Environmental Health Criteria 62

1,2-DICHLOROETHANE

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INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

ENVIRONMENTAL HEALTH CRITERIA 62

1,2-DICHLOROETHANE

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The International Programme on Chemical Safety (IPCS) is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by the IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

Every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors that may have occurred to the Manager of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda, which will appear in subsequent volumes.

* * *
A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Palais des Nations, 1211 Geneva 10, Switzerland (Telephone no. 988400 - 985850).

ENVIRONMENTAL HEALTH CRITERIA FOR 1,2-DICHLOROETHANE

A WHO Task Group on Environmental Health Criteria for 1,2-Dichloroethane met in Geneva from 25 to 30 August, 1986. Professor F. Valic opened the meeting on behalf of the Director-General. The Task Group reviewed and revised the draft criteria document and made an evaluation of the health risks of exposure to 1,2-dichloroethane.

The drafts of this document were prepared by DR T. VERMEIRE of the National Institute of Public Health and Environmental Hygiene, Bilthoven, the Netherlands.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

* * *

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1. SUMMARY AND CONCLUSIONS

1,2-Dichloroethane (DCE) is a colourless, flammable, and volatile liquid that decomposes slowly in the presence of air, moisture, and light; its vapour decomposes in flame and on hot surfaces yielding hydrogen chloride, phosgene, and other chlorine-containing compounds.

Sensitive analytical methods have been developed for the determination of 1,2-dichloroethane using gas chromatography. Detection limits are in the range of 0.02 - 1.2 µg/m³ air, 0.001 - 10 µg/litre water, 25 µg/litre blood, and 44 - 100 µg/kg food or tissue. Methods used for air analysis include direct ultraviolet or infrared spectroscopy and direct reading colorimetry tubes.

World production of 1,2-dichloroethane in 1981 was estimated to be about 23,000 kilotonnes. In 1983, the chemical was ranked as the 15th highest volume chemical produced in the USA. It is principally used in the synthesis of vinyl chloride. Human exposure mainly occurs at, and in the vicinity of, production facilities, through skin contact and inhalation. Almost 60% of the total emission (about 0.2% of production) is estimated to be lost to the air, water, and soil from these industries; nearly one-third of this loss is estimated to occur via disposal of heavy ends in vinyl chloride production (EDC tars). Human
exposure to the vapour as a result of dispersive uses of 1,2-
dichloroethane can occur when it is used in gasoline or as a
solvent or seed fumigant. Losses via dispersive uses account
for about 40% of the total emission. Emissions also occur from
contaminated water and from waste-disposal sites.

Average concentrations found in the vicinity of production
facilities have been below 40 µg/m³. In the air of cities,
average concentrations of between 0.3 and 6.5 µg/m³, with a
reported maximum of 30 µg/m³, have been measured. Only two old
reports on small groups of occupationally-exposed men are
available, indicating exposure levels of 40 – 800 mg/m³.

In air, 1,2-dichloroethane is degraded by sunlight fairly
rapidly yielding mainly carbon oxides and hydrogen chloride.
This prevents accumulation in the atmosphere.

Emissions of 1,2-dichloroethane entering water may amount to
about 0.1% of production volume; in addition, some of the
emissions from EDC tars will also contaminate water. However,
average levels in drinking-water are generally below 1
µg/litre. The main removal process from water is
evaporation, since chemical degradation, biodegradation, and
bioconcentration are unlikely to occur.

LC50 values for fish exposed for 1 - 4 days ranged between
85 and 550 mg/litre water, with bioaccumulation unlikely. A no-
observed-adverse-effect level of 11 mg/litre was found for

_Daphnia magna_, following long-term exposure. 1,2-Dichloro-
ethane does not pose a significant hazard for the aquatic
environment, except in cases of accident or inappropriate
disposal.

1,2-Dichloroethane is readily absorbed via the dermal, oral,
or inhalation routes.

After oral administration, blood levels peak earlier with
low than with high doses, and are 5 times higher with oral
exposure to doses of the order of 150 mg/kg body weight than
with similar inhalation exposure. After inhalation, a
disproportionate increase in blood level occurs with increasing
dose. At an exposure level of 3200 mg/m³, a steady blood level
is achieved after 2 – 3 h. After oral dosing, 1,2-dichloro-
ethane showed a preference for adipose tissue and liver. Following
inhalation, accumulation was mainly observed in
adipose tissue, but not in the liver. At higher levels of
exposure, relatively more 1,2-dichloroethane accumulated.

1,2-Dichloroethane was found in fetal tissues and in the
placenta, when pregnant rats were exposed by inhalation to the
compound at 1000 mg/m³ for 3 days.

When administered orally, parenterally, or by inhalation to
rats and mice, it is extensively biotransformed to urinary
metabolites (55 – 90%). Relatively more is metabolized at lower
doses. Metabolism may occur via two known pathways: one via
cytochrome P-450-mediated oxidation and the other via
glutathione conjugation. The former pathway involves the
formation of 2-chloroacetaldehyde and 2-chloroethanol. Although
this pathway appears to be important in vitro in producing
intermediates capable of interacting with DNA, it does not
appear to be important in vivo. Reactive intermediates are
formed when 1,2-dichloroethane is metabolized via glutathione
conj u gation. The identity of these intermediates has not been confirmed, though some evidence suggests the formation of \( \text{S-} (2\text{-chloroethyl}) \text{ glutathione and its alkylating episulfonium ion, which, by reaction with DNA, yield an indicated adduct, S-} [2\text{-}(N^7\text{-guanyl})\text{-ethyl}] \text{ glutathione.} \)

Excretion of 1,2-dichloroethane or its metabolites from rodents is rapid. At least 89% of the body burden was excreted via the lungs or urine within 24 h in intraperitoneally-injected mice and within 48 h in orally-dosed mice.

The oral LD\(_{50}\) was found to be 413 - 489 mg/kg body weight in the mouse, 680 - 850 mg/kg body weight in the rat, and 2500 mg/kg body weight in the dog. The 6-h LC\(_{50}\) was estimated to be 1060 mg/m\(^3\) in the mouse and 5100 - 6660 mg/m\(^3\) in the rat. Deaths occurred within a narrow range of concentrations.

In an exposure-response inhalation study on rats, no adverse effects were observed in a 7-h exposure to 1200 mg/m\(^3\). At the next higher exposure level (2400 mg/m\(^3\)), depression of the central nervous system (CNS) was observed, and some of the rats died after 7 h. As the exposure levels increased, depression of the CNS became more severe, and deaths occurred after progressively shorter exposure periods. At the highest concentration (81 000 mg/m\(^3\)), rats became comatose and some died within 0.3 h. Liver and kidney damage was found in most of the animals that died.

After single oral doses of 615 - 770 mg/kg body weight, liver damage was observed histologically in rats. Myocardial oedema and damage to coronary vessels were observed.

In 3 short-term inhalation studies, various species were exposed to concentrations of between 405 and 3900 mg 1,2-dichloroethane/m\(^3\) air, 6 or 7 h per day, for 5 days/week. Mice and rats appeared to be more sensitive than guinea-pigs, rabbits, monkeys, dogs, and cats. The overall no-observed-adverse-effect level for exposure periods ranging from 4 to 9 months in the rat was about 400 mg/m\(^3\). Signs of intoxication, including central nervous system depression and death, were observed in all species exposed to the higher concentrations of between 1620 and 3900 mg/m\(^3\). For rats, liver damage, mainly consisting of fatty changes, was observed after exposure to 1540 mg/m\(^3\) for up to 12 weeks, 1620 mg/m\(^3\) for up to 8 weeks, and 1900 mg/m\(^3\) for up to 1 week. In rats, guinea-pigs, and mice, an increased mortality rate was observed at concentrations of 730 mg/m\(^3\) or more. In rabbits, there was an increase in the mortality rate from 1540 mg/m\(^3\) and, in monkeys, from 1620 mg/m\(^3\). Dogs and cats only showed increased mortality at 3900 mg/m\(^3\).

Repeated oral administration of 1,2-dichloroethane at a dose of 300 mg/kg body weight was lethal for rats after 5 doses and produced necrosis and fatty changes in the liver. No effects were observed when the chemical was given orally to rats at 10 mg/kg body weight daily for 90 days or at 150 mg/kg, 5 times per week, for 2 weeks.

