg/ℓ)	Hardness (mgCaCO3/ℓ)	Flow/Static	Parameter	Concentration (mg/ℓ)	References and remarks
Crustacea	Water flea (Daphnia magna)	22	7.4-9.4/ 6.5-9.1	173	Static	48h-LC$_{50}$ 48h-NOEC	220 68	Le Blanc (1980) Nominal concentration
Crustacea	Water flea (Daphnia magna)	20-22	7.6-7.7	Unknown	Static	24h-EC$_{50}$ 24h-NOEC	2100-2270 1550-1707	Bringmann & Kühn (1977a, 1982) Nominal concentration
Crustacea	Water flea (Daphnia magna)	Unknown	Unknown	Unknown	Static	48h-LC$_{50}$	270	Daniels et al. (1985)
Crustacea	Water flea (Daphnia magna)	Unknown	Unknown	Unknown	Static	48h-LC$_{50}$	1250 mg/ℓ	Bringmann & Meinck (1964)
Crustacea	Water flea (Daphnia magna)	Unknown	Unknown	Unknown	Static	24h-EC$_{50}$ 48h-EC$_{50}$	1959 1682	Kühn et al. (1989) (closed system)
Crustacea	Water flea (Daphnia magna)	Unknown	Unknown	Unknown	Static	48h-EC$_{50}$	135	Abernethy et al. (1986) (closed system)
Crustacea	Water flea (Daphnia magna)	Unknown	Unknown	Unknown	Unknown	24h-EC$_{50}$	12.5	Knie (1988) Nendza & Seydel (1988)
Crustacea	Water flea (Daphnia magna)	18-20	8/ 8.7-8.8	11.7	Unknown	48h-LC$_{50}$ 48h-NOEC	480 100	RIVM (1986) Nominal concentration; closed system
Fish	Goldfish (Carrasslus auratus)	Unknown	Unknown	Unknown	Static	24h-$_{50}$	420	Jansen (1978) Nominal concentration
Fish	Fathead minnow (Pimephales promelas) (adult)	12	7.8-8.0/ > 5	> 5	Static Flow	96h-LC$_{50}$ 96h-LC$_{50}$ 96h-NOEC	310 193 66.3	Alexander et al. (1978) Static test nominal, flow-through measured concentrations; aquarium covered with plastic film for the first 24 h
Fish	Fathead minnow (Pimephales promelas) (juvenile)	25	7.6-8.1	73-82	Flow	96h-LC$_{50}$	502	Dill et al. (1987) Analysed concentration
Fish	Bluegill, (Lepomis macro-chirus)	21-23	6.5-7.9/ 9.7-0.3	32-48	Static	96h-LC$_{50}$	220	Buccafusco et al. (1981) Nominal concentration, aquarium not capped

Table 11. Methylene Chloride: Acute aquatic toxicity to algae

Organism	Description	Method	Parameter	Concentration (mg/ℓ)	Reference
Diatom	*Skeletonema costatum* (salt water)	Chlorophyll *a* content, cell number	96h-EC_{50}	> 662	EPA (1980)
Green alga	*Selenastrum capricornutum*	Chlorophyll *a* content, cell number	96h-EC_{50}	> 662	EPA (1980)
Green alga	*Scenedesmus subspicatus*	Unknown	7d-EC_3	1450	UBA (1986) (Kühn (1979)
Green alga	*Scenedesmus quadricauda*	Cell number	EC_0	1450	Bringmann & Kühn (1978)
Green alga	*Scedenesmus sp.*	Unknown	LD_{50}	125	Selenka & Bauer (1976)
Green alga	*Chlorella vulgaris*	CO_2 uptake	3h EC_{50}	2292	Hutchinson et al. (1978)
Green alga	*Chlamydomonas angulosa*	CO_2 uptake	3h EC_{50}	1477	Hutchinson et al. (1978)
Blue-green alga	*Microcystis aeruginosa*	Cell number	7d-EC_3	550	Bringmann & Kühn (1978)

7.2   Aquatic Organisms

The volatility of methylene chloride presents difficulties in aquatic toxicity testing. Flow-though systems or closed static systems are necessary to adequately conduct toxicity studies. These systems were not always used (Table 12).