1,2-Dichloroethane is weakly mutagenic in Salmonella typhimurium TA 1535, both in the absence of, and in the presence of, a microsomal activation system. However, in the presence of cytosolic glutathione-\( \Gamma \)-transferase, a stronger positive
response was obtained. Negative results were obtained with strains TA 1537, TA 1538, and TA 98. Mutagenicity occurs in fungi, Drosophila, and mammalian cells in vitro. In two human cell lines exposed to 1,2-dichloroethane, the incidence of gene mutations was found to increase with increasing levels of glutathione-S-transferase. Micronuclei or dominant lethals were not induced, and a weak mutagenic effect was reported in a spot test on mice. DNA damage has been observed in bacteria, mammalian cells in vitro, and in mammals in vivo. 1,2-Dichloroethane did not induce cell transformation in one of two assays, and enhanced virus-induced cell transformation in the other.

1,2-Dichloroethane is carcinogenic in B6C3F1 mice and Osborne-Mendel rats following administration of doses of 50 - 300 mg/kg body weight, given by gavage, in oil. In male rats, squamous cell carcinomas of the forestomach, subcutaneous fibromas, and haemangiosarcomas in several organs (mainly the spleen) were produced following gavage; in female rats, mammary gland fibromas and mammary adenocarcinomas were increased. In mice, increased incidences of hepatocellular carcinomas in males and mammary gland adenocarcinomas in females, and lung adenomas in both sexes were observed. No increase in tumour incidence was reported in inhalation studies on Swiss mice and Sprague Dawley rats exposed to concentrations of up to 607 mg/m³.

A prolongation of the estrus cycle, an increase in embryonal mortality, pre-implantation losses, and haematomas were found when female rats were exposed to 15 mg/m³, 4 h per day, 6 days/week, for 4 months prior to mating and during pregnancy. While the fetal toxicity of 1,2-dichloroethane was not confirmed at higher exposure levels, severe toxic effects on rats were observed and all implantation sites resorbed. No fetal abnormalities were observed in the rabbit. Oral administration to male and female rats of up to 35 mg 1,2-dichloroethane/kg body weight per day, via the food, for up to 2 years, did not affect reproduction. No effects on fertility or gestation index, and no teratological effects were observed in a 2-generation study on mice treated with 5 - 50 mg 1,2-dichloroethane/kg body weight per day, via drinking-water, for up to 25 weeks.

1,2-Dichloroethane may cause severe corneal damage in animals, but no gross skin reactions occurred in a 12-h occluded patch test on guinea-pigs. Corneal opacity was observed in dogs, following subcutaneous injection.

In man, immersion of the hands for 4 h at intermittent intervals caused severe dermatitis. Conjunctivitis has been reported from exposure to vapour, and corneal opacity from accidental ingestion.

Two early reports describe human effects from occupational exposure, and a number of fatal case histories through accidental oral ingestion. Complaints referable to the CNS, liver, and gastrointestinal tract were reported in workers occupationally exposed to concentrations of 1,2-dichloroethane of 250 - 800 mg/m³. Similar complaints were reported less frequently by workers exposed to concentrations of 40 - 150 mg/m³. Liver and bile-duct disorders, neurotic conditions, autonomous dystonia, neuromyalgia, and hyperthyroidism have been reported in workers exposed to 5 - 150 mg 1,2-dichlorethane/m³.

Accidental ingestion of 10 - 250 g 1,2-dichloroethane
resulted in death in all instances. Haemorrhage at various sites, depression of the CNS, liver and kidney damage, and pulmonary oedema occurred.

Making an overall evaluation, in the absence of human data, and taking into account that: (a) 1,2-dichloroethane produces a reactive intermediate that alkylates DNA, (b) it is positive in a number of mutagenicity tests in vitro, though weakly so, and (c) both rare and common tumours are produced in rats and mice, it would be prudent to consider 1,2-dichloroethane as a possible human carcinogen. Thus, it should be regarded, for practical purposes, as if it presented a carcinogenic risk for man. In evaluating reproduction hazards and teratogenicity, it is necessary to rely on the limited data available from laboratory investigations since there are no human data. The weight of evidence does not suggest that exposure to prevailing environmental levels poses a reproductive or teratogenic hazard.

Degradation processes are rapid enough to prevent accumulation of 1,2-dichloroethane in the atmosphere. Except in the case of accidents or inappropriate disposal, 1,2-dichloroethane does not present a significant hazard for the aquatic environment. Available data are not sufficient to evaluate its effects on soil.

Further studies are needed on: (a) DNA alkylation (adduct identification); (b) sub-chronic toxicity by various routes of exposure; (c) assessment of the extent to which EDC tars contribute to contamination of groundwater by 1,2-dichloroethane; and (d) dose-response on sensitive, commercially important fish species (particularly studies relevant to EDC tar spills).

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Structural formula:  
\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{H}
\end{array}
\begin{array}{c}
\text{Cl} \\
\text{C} \\
\text{Cl}
\end{array}
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{H}
\end{array}
\]

Molecular formula:  \( \text{C}_2\text{H}_4\text{Cl}_2 \)

Abbreviation:  EDC

Synonyms:  alpha,beta-dichloroethane, 1,2-bichloroethane, ethane dichloride, ethylene chloride, ethylene dichloride, 1,2-ethylene dichloride, sym-(metric)-dichlorehane

Common trade names:  Borer-Sol, Brocide, Destruxol Dichlor-emulsion, Dichlor-mulsion, Dutch Liquid, Dutch Oil, ENT 1656, Gaze Oleflant

CAS registry number:  107-06-2

Conversion factor:  1 ppm = 4.05 mg/m\(^3\) air at 25 °C and 101.3 kPa (760 mmHg)
2.2 Physical and Chemical Properties

1,2-Dichloroethane is a flammable compound that burns with a smoky flame. When dry, 1,2-dichloroethane is stable at ordinary temperatures. In the presence of air, moisture, and light, the liquid decomposes slowly, yielding hydrogen chloride and other corrosive products. Vapour-air mixtures are readily ignited. In a flame, or at a hot surface, 1,2-dichloroethane decomposes, yielding hydrogen chloride, phosgene, and other chlorine-containing compounds. Some physical characteristics of 1,2-dichloroethane are given in Table 1.

2.3 Analytical Methods

A summary of relevant methods of sampling and analysis is presented in Table 2.

Table 1. Some physical characteristics of 1,2-dichloroethane

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical state</td>
<td>liquid</td>
</tr>
<tr>
<td>Colour</td>
<td>colourless</td>
</tr>
<tr>
<td>Taste</td>
<td>sweet</td>
</tr>
<tr>
<td>Odour</td>
<td>chloroform-like</td>
</tr>
<tr>
<td>Odour threshold</td>
<td>25 - 450 mg/m³, for perception; 162 - 750 mg/m³ for recognitiona</td>
</tr>
<tr>
<td>Relative molecular mass</td>
<td>98.96</td>
</tr>
<tr>
<td>Melting point</td>
<td>-35 °C</td>
</tr>
<tr>
<td>Boiling point</td>
<td>83 °C</td>
</tr>
<tr>
<td>Water solubility</td>
<td>8.69 g/litre, 20 °C</td>
</tr>
<tr>
<td>log n-Octanol/water partition coefficient</td>
<td>1.48</td>
</tr>
<tr>
<td>Relative density</td>
<td>1.23, 20 °C</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>3.42</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>8.53 kPa (64 mmHg), 20 °C</td>
</tr>
<tr>
<td>Flash point</td>
<td>13 °C (closed cup)</td>
</tr>
<tr>
<td>Flammable limits</td>
<td>0.25 - 0.64 g/litre, 6 to 16 vol %</td>
</tr>
</tbody>
</table>


Table 2. Sampling, preparation, analysis

<table>
<thead>
<tr>
<th>Medium</th>
<th>Sampling method</th>
<th>Analytical method</th>
<th>Detection limit</th>
<th>Sample size</th>
<th>Comment</th>
</tr>
</thead>
</table>

Dichloroethane, 1,2- (EHC 62, 1987, 1st edition)
<table>
<thead>
<tr>
<th>Sample Medium</th>
<th>Method of Sampling</th>
<th>Analytical Technique</th>
<th>Limit</th>
<th>Volume or Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>Manual sampling</td>
<td>Colorimetry, direct reading</td>
<td>not specified</td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td>Continuous monitoring with or without built-in aspirator</td>
<td>UV-photodetection</td>
<td>approximately 4 mg/m³</td>
<td>not specified</td>
</tr>
<tr>
<td>Air</td>
<td>Continuous monitoring and breath analysis</td>
<td>Infra-red spectroscopy</td>
<td>subject to analysis by pounds</td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td>Sampling on charcoal</td>
<td>Desorption by carbon disulfide, gas chromatography with flame ionization detection</td>
<td>0.013 ug/litre per sample</td>
<td>3 - 40 litres</td>
</tr>
<tr>
<td>Air</td>
<td>Sampling on charcoal or Chromosorb</td>
<td>Thermal desorption; gas chromatography with flame ionization detection</td>
<td>1.2 ug/m³</td>
<td>10 litres</td>
</tr>
<tr>
<td>Air</td>
<td>Sampling on Tenax polymeric beads</td>
<td>Thermal desorption; gas chromatography with mass spectrometric detection</td>
<td>0.032 ug/m³</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>Stripping by helium adsorption on Tenax</td>
<td>Thermal desorption; gas chromatography with flame ionization detection or mass spectrometric detection</td>
<td>0.001 ug/litre</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>Stripping by helium or nitrogen, sorption on Tenax or Chromosorb</td>
<td>Thermal desorption; gas chromatography with microcoulo-metric detection</td>
<td>0.1 - 0.4 ug/litre</td>
<td>5 ml</td>
</tr>
<tr>
<td>Water</td>
<td></td>
<td>Gas chromatography with mass spectrometric detection</td>
<td>0.5 ug/litre</td>
<td>0.1 ml</td>
</tr>
<tr>
<td>Water</td>
<td></td>
<td>Gas chromatography with electron capture detection</td>
<td>10 ug/litre</td>
<td>1 litre</td>
</tr>
<tr>
<td>Blood, Tissue</td>
<td></td>
<td>Gas chromatography with flame ionization detection</td>
<td>25 ug/litre blood, 50 ug/kg tissue (wet weight)</td>
<td>1 ml</td>
</tr>
</tbody>
</table>
3. SOURCES IN THE ENVIRONMENT, ENVIRONMENTAL TRANSPORT AND DISTRIBUTION

3.1 Natural Occurrence

There are no reports of 1,2-dichloroethane occurring as a natural product.

3.2 Man-Made Sources

3.2.1 Production, disposal of waste, and uses

3.2.1.1 Production levels

In 1983, 1,2-dichloroethane was ranked as the 15th highest volume chemical produced in the USA (Webber, 1984). World production in 1981 was estimated to be 23,130 kilotonnes (Gold, 1980). In the countries of the European Community, the production capacity was estimated to be 9,446 kilotonnes in 1982 (DeQuinze et al., 1984), an increase over the estimated 5,290 kilotonnes capacity reported for 1977 (Atri, 1984). In the USA, production increased from 4,750 kilotonnes in 1977 (Drury & Hammons, 1979) to 5,740 kilotonnes in 1983 (Webber, 1984). In Japan, a total production of 1,800 kilotonnes was reported in 1976 (IARC, 1979).

3.2.1.2 Production processes

Two processes are used, which are very often combined into one so-called "balanced process". The first is the vapour or liquid phase reaction of chlorine with ethene in the presence of a catalyst, usually 1,2-dibromoethane or metal chlorides. The second is the reaction of ethene with oxygen and hydrogen chloride in the presence of the catalyst, copper (II) chloride (Drury & Hammons, 1979).

Most commercial 1,2-dichloroethane is 97 - 99% pure and contains approximately 0.1% by weight of alkylamines to inhibit decomposition. Impure 1,2-dichloroethane may contain polychlorinated ethanes, and the uninhibited product may also contain chlorine and/or hydrogen chloride (Drury & Hammons, 1979; IARC, 1979).

The above production processes and the production of end-products, mainly vinyl chloride, are important sources of emission of 1,2-dichloroethane into the environment. In 1979, in the USA, almost 60% of the total emission of 12 kilotonnes was lost by these industries to the air, water, and soil and about 40% via dispersive uses as a solvent (Seufert et al., 1980). In the USA, in 1977, approximately 35% of the emissions of 1,2-dichloroethane associated with the production of the compound itself and end-products were estimated to occur via disposal of heavy ends, the so-called EDC tars, a mixture of
low- and high-boiling chlorinated hydrocarbons (Gold, 1980).

3.2.1.3 Disposal of wastes

Large amounts of western European tars used to be dumped in the North Sea, but incineration at sea seems to be the present practice (Jensen et al., 1975). In the USA, disposal of EDC tars is usually by burial in a landfill or incineration (Drury & Hammons, 1979; Gold, 1980).

3.2.1.4 Uses

The major industrial use of the compound is in the synthesis of vinyl chloride (approximately 90% of the total production in Japan and approximately 85% of total production in the USA) (IARC, 1979). Other chemicals produced from 1,2-dichloroethane are 1,1,1-trichloroethane, ethyleneamines, vinylidene chloride, trichloroethylene, and tetrachloroethylene. In 1977, 2 - 4% of the total production of 1,2-dichloroethane in the USA was used for the synthesis of each of these chemicals. Another 2% was used in the USA as a lead scavenger in gasoline. This application will decline in importance with the world-wide conversion to unleaded fuel. A small fraction of the total production, approximately 0.1% in the USA in 1977, was used for solvent and fumigant applications (Gold, 1980). When used as a fumigant, 1,2-dichloroethane is usually mixed with carbon tetrachloride to reduce the fire hazard, and small portions of other fumigants may be added (WHO, 1972).

3.3 Transport and Fate in the Environment

Out of the total production of 1,2-dichloroethane in the USA in 1977, approximately 0.2% was estimated to be lost to the atmosphere, 40% of this during dispersive use as a solvent or fumigant (Seufert et al., 1980). Evaporation from disposal sites also occurs. In 1977, losses to the atmosphere were estimated to be higher (1% of total production). Minimal estimates for emissions entering water and for emissions via EDC tars in 1977 were 0.1 and 0.5% of total production, respectively (Gold, 1980).

Evaporation appears to be the major pathway by which 1,2-dichloroethane is lost from water. In a controlled outdoor experiment, the half-life for the disappearance from running river water was found to be 1.4 h (Scherb, 1978). This agrees well with laboratory findings (Dilling et al., 1975). Loss by chemical reaction with water is insignificant (Radding et al., 1977).

In the troposphere, rain-out and adsorption on atmospheric aerosols are unlikely because of the high vapour pressure and the low solubility of the compound (Cupitt, 1980). The major part of the 1,2-dichloroethane is removed from the atmosphere via oxidation by hydroxyl radicals. On the basis of experimentally-derived rate constants, and hydroxyl radical concentrations of 4.8 x 10^6 and 1.0 x 10^6 radicals/ml, respectively, half-lives for this reaction have been calculated of 10 days (Radding et al., 1977) and 36 days (Howard & Evenson, 1976). A lifetime of 53 days was predicted, which would preclude accumulation in the troposphere and transport to the stratosphere (Howard & Evenson, 1976). The reported degradation products are formyl chloride, hydrogen chloride, carbon dioxide, carbon monoxide, and monochloroacetyl chloride (Pearson &
McConnell, 1975; Spence & Hanst, 1978). Since 1,2-dichloroethane absorbs light within the solar spectral region, photolytic transformation is possible (Cupitt, 1980). However, the extent of this reaction has not been verified experimentally.

Slow biodegradation of 1,2-dichloroethane was observed in fresh water, seeded by settled domestic waste water. Non-acclimated cultures caused a biological demand of 16% of the theoretical oxygen demand for the compound in 10 days (Price et al., 1974). 1,2-Dichloroethane was biodegraded in aqueous media by acclimated aerobic mixed cultures from soil or sewage samples (Stucki et al., 1981; Tabak et al., 1981). An aerobic bacterium G10, a Pseudomonas strain, that was able to use 1,2-dichloroethane as a sole source of carbon and energy for growth, was isolated from samples containing a mixture of activated sludge and soil samples (Janssen et al., 1984). In addition, slow anaerobic biodegradation, mainly to carbon dioxide, was observed in an aqueous medium with a mixed methanogenic culture, grown on waste activated sludge with sodium acetate as a primary substrate (Bouwer & McCarty, 1983).

In soil, 1,2-dichloroethane adsorbs aselectively to bentonite clay and peat moss, but not to dolomitic limestone and silica (Dilling et al., 1975).

4. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

4.1 Environmental Levels

4.1.1 Water

Concentrations of 1,2-dichloroethane measured at different locations are summarized in Table 3. It will be noted that Symons et al. (1975) observed more positive samples in finished water than in untreated water. This suggests treatment-related contamination during water chlorination.