Table 12. Methylene chloride - Acute aquatic toxicity/salt water

Organism	Description	T (°C)	pH/Dissolved oxygen (mg/ℓ)	Hardness (mgCaCO₃/ℓ)	Flow/ Stat	Parameter	Concentration (mg/ℓ)	References and remarks
Fish	Golden orfe (*Leuciscus idus*)	Unknown	Unknown	Unknown	Static	48h-LC_{50}	521-528	Juhnke & Lüdemann (1978)
Fish	Killifish (juvenile) (*Fundulus heteroclitus*)	20±2	6.1-8.0/ > 4	Unknown	Static	48h-LC_{50}	97.0	Burton & Fisher (1990)
Crustacea	Mysid shrimp (*Mysidopsis bahia*)	Unknown	Unknown	Unknown	Static	96h-LC_{50}	260	EPA (1980) Nominal concentration
Crustacea	Grass shrimp (*Palaemonetes pugia*)	20 ± 2	6.1 - 8.0 > 4	8 - 12	Static	48h-LC_{50}	108.5	Burton & Fischer (1990)
Fish	Sheepshead minnow (*Cyprinodon variegatus*)	25-31	Unknown	10-31	Static	96h-LC_{50} 96h-NOEC	330 130	Heitmuller et al. (1981) Nominal concentration

7.2.1 Plants

The EC_{50} for *Lemna minor* growth was 2,000 mg/ℓ, whilst both growth and photosynthesis of the plant *Groenlandia densa* were totally inhibited at this concentration after 7 days (Merlin et al., 1992).

7.2.2 Invertebrates

7.2.2.1 Insects

The toxicity of methylene chloride for insects was investigated in adult *Tribolium confusum* and grain weevil (*Calandra granaria*). The LC_{50} for a 5h exposure in fumigation vessels was 82 and 380 mg/ℓ, respectively (Back and Cotto as cited in Negherbon, 1959; Ferguson and Pirie, 1948).

7.2.2.2 Crustaceans (Table 12)

The acute toxicity of methylene chloride to *Daphnia magna* has been repeatedly studied. A relative high 24h-EC_{50} value of 2100-2270 mg/ℓ and a NOEC of 1550-1700 mg/ℓ were found in a static study (Bringmann and Kühn, 1977a, 1982).

The static 48 h-LC_{50} and NOEC values were respectively 220 mg/ℓ and 68 mg/ℓ in one study, whilst the 48h-LC_{50} was reported to be 27 mg/ℓ in another (Le Blanc 1980, Daniels et al., 1985). In an earlier study the mobility of *Daphnia magna* was affected after 48h exposure to 1250 mg/ℓ (Bringmann and Meinck, 1964). In none of these studies the water concentration of methylene chloride was analytical determined, nor where precautions described to avoid evaporation.

In more recent studies using closed exposure systems static 24h and 48h-EC_{50} values of 1959 and 1682 mg/ℓ were obtained (Kühn et al., 1989). Lower 48h-EC_{50} values of 480 and 135 mg/ℓ were reported using closed systems (RIVM, 1986; Abernethy et al., 1986). In the static DIN 38 412 11 test with *Daphnia magna* the 24h EC_{50} was 12.5 mg/ℓ (Knie, 1988; Nendza & Seydel, 1988).

In the marine environment, mysid shrimp (*Mysidopsis bahia*) has been investigated; in a static system the 96h LC_{50} was 256 mg/ℓ (Le Blanc, 1984). The static 48h LC_{50} for grass shimp (*Palaemonetes pugio*) was measured to be 108.5 mg/ℓ (Burton and Fischer, 1990).

7.2.2.3 Molluscs

In seawater metamorphoses was induced in up to 63% of the larvae of the nudibranch mollusc (*Phestilla sibogae*) when exposed to 8.500-25.500 mg/ℓ of methylene chloride (Pennington and Hadfield, 1989).

7.2.3 Fish (Table 12)

7.2.3.1 Acute toxicity

In the golden orfe (*Leuciscus idus*) the nominal static $48h\text{-}LC_{50}$ value was found to be 521-528 mg/ℓ and in the bluegill (*Lepomis macrochirus*) the nominal static 96h LC_{50} appeared to be 220 mg/ℓ (Buccafusco et al., 1981; Juhnke and Lüdemann, 1978).

In the goldfish (*Carassius auratus*) the nominal static 24h LC_{50} was found to be 420 mg/ℓ (Jansen, 1978 as cited in EUCLID, 1992).

The acute toxicity of methylene chloride to adult fathead minnows (*Pimephales promelas*) has been studied both in a static and a flow-though system. The $96h\text{-}LC_{50}$ was 310 (nominal) and 193 (measured) mg/ℓ, respectively. The observed effects (loss of equilibrium, melanisation, narcosis and swollen, haemorrhaging gills) were reversible at a sublethal level. The no-observed effect concentration (NOEC) was 66.3 mg/ℓ (Alexander et al., 1978).

In a flow-through study with juvenile fathead minnow (*Pimephales promelas*) the $96h\text{-}LC_{50}$ value was significantly higher than adults at 502 mg/ℓ (Dill et al., 1987).