4.1.2 Air

Concentrations of 1,2-dichloroethane measured in air at various locations are summarized in Table 4.

4.1.3 Food

Reports on 1,2-dichloroethane in food are scarce. Bauer (1981) found that levels were generally low in the Federal Republic of Germany. Milk products with added fruits contained an average of 0.8 µg/kg. In Canada, 15 out of 34 samples of spice oleoresins contained between 2 and 34 mg of 1,2-dichloroethane, used as an extractant, per kg (Page & Kennedy, 1975).

In residue studies, various amounts of 1,2-dichloroethane were found to remain in fumigated grain, depending on the type of grain and fumigation mixture, exposure conditions, and the extent of subsequent ventilation (Berck, 1965, 1974). Wheat was found to contain the highest residue levels, varying from 16 to 213 mg/kg following common fumigation practices. Processing reduces residue levels; for example, 1 – 10 mg/kg were recovered in ground wheat flour; less than 2 mg/kg was present in bread (Lynn & Vorhes, 1957; Wit et al., 1969). In the United Kingdom, 1 out of 281 samples of wheat contained 1,2-dichloroethane at a level of 290 mg/kg; in the remaining samples, the concentration was below the detection limit of 4.0 mg/kg (Bailey et al.,
1982). 1,2-Dichloroethane at a level of 51 mg/kg in fumigated soybeans was completely extracted by hexane, during the production of oil by solvent extraction (Storey et al., 1972).

### 4.1.4 Industrial wastes

EDC tar originating from vinyl chloride production in 1974 (400 000 tonnes on a global basis) contained up to 35% 1,2-dichloroethane together with other components, seven of which have been identified.

#### Table 3. Environmental levels in water

<table>
<thead>
<tr>
<th>Type of water</th>
<th>Location</th>
<th>Detection limit (µg/litre)</th>
<th>Levels observed (µg/litre)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sea water</td>
<td>Gulf of Mexico, open ocean; near Mississippi mouth</td>
<td>0.001</td>
<td>nd</td>
<td>Sauer (1980); Osaka Bay</td>
</tr>
<tr>
<td>River water</td>
<td>Germany, Federal Republic of; 3 rivers</td>
<td>1.0</td>
<td>1.0 (average)</td>
<td>nd - 4.0</td>
</tr>
<tr>
<td></td>
<td>USA; 14 industrial river basins</td>
<td>1.0</td>
<td>5.6 (average in 25% of samples)</td>
<td>nd - 90</td>
</tr>
<tr>
<td>Untreated water</td>
<td>USA; 80 drinking-water stations</td>
<td>0.2 - 0.4</td>
<td>nd (86%) (maximum)</td>
<td>Symons (1975)</td>
</tr>
<tr>
<td></td>
<td>Netherlands; 232 ground-water stations</td>
<td>0.5</td>
<td>nd (229 stations) (3 stations)</td>
<td>Zoetema et al.</td>
</tr>
<tr>
<td>Drinking-water</td>
<td>USA; 80 stations</td>
<td>0.2 - 0.4</td>
<td>nd (68%) (maximum)</td>
<td>Symons al. (1985)</td>
</tr>
<tr>
<td></td>
<td>Japan; 5 locations</td>
<td>0.5</td>
<td>nd (4 locations) (1 location)</td>
<td>Fujii (1985)</td>
</tr>
<tr>
<td></td>
<td>Germany, Federal Republic of; 100 cities</td>
<td>1.0</td>
<td>nd</td>
<td>Bauer (1987)</td>
</tr>
</tbody>
</table>

*a* nd = not detected.

### 4.2 General Population Exposure

Daily intake from urban air in the USA has been estimated to be between 8 and 140 µg per day (Singh et al., 1983). In the Netherlands, the figure is 26.5 µg per day (Guicherit & Schulting, 1985).

More specifically, people can be exposed via air at, or near, sites of production and dispersive use, notably in anti-knock agents in gasoline. At 12 locations near production facilities in each of 3 areas in the USA, average air concentrations gradually decreased from 61 µg/m³ to 2 µg/m³ at distances of 1 km and 3 - 4 km, respectively. Thus, near
production facilities, approximately 12.5 million people in the USA were estimated to be exposed to average annual concentrations of up to 40 µg/m³ (Elfers, 1979; Kellam & Dusetzina, 1980).

The annual average population exposure to 1,2-dichloroethane from gasoline, in the USA, has been estimated to remain below 0.12 µg/m³ (Kellam & Dusetzina, 1980).

4.3 Occupational Exposure

No data were available to the Task Group concerning exposure levels in the 1,2-dichloroethane- and vinyl chloride-synthesizing industries. Poisoning incidents following inhalation or skin exposure have been reported frequently for places of work where 1,2-dichloroethane is used as a solvent or fumigant, but data concerning exposure levels are scarce (Hadengue & Martin, 1953; Paparopoli & Cali, 1956; Suveev & Babichenko, 1969).

1,2-Dichloroethane levels of up to 150 mg/m³ (Kozik, 1957) and ranging from 40 to 800 mg/m³ (Cetnarowicz, 1959) were detected in industrial plants using the chemical as a solvent.

Time-weighted averages of 0.1 and 1 mg/m³, respectively, have been reported for 2 different jobs in an anti-knock agent blending plant in the USA. The maximum exposure level measured was 8.9 mg/m³ (Jacobs, 1980).

Table 4. Environmental levels in air

<table>
<thead>
<tr>
<th>Type of site</th>
<th>Location</th>
<th>Detection limit (µg/m³)</th>
<th>Average levels observed (µg/m³)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marine</td>
<td>Osaka Bay</td>
<td>8.4</td>
<td></td>
<td>Okamoto &amp; Tatsukawa (1981)</td>
</tr>
<tr>
<td></td>
<td>Pacific</td>
<td>0.168</td>
<td></td>
<td>Singh et al. (1982)</td>
</tr>
<tr>
<td>Rural</td>
<td>USA</td>
<td>0.02</td>
<td>nd</td>
<td>Grimsrud &amp; Rasmussen (1975)</td>
</tr>
<tr>
<td></td>
<td>Japan</td>
<td>0.05</td>
<td>0.3 - 0.4a</td>
<td>Environment Agency, Japan (1983)</td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td>0.08</td>
<td></td>
<td>Clark et al. (1984a,b)</td>
</tr>
<tr>
<td></td>
<td>Netherlands</td>
<td>0.2</td>
<td></td>
<td>Guicherit &amp; Schulting (1985)</td>
</tr>
<tr>
<td>Urban</td>
<td>United Kingdom</td>
<td>0.48 - 2.14a</td>
<td></td>
<td>Tsani-Bazaca et al. (1981)</td>
</tr>
<tr>
<td></td>
<td>USA; 10 cities</td>
<td>0.335 - 6.11</td>
<td>30 (maximum)</td>
<td>Singh et al. (1983)</td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td>1.2</td>
<td></td>
<td>Clark et al. (1984a,b)</td>
</tr>
</tbody>
</table>
### Table 4 (contd.)

<table>
<thead>
<tr>
<th>Type of site</th>
<th>Location</th>
<th>Detection limit (µg/m³)</th>
<th>Average observed levels (µg/m³)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parking garage and repair shop</td>
<td>Sweden</td>
<td>0.01</td>
<td>2.0 - 6.5</td>
<td>Jonsson &amp; Berg (1980)</td>
</tr>
<tr>
<td>Inside cars</td>
<td>Sweden</td>
<td>0.01</td>
<td>0.4 - 1.2</td>
<td>Jonsson &amp; Berg (1980)</td>
</tr>
<tr>
<td>Exhaust gases (cars)</td>
<td>United Kingdom</td>
<td>38 - 3250&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>Tsani-Bazaca et al. (1981)</td>
</tr>
<tr>
<td>Airport vicinity</td>
<td>USA</td>
<td>nd</td>
<td></td>
<td>Tsani-Bazaca et al. (1982)</td>
</tr>
<tr>
<td>Motorway</td>
<td>United Kingdom</td>
<td>0.08</td>
<td></td>
<td>Clark et al. (1984a)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Range of values (not average).

<sup>b</sup> Many sites with undetectable levels of 1,2-dichloroethane were not considered in the average.

nt = not detected.

### 5. KINETICS AND METABOLISM

#### 5.1 Absorption

1,2-Dichloroethane can be found in the blood of rodents, almost immediately after dermal, oral, or inhalation exposure.