Juvenile killifish (*Fundulus heteroclitus*) was more sensitive to methylene chloride, the static $48\ h\text{-}LC_{50}$ being 97 mg/ℓ (Burton and Fischer, 1990).

The acute toxicity of methylene chloride to marine species was only evaluated in sheepshead minnow (*Cyprinodon variegatus*) showing in a static test a $96\ h\text{-}LC_{50}$ value of 330 mg/ℓ and no effects at 130 mg/ℓ (Heitmuller et al., 1981).

7.2.3.2 Chronic toxicity and reproduction

In the guppy (*Poecilia reticulata*) the nominal LC_{50} after 14 days exposure to a daily renewed methylene chloride solution was 295 mg/ℓ (Könemann, 1981).

In an egg-larva test in the rice fish (*Oryzias latipes*) with exposure up to 3 weeks after hatching and renewal of the test solution 3 times per week, an analytically determined EC_{50} and LC_{50} of 106 mg/ℓ was found. The NOEC in this study was 75 mg/ℓ (RIVM, 1986).

Fish embryos are the most sensitive to methylene chloride with analytical determined $96\ h\text{-}LC_{50}$ values of 13.1 mg/ℓ in Rainbow trout (*Salmo gairdneri*; flow-through, fertilisation to 4 d post hatching) and about 34 mg/ℓ in fathead minnow (flow-through, embryo-larval test). In the rainbow trout teratics were observed from 5.5 mg/ℓ (Black et al., 1982).

In a flow though study with juvenile fathead minnow (*Pimephales promelas*) the LC_{50} and the threshold for effects after 8 days exposure were 471 and 357 mg/ℓ methylene chloride, respectively. In a 32 d embryo-larval test in the same species the larval survival and weight was affected from 209 and 142 mg/ℓ respectively. The maximum acceptable

toxicant concentration (MATC) based on body weight was calculated to be 108 mg/ℓ. The ratio between the acute 8 d LC_{50} value and the 32 d embryo-larval MATC is 4.6, indicating a small difference between acute and chronic effects of methylene chloride (Dill et al., 1987).

7.2.4 Amphibians

In closed flow-though systems short-term embryo-larval tests were carried out with amphibian eggs of *Rana catesbeiana, R. palustris* and *Bufo fowleri*. Combining frequencies for lethality and teratogenesis the analytical determined 96 h post hatching LC_{50}s were > 32 mg/ℓ for pickerel frog (*R. palustris*) and Fowler's toad (Bufo Fowleri) and 17.78 mg/ℓ for bullfrog (*R. catesbeiana*). In the latter anomalous larvae and 16% decreased hatching were observed at 6.73 mg/ℓ. In pickerel frog and Fowler's toad hatching was decreased by 14 and 20% at 10 and 32 mg/ℓ, respectively. In the hatched populations slightly higher incidences of teratics were observed. The probit LC_{10} and LC1 for the most sensitive species were 0.98 and 0.09 mg/ℓ, respectively (Birge et al., 1980).

In the same test system 96 h LC_{50} values ranging from 16.9 to above 48 mg/ℓ were found for eggs of the European common frog (*R. temporaria*), Northwestern salamander (*Ambystoma gracile*), African clawed frog (*Xenopus laevis*) and the Leopard frog (*R. pipiens*). The European common frog and the Northwestern salamander were the most sensitive to methylene chloride. For the European salamander the probit LC10 and LC1 were 0.82 mg/ℓ and 0.07 mg/ℓ, respectively (Black et al. 1982).

7.3 Terrestrial Organisms

In a 48-h filter paper contact toxicity test in the earthworm *Eisenia fetida* the LC_{50} was 304 µg/cm² in one study and higher than 1000 µg/cm² in another, and therefore methylene chloride was classified as moderately toxic (100-1000 $\mu g/cm^2$) (Roberts and Dorough, 1984; Neuhauser et al., 1985).

The toxicity of methylene chloride to higher plants (*Phaseolus vulgaris, Raphanus sativus radicula, Lepidum sativum, Trifolium pratense, Saintpaula ionatha, Petunia hybrida*) was evaluated, using the LIS (Landesanstalt für Immissionsschutz, Essen) test; no effect was observed at 100 mg/m³ exposure over 14 days (Van Haut and Prinz, 1979).

In leaves of alfalfa (*Medicago sativa*) the effect of methylene chloride vapours on the photosynthetic fixation of $^{14}CO_2$ was tested; photosynthesis appeared to be reduced from 388,000 mg/m³ (Lehman and Paech, 1972).

In chicken embryos of the White leghorn the LD_{50} for injection of methylene chloride in the yolk sack is 14 mg/egg (Verrett et al., 1980).