During a 12-h dermal exposure of guinea-pigs to undiluted 1,2-dichloroethane, blood concentrations of 1,2-dichloroethane increased rapidly during the first half hour and then more slowly, up to the end of exposure (Jakobson et al., 1982). In mice, a dermal absorption rate of 47 µg/cm² per min was measured over the first 15 min following application of undiluted 1,2-dichloroethane (Tsuruta, 1975).
Oral exposure of rats to 25 or 250 mg EDC/kg body weight in corn oil produced peak blood levels within 9 and 90 min, respectively. Blood levels appeared to increase linearly with exposure from 13 mg/litre at 25 mg/kg up to levels of between 30 and 70 mg/litre at 150 and 250 mg/kg. Small quantities of metabolites, but no detectable amounts of 1,2-dichloroethane, were recovered in faeces (Sopikov & Gorshunova, 1979; Reitz et al., 1982).

During inhalation at concentrations of up to 3200 mg/m³, steady-state blood levels of the chemical in rats were reached within 2 - 3 h. The blood levels increased disproportionally with exposure from 1.4 mg/litre at 202 mg/m³ to 8.3 mg/litre at 607 mg/m³ and 56 mg/litre at 3200 mg/m³. These data suggest saturation of the metabolic capacity at a blood level of approximately 5 mg/litre. Peak blood levels of 1,2-dichloroethane were almost 5 times higher following oral exposure to 150 mg/kg body weight than after inhalation exposure to 607 mg/m³, which appeared equivalent to 113 mg/kg body weight (Sopikov & Gorshunova, 1979; Spreatico et al., 1980; Reitz et al., 1982). These exposure concentrations were the high dose levels for the NCI (1978) oral study and the Maltoni et al. (1980) inhalation study.

5.2 Distribution

The distribution of 1,2-dichloroethane in tissue has mainly been investigated during exposure of laboratory animals. However, one report, has been identified that gives an indication of the relative distribution of 1,2-dichloroethane in human tissues (Luznikov et al., 1985). As shown in Table 5, 1,2-dichloroethane concentrations were measured in ten biological compartments following acute oral poisoning. 2-Chloroacetaldehyde, a metabolite of 1,2-dichloroacetaldehyde, was not detected. In addition to 1,2-dichloroethane, detectable quantities of 2-chloroethanol and monochloroacetic acid were reported. In this report, the omentum and stomach contained similar high levels of 1,2-dichloroethane; liver and kidney contents were comparable, but approximately 10 times less. The detectable amounts of metabolites were too low to make comparisons.

Table 5. Levels of 1,2-dichloroethane and its metabolites determined by gas chromatography in cadaveric organs and tissues of 15 human beings who died after acute oral poisoning.

<table>
<thead>
<tr>
<th>Tissues/ organs</th>
<th>1,2-dichloroethane (mg/kg)</th>
<th>2-chloroacetaldehyde (mg/kg)</th>
<th>2-chloroethanol (mg/kg)</th>
<th>Monochloroacetic acid (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>5 - 100</td>
<td>nd</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Kidney</td>
<td>5 - 80</td>
<td>nd</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Myocardium</td>
<td>10 - 150</td>
<td>nd</td>
<td>0.12 - 1.1</td>
<td>2.3 - 3.8</td>
</tr>
<tr>
<td>Spleen</td>
<td>1 - 50</td>
<td>nd</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Omentum</td>
<td>100 - 950</td>
<td>nd</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Tissue</td>
<td>10 - 100</td>
<td>nd</td>
<td>0.12 - 0.28</td>
<td>1.0 - 2.0</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------</td>
<td>-----</td>
<td>-------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Stomach</td>
<td>100 - 1000</td>
<td>nd</td>
<td>0.14 - 0.56</td>
<td>1.0 - 2.0</td>
</tr>
<tr>
<td>Small intestine</td>
<td>10 - 90</td>
<td>nd</td>
<td>0.13 - 0.21</td>
<td>0</td>
</tr>
<tr>
<td>Large intestine</td>
<td>5 - 60</td>
<td>nd</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Blood</td>
<td>10 - 150</td>
<td>nd</td>
<td>nd</td>
<td>nd</td>
</tr>
</tbody>
</table>

---
a From: Luznikov et al. (1985).

**Note:** The analytical detection limit for 1,2-dichloroethane and all metabolites except monochloroacetic acid was 100 g/litre or 100 g/kg tissue; for monochloroacetic acid, the limit was 100 g/litre or 100 g/kg tissue.

After oral exposure of rats to 25, 50, or 150 mg 1,2-dichloroethane/kg, in corn oil, peak levels of the parent compound in adipose tissue at 45 - 60 min exceeded those in blood by 3.9 - 8.3 times. Peak levels in the liver, 10 min after exposure, exceeded those in blood by 1.3 - 2.2 times. This accumulation was lower than expected at the 2 higher exposure levels, indicating saturation of the tissues at higher doses. During inhalation, steady-state levels in rat tissues were reached within 2 - 3 h and increased 20- to 30-fold when the exposure increased from 202 to 1012 mg/m³, suggesting a saturable metabolic capacity (section 5.3). Levels in adipose tissue, at steady-state, were 7 - 8 times higher than those in blood, while levels in the liver were 20% below those in blood. At comparable blood levels, the maximum concentration of 1,2-dichloroethane after inhalation was lower in the liver and higher in lung and adipose tissue than after oral exposure. Levels in the spleen, brain, and kidney were similar to those in the blood, irrespective of the route of administration (Spreafico et al., 1980).

Forty-eight h after ingestion of 150 mg/kg body weight or inhalation exposure to a concentration of 607 mg/m³, 3 - 4% of the body burden of labelled 1,2-dichloroethane was recovered in the carcass of rats. Most radioactivity was found in the liver and kidneys. Residual radioactivity in selected tissues was 1 - 2 times higher after oral exposure than after inhalation. Another difference between oral and inhalation exposure was the higher residual activity in the forebrain, well after the oral exposure. A similar distribution pattern emerged for macromolecular binding, as determined 4 h after oral ingestion or directly after inhalation. At these times, oral exposure produced lower levels of total macromolecular binding, but higher levels of DNA alkylation than inhalation exposure. The absolute levels of DNA alkylation (2 - 14 µmol equivalents of 1,2-dichloroethane per mol DNA at 1 mmol/kg body weight) were considered low (Reitz et al., 1982).

In another study, rats and mice were compared with respect to DNA binding in liver, kidney, stomach, and lung, 22 h after a single intraperitoneal injection of 0.86 mg labelled 1,2-dichloroethane/kg body weight in ethanol. Binding to lung DNA was low compared with that in the other tissues. Binding to DNA of mouse organs was always greater than that to DNA of rat organs (Arfellini et al., 1984).
When pregnant rats inhaled 1,2-dichloroethane at a level of 1000 mg/m³, for 4 h per day, the compound was found to accumulate in the placental and fetal tissues over a period of 7 days (Vosovaya, 1977). Withey & Karpinski (1985) also obtained evidence that exposure of rats to 1,2-dichloroethane via inhalation results in detectable levels in fetuses in a dose-related manner.

Binding of 1,2-dichloroethane to protein, lipid, and DNA was also observed in vitro (Guengerich et al., 1980).

5.3 Metabolism

Metabolism of 1,2-dichloroethane appears to have a significant role in the manifestation of the toxic, carcinogenic, and mutagenic effects of this chemical.

Biotransformation of 1,2-dichloroethane is extensive in the mouse; ip doses of 50 and 170 mg/kg body weight were associated with 88 and 55% conversion to metabolites, respectively (Yllner, 1971). The metabolites identified by Yllner (1971) are shown in Table 6. Reitz et al. (1982) observed extensive metabolism of 1,2-dichloroethane in the rat, i.e., 70 and 91% transformation, with oral (150 mg/kg) and inhalation (607 mg/m³; 6 h) exposures, respectively, 85% of the metabolites appearing in the urine. Biotransformation of 1,2-dichloroethane approaches saturation at high blood levels.

Table 6. Non-volatile urinary metabolites of 1,2-dichloroethane in rodents

<table>
<thead>
<tr>
<th>Species</th>
<th>Route</th>
<th>Metabolite</th>
<th>Fraction of total (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>mouse</td>
<td>oral</td>
<td>(conjugated) S-carboxy-methylcysteine</td>
<td>48</td>
<td>Yllner (1971)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>thiodiacetic acid</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>chloroacetic acid</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>S,S'-ethene-bis-cysteine</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-chloroethanol</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>rat</td>
<td>inhala-</td>
<td>thiodiacetic acid</td>
<td>67 - 68</td>
<td>Reitz et al.</td>
</tr>
<tr>
<td></td>
<td>tion</td>
<td>or oral</td>
<td></td>
<td>(1982)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(in oil) thiodiacetic acid sulfoxide</td>
<td>26 - 29</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>S-(2-hydroxyethyl)mercap- turic acid</td>
<td></td>
<td>Nachtomi et al.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S-(2-hydroxyethyl)cysteine</td>
<td></td>
<td>(1966)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-chloroethanol</td>
<td></td>
<td>Kokarovtseva &amp; Kiselyova (1978)</td>
</tr>
</tbody>
</table>
1,2-Dichloroethane metabolism involves the formation of sulfur-containing metabolites, which appear in the urine. Two proposed pathways of metabolism of 1,2-dichloroethane are depicted in Fig. 1; one pathway begins with cytochrome P-450-mediated oxidation, and the other begins with glutathione conjugation. There is a lack of evidence that doses of 1,2-dichloroethane, either by gavage or inhalation, have any effects on the distribution of its metabolites between these pathways. Cytochrome P-450 enzymes catalyse an oxidative transformation of 1,2-dichloroethane to form reactive intermediates, which result in the formation of 2-chloroacetaldehyde and 2-chloroethanol (Guengerich et al., 1980) (Fig. 1). Johnson (1965, 1966, 1967) has shown that 2-chloroacetaldehyde reacts both enzymatically and non-enzymatically with glutathione (GSH).

[Diagram of proposed pathways for 1,2-dichloroethane metabolism]

Rannug et al. (1978) first reported that mutagenic compounds could be formed by the reaction of GSH with 1,2-dihaloalkanes in the presence of cytosolic glutathione-$\mu$-transferases. This observation led workers to investigate in greater detail the role of glutathione-$\mu$-transferases in the metabolism and bio-
activation of both dibromoethane (DBE) and 1,2-dichloroethane (Rannug, 1980; Sundheimer et al., 1982; Ozawa & Guengerich, 1983; Inskeep & Guengerich, 1984). This pathway (Fig. 1) involves the direct reaction of GSH with 1,2-dichloroethane to form S-(2-chloroethyl) glutathione, which is a half mustard with a half-life of 69 min at 20 °C (Schasteen & Reed, 1983) and less than 15 min at 37 °C (Foureman & Reed, 1985). Non-enzymic conversion of the half mustard to the corresponding episulfonium ion gives a putative alkylating agent (episulfonium ion) that has several fates (Fig. 1). Reaction can occur with water to form S-(2-hydroxyethyl) glutathione or reaction with thiols such as GSH to form ethene bis-glutathione or with DNA to form adducts. With the exception of DNA adducts, the reaction products are considered non-toxic and undergo further metabolism. These reactions and subsequent metabolism of the products can account for all of the known sulfur-containing metabolites found in the urine of 1,2-dichloroethane-treated animals.

Although much evidence has been reported that supports the P-450 mediated metabolism of 1,2-dihaloethanes, this branch of the pathway (Fig. 1) does not appear relevant to DNA adduct formation by 1,2-dichloroethane (Koga et al., 1986). Guengerich et al. (1980) proposed the possibility of chloroso oxidation products of 1,2-dichloroethane in DNA adduct formation (Fig. 1). However, they observed that the apparent stimulation of P-450-directed DNA adduct formation by GSH was a result of incomplete removal of GSH conjugates during analysis (Koga et al., 1986). In addition, they concluded that 2H and 18O studies on the formation of 2-haloethanols and 2-haloacetaldehydes from 1,2-dihaloethanes are inconsistent with a major role of such a mechanism for DNA damage (Guengerich et al., 1986; Koga et al., 1986).

It should be pointed out that the P-450 directed pathway can presumably form considerable quantities of 2-haloacetaldehydes, which readily bind to protein and non-protein thiols, as shown for vinyl bromide and vinyl chloride (Guengerich et al., 1981) and dibromoethane (DBE) (van Bladeren et al., 1981).

Although some DNA damage can be produced via the P-450 pathway under in vitro conditions (Hill et al., 1978; Banerjee et al., 1980; Guengerich et al., 1980; Lin et al., 1985), several lines of evidence suggest that the GSH conjugation pathway is probably of greater significance than the P-450 pathway as the major in vivo route for DNA damage (Guengerich et al., 1980; Rannug, 1980; Sundheimer et al., 1982; Inskeep et al., 1986).

It has been possible to correlate the 1,2-dichloroethane-induced mutation frequency of two human cell lines with the difference in levels of glutathione-S-transferase activities. AHH-1 cell line mutation frequency was 25 times that in the TK6 cell line in the presence of 1,2-dichloroethane. The difference was attributed to the fact that the AHH-1 cell line possesses 5 times more glutathione-S-transferase activity than the TK6 cell line (Crespi et al., 1985).

Male B6C3F1 mice, pretreated with piperonyl butoxide (PIB), were examined for the extent of hepatic DNA damage produced 4 h after 1,2-dichloroethane administration (Storer & Conolly, 1985). PIB is a P-450 inhibitor. Hepatic DNA damage, as measured by the alkaline DNA unwinding assay for single-strand breaks and alkali-labile lesions, was potentiated by PIB. Treatment of mice with high doses of 2-chloroethanol failed to
produce DNA damage, as measured by this assay. Diethylmaleate, a GSH depletor, potentiated the hepatotoxicity of 2-chloroethanol but not DNA damage. Although the significance of this observation is uncertain, it is not inconsistent with the hypothesis that reduction of GSH levels is associated with a reduction in DNA damage.

Recent evidence suggests that the putative episulfonium ion, resulting from a non-enzymatic conversion of S-(2-chloroethyl) glutathione, is a major intermediate in the formation of DNA adducts in vivo from 1,2-dichloroethane exposures (Fig. 2) (Inskeep et al., 1986). When rats were administered a single dose of 14C-1,2-dichloroethane in vivo and the liver analysed 8 h later, 78% of the DNA adducts (0.25 nmol/mg DNA) could be released by neutral thermal hydrolysis. A major adduct and several minor adducts were present; the major adduct co-chromatographed with S-[2-(N7-guanyl)ethyl] glutathione. DNA adducts released from kidney preparations by neutral thermal hydrolysis were represented by 5 different fractions containing radioactivity after chromatography. The postulated adduct of liver DNA after 14C-1,2-dichloroethane exposure, S-[2-(N'-guanyl)ethyl] glutathione, appears to be chromatographically identical to the major adduct in rats after exposure to DBE (Koga et al., 1986). This DBE adduct, which has been isolated and characterized by NMR and mass spectrometry, gives strong support to an identical adduct being the principal DNA adduct from exposure to 1,2-dihaloethanes. The formation of apurinic sites, as this adduct cleaves from DNA, may be a key factor in the mutagenic and carcinogenic effects of these compounds.

5.4 Excretion and Elimination

Excretion of 1,2-dichloroethane from rodents is rapid. Approximately 89% or more of the body burden of the compound was
excreted within 24 h in ip-injected mice (Yllner, 1971), within 48 h in orally exposed mice (Mitoma et al., 1985), and within 48 h in rats exposed orally or via inhalation (Reitz et al., 1982; Mitoma et al., 1985). In the 3 studies cited above, excretion of 1,2-dichloroethane or its metabolites mainly occurred in exhaled air via the lungs and in urine via the kidneys. In both species, and at various exposure levels, 7 - 18% of the metabolized 1,2-dichloroethane was excreted as carbon dioxide (CO₂) and approximately 80 - 85% as non-volatile metabolites (Table 6). The metabolism of 1,2-dichloroethane in mice and rats is dose-dependent. For example, in mice, 11 and 45% of the body burdens of 1,2-dichloroethane, resulting from ip exposure to 50 and 170 mg/kg body weight, respectively, were excreted unchanged via the lungs within 72 h (Yllner, 1971). In rats, 1.8, 11.5, and 29% of the body burdens were excreted unchanged via the lungs within 48 h following: an inhalation exposure at 607 mg/m³ for 6 h (equivalent to a dose of 113 mg/kg body weight) (Reitz et al., 1982), an oral dose of 100 mg/kg body weight (Mitoma et al., 1985), and an oral dose of 150 mg/kg body weight (Reitz et al., 1982), respectively.

The rate of elimination from blood and tissues appears to depend on the exposure level; the higher the exposure level, the slower the elimination rate of 1,2-dichloroethane, after both oral and inhalation exposure. Half-lives in the blood of rats, exposed orally, increased from 25 min at 25 mg/kg body weight to 57 min at 150 mg/kg body weight. With inhalation exposure, half-lives increased from 13 min at 202 mg/m³ to 22 min at 1012 mg/m³, after a 6-h inhalation exposure (Sprefico et al., 1980). In addition, after oral exposure of rats to 150 mg/kg body weight, an initial half-life of 90 min in blood decreased to 20 - 30 min, when blood levels fell below 5 - 10 mg/litre after 3 h (Reitz et al., 1982). Elimination of 1,2-dichloroethane from blood, adipose tissue, lung, liver, brain, kidneys, and spleen was comparable after oral exposures of up to 150 mg/kg body weight. Elimination from the liver was reported to be biphasic with a higher elimination rate just after reaching peak levels of 1,2-dichloroethane. Elimination from other organs was monophasic. Following inhalation, elimination was the slowest in adipose tissue and the most rapid in the lung, up to an exposure level of 1012 mg/m³ (Sprefico et al., 1980). Withey & Collins (1980) also reported that the elimination of 1,2-dichloroethane was dose-dependent. After iv administration of from 3 to 15 mg/kg body weight to male Wistar rats, the authors found that the elimination fitted a two-compartment model at a low-dose level and a three-compartment model at high-dose levels.

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

6.1 Aquatic Organisms

6.1.1 Acute toxicity

The acute toxicity of 1,2-dichloroethane for aquatic organisms is summarized in Table 7. The concentration of 1,2-dichloroethane was measured in four of the studies cited (see footnote⁸ in Table 7); the concentrations reported in the other studies were nominal. It should be noted that, in open systems, the toxic effects observed must have occurred at concentrations lower than the nominal ones reported in latter studies, due to the anticipated evaporation of 1,2-dichloro-
ethane in the aquatic media.

The species most sensitive to 1,2-dichloroethane were members of the class Crustacea. A no-observed-adverse-effect level below 68 mg/litre was found for *Daphnia magna* (Le Blanc, 1980). The shrimp *Crangon crangon* showed a 96-h LC$_{50}$ of 85 mg/litre in sea water, measured by the flow-through method (Adema, 1976). When the brine shrimp *Artemia salina* was exposed to 1,2-dichloroethane at levels ranging from 0.25 to 25 mg/litre, growth inhibition was noted 24 h after cyst wetting (Kerster & Schaeffer, 1983).

EDC tar is much more toxic for marine species than 1,2-dichloroethane, the heavy fractions of the tar being responsible for the high toxicity observed (Jernelöv et al., 1972; Rosenberg, 1972; Jensen et al., 1975; Rosenberg et al., 1975).

6.1.2 Short-term exposures

When blue algae *Mycrocystis aeruginosa* and green algae *Scenedesmus quadricauda* were exposed in closed containers to 1,2-dichloroethane at 105 and 710 mg/litre, respectively, for 8 days, cell multiplication started to be inhibited (Bringmann & Kühn, 1978). Guppies (*Poecilia reticulata*) were exposed for 7 days in a static test, and an LC$_{50}$ of 106 mg/litre was found. Solutions were renewed daily, but no water analysis data were reported (Könemann, 1981). Finally, an early life stage flow-through test was done. Fathead minnows (*Pimephales promelas*) were exposed to concentrations of between 4 and 56 mg/litre beginning from 2 to 5 days after spawning and continuing throughout the subsequent embryonal, larval, and juvenile stages up to 28 days after hatching. Water was analysed for 1,2-dichloroethane. Body weight was reduced at 59 mg/litre. The survival of juveniles, the percentage of normal larvae at hatch, and the hatchability of embryos were not affected (Benoit et al., 1982).

Table 7. Acute aquatic toxicity

<table>
<thead>
<tr>
<th>Organism</th>
<th>Description</th>
<th>t (°C)</th>
<th>pH</th>
<th>Dissolved oxygen (mg CaCO$_3$/liter)</th>
<th>Hardness (mg/litre)</th>
<th>Flow/Parameter stat/open/closed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteria</td>
<td><em>Pseudomonas putida</em></td>
<td>25</td>
<td>7</td>
<td>stat</td>
<td>16-h MI closed</td>
<td></td>
</tr>
<tr>
<td>Protozoa</td>
<td><em>Entosipon sulc-atum</em>, <em>Uronema parduczi</em>, <em>Chilomonas paramecium</em></td>
<td>25</td>
<td>7</td>
<td>stat</td>
<td>72-h MI closed</td>
<td></td>
</tr>
<tr>
<td>Crustacea</td>
<td>water flea</td>
<td>22</td>
<td>6.7-8.1</td>
<td>6.5-9.1</td>
<td>72</td>
<td>stat</td>
</tr>
<tr>
<td>(Daphnia magna)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crustacea</td>
<td>water flea</td>
<td>20</td>
<td>8.0</td>
<td>&gt; 2</td>
<td>stat</td>
<td>24-h EC$_{50}$</td>
</tr>
<tr>
<td>(Daphnia magna)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organism &amp; Species</td>
<td>Toxicity Level</td>
<td>Observed Effect</td>
<td>Method</td>
<td>Experimental Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>----------------</td>
<td>-----------------</td>
<td>--------</td>
<td>-----------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Crustacea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>water flea (Daphnia magna)</td>
<td>20 7.1-7.7 7.9-9.9 44.7</td>
<td>stat closed 48-h LC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish (Daphnia magna)</td>
<td>20 7.0-7.5 4.1-8.4 44.7</td>
<td>stat closed 48-h EC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fish</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bluegill sunfish (Lepomis macrochirus)</td>
<td>21-23 6.5-7.9 32-48</td>
<td>stat closed</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bluegill sunfish (Lepomis macrochirus)</td>
<td>23 7.6-7.9 55</td>
<td>stat open</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fathead minnow (Pimephales promelas)</td>
<td>25 6.7-7.6 8.0 45.1</td>
<td>flow open</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Table 7 (contd.)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sea water</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alga Phaeodactylum tricornutum</td>
<td>stat</td>
<td>EC50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worm chaetopod (Ophryotrocha labronica)</td>
<td>23</td>
<td>stat closed</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crustacea shrimp (Crangon crangon)</td>
<td>15 8.0 &gt; 8.0</td>
<td>flow open</td>
<td>96-h LC50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crustacea shrimp (Crangon crangon)</td>
<td>16</td>
<td>stat open</td>
<td>24-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mollusca barnacle nauplii (Elminius modestus)</td>
<td>stat closed</td>
<td>48-h LC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish dab (Limanda limanda)</td>
<td>stat</td>
<td>flow open</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish tidewater silver- sides (Menidia beryllina)</td>
<td>20 7.6-7.9 55</td>
<td>stat open</td>
<td>96-h LC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish sheephead minnow (Cyprinodon variegatus)</td>
<td>stat open</td>
<td>96-h LC</td>
<td>no-obse adverse effect</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish goby (Gobius minutus)</td>
<td>15 8.0 &gt; 8.0</td>
<td>flow open</td>
<td>96-h LC50</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Notes:**

a  Water analysis for 1,2-dichloroethane was reported.
b  Flow-through or static method; open or closed system.
c  MIC = minimum inhibitory concentration for cell multiplication. EC50 and LC50.
causing an effect and death, respectively, in 50% of the population. Fleas unfed. Effect was complete immobilization. Fleas fed. Effect was complete immobilization. Effect was growth inhibition, measured by $^{14}$C uptake during photosynthesis. When the concentration was gradually built up during the first hour, the 96-hour 900 mg/litre, and the percentage of hatched eggs, laid within 15 days, was decreased to 400 mg/litre. The latter was not noted at 200 mg/litre.

Concentration was gradually built up during the first hour.

### 6.1.3 Long-term exposure

No-observed-adverse-effect and effect concentrations were determined on the basis of reproduction or length for *Daphnia magna* in a 28-day test, in stopped flasks. The test solution was analysed by gas chromatography. The lowest observed adverse effect concentrations were 21 mg/litre, on the basis of reproduction, and 72 mg/litre, on the basis of length. The no-observed-adverse-effect concentrations were 11 mg/litre, on the basis of reproduction and 42 mg/litre, on the basis of length (Richter et al., 1983).

### 6.1.4 Bioconcentration

Bioconcentration of 1,2-dichloroethane in aquatic species is unlikely in view of its physical and chemical properties. In a tracer study, a bioconcentration factor of 2 was found for bluegill sunfish (*Lepomis macrochirus*) in flowing water. The half-life for the elimination of 1,2-dichloroethane from tissues was 1 - 2 days (Barrows et al., 1980).

When tissues of several aquatic species, collected from near the discharge zone of a wastewater treatment plant, were analysed for 1,2-dichloroethane, the concentration of the compound was less than 0.5 µg/kg wet weight in all cases, while the average effluent concentration was 41 µg/litre and the average sediment concentration was less than 0.5 µg/kg dry weight (Gossett et al., 1983).

### 6.2 Microorganisms

1,2-Dichloroethane at an influent concentration of 258 mg/litre did not affect the treatment efficiency of a bench-scale activated sludge system. The compound itself was virtually completely removed by stripping but not by biodegradation (Stover & Kincannon, 1983). In a batch anaerobic toxicity assay, 1,2-dichloroethane was slightly toxic to the anaerobic digestion process from a concentration of 2.5 mg/litre, though acclimation was observed after several days. A concentration of 20 mg/litre caused more severe retardation, while acclimation was slow. In semi-continuous assays, stress became evident at 1,2-dichloroethane concentrations of between 5 and 7.5 mg/litre (Stuckey et al., 1980).

### 6.3 Terrestrial Organisms

#### 6.3.1 Birds

The effects on reproduction were investigated in groups of 10 male and 20 female white leghorn chickens after 2 years of oral exposure to 0, 250, or 500 mg 1,2-dichloroethane/kg feed mash. From the fourth month of laying onwards, decreased egg weight was observed at both dose levels, while at the higher dose level, the number of eggs and the feed intake were also
reduced. 1,2-Dichloroethane did not affect serum composition and growth, semen characteristics, or fertility of chickens (Alumot et al., 1976b).

6.3.2 Plants

1,2-Dichloroethane is used as a seed fumigant, usually in combination with compounds such as carbon tetrachloride, 1,2-dibromomethane, or 2-chloroethanol. Such fumigants inhibited the germination of seeds (Caswell & Clifford, 1958; Kamel, 1959), broke the dormancy period of potato tubers (Varga & Ferenczy, 1956; Jolivet, 1968) and beech (Thorup, 1957), and adversely affected the nodulation status and yield of groundnuts treated with Rhizobium (Kulkarni et al., 1975). 1,2-Dichloroethane vapour was both lethal and mutagenic for barley seeds at 3 mg/m³ during 24 h (Ehrenberg et al., 1974).

7. EFFECTS ON ANIMALS

7.1 Single Exposures

7.1.1 Inhalation and oral exposure

The available acute mortality data following inhalation and oral exposure are summarized in Table 8.

Table 8. Acute mortality after inhalation or oral exposure to 1,2-dichloroethane

<table>
<thead>
<tr>
<th>Species/strain</th>
<th>Route</th>
<th>Vehicle</th>
<th>Parameter</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>dog</td>
<td>oral</td>
<td>acacia gum</td>
<td>LD₅₀</td>
<td>2500 mg/kg</td>
<td>Barsoum &amp; Saad (1934)</td>
</tr>
<tr>
<td>rat</td>
<td>oral</td>
<td>corn oil</td>
<td>LD₅₀</td>
<td>680 mg/kg</td>
<td>McCollister et al. (1956)</td>
</tr>
<tr>
<td>CD-1 mouse</td>
<td>oral</td>
<td>water</td>
<td>LD₅₀</td>
<td>489 mg/kg</td>
<td>Munson et al. (1982)</td>
</tr>
<tr>
<td>(male)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD-1 mouse</td>
<td>oral</td>
<td>water</td>
<td>LD₅₀</td>
<td>413 mg/kg</td>
<td>Munson et al. (1982)</td>
</tr>
<tr>
<td>(female)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wistar rat</td>
<td>inhalation</td>
<td>-</td>
<td>6-h LC₅₀</td>
<td>5100 mg/m³</td>
<td>Spencer et al. (1951)</td>
</tr>
<tr>
<td>Sprague Dawley</td>
<td>inhalation</td>
<td>-</td>
<td>6-h LC₅₀</td>
<td>6660 mg/m³</td>
<td>Bonnet et al. (1980)</td>
</tr>
<tr>
<td>OF₁ mouse</td>
<td>inhalation</td>
<td>-</td>
<td>6-h LC₅₀</td>
<td>1060 mg/m³</td>
<td>Gradiski et al. (1978)</td>
</tr>
<tr>
<td>(female)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rat</td>
<td>oral</td>
<td></td>
<td>LD₅₀</td>
<td>850 mg/kg</td>
<td>Larionov &amp; Kokarovtseva (1976)</td>
</tr>
</tbody>
</table>
Deaths occur within a narrow range of concentrations. In rats, the difference between the 6-h LC$_{10}$ and 6-h LC$_{90}$ was approximately 2800 mg/m$^3$ (Bonnet et al., 1980). No deaths were observed in rats after 6 h of exposure to 2000 mg/m$^3$ (Spencer et al., 1951). In mice, an extremely narrow range of about 500 mg/m$^3$ was observed between the 6-h LC$_{10}$ and the 6-h LC$_{90}$ (Gradiski et al., 1978).

Exposure of rats to single high doses of 1,2-dichloroethane resulted in adverse effects on the CNS, liver, kidneys, adrenals, and lungs (Spencer et al., 1951). Groups of 10 – 52 Wistar rats were exposed to 81 000, 48 600, 12 100, 6100, 4000, 3200, 2400, or 1200 mg 1,2-dichloroethane/m$^3$ for various lengths of time. At the highest concentration (81 000 mg/m$^3$), deaths were observed in animals exposed for 0.3 h or longer. Deaths were observed at all except the lowest of the other concentrations with exposure periods of 0.4, 0.7, 3.0, 4.0, 7.0, and 7.0 h, respectively. No deaths were observed in rats exposed to the lowest concentration for 7 h.

Severe depression of the central nervous system resulting in coma was observed in rats exposed to the highest concentration. At lower concentrations, this depressant action expressed itself as various levels of “drunkeness”. In this investigation, Spencer et al. (1951) did not specify the sex of the rats.

In the same publication, the authors reported another study in which groups of 4 – 6 female rats were exposed to 48 600, 12 100, 4000, 1200, or 800 mg/m$^3$. “Adverse effects” (not described by the authors) were observed at the 4 highest levels in rats exposed for 0.2, 0.5, 3.0, and 5.5 h, respectively. No adverse effects were observed in female rats exposed to the lowest concentration, for 7 h.

Examination of internal organs in groups of rats killed, either when moribund or 24 h after the last exposure, showed that, after exposure to 1,2-dichloroethane levels of 2400 mg/m$^3$ or more, the most severe damage occurred in the kidney and consisted of haemorrhage and tubular necrosis. The liver showed fatty changes and hepatocellular necrosis with haemorrhage, and adrenal glands were haemorrhagic. Lung oedema was observed at concentrations above 12 100 mg/m$^3$. The injury to organs in this study was accompanied by high blood-urea levels, a decrease in serum-phosphatase activity, and increased lipid concentration in the liver (Spencer et al., 1951).

Depression of the central nervous system was noted during exposure of rats to 1,2-dichloroethane concentrations exceeding 1200 mg/m$^3$ (Bonnet et al., 1980). From an exposure level of 4000 mg/m$^3$, for 4 h, rats showed altered behaviour. A narcotic effect was observed at 9100 mg/m$^3$ (Wolff et al., 1979).

Albino rats, given a single oral dose of 615 mg/kg body weight, showed congested livers with cloudy swelling and fatty degeneration. The myocardium showed oedema and haemorrhaging in
the walls of the coronary vessels, stasis, and thrombi in the vessels. These changes were associated with an increased activity of alanine- and aspartate aminotransferase in the serum and decreased tissue levels of nicotinamide coenzymes (Natsyuk & Chekman, 1975). A single administration of 861 mg/kg, by gavage, was reported to partially uncouple oxidative phosphorylation measured in vitro in albino rat livers, 1, 3, or 6 days after exposure (Natsyuk et al., 1974). In rat liver microsomes, cytochrome P-450 levels were slightly decreased after an oral dose of 625 mg/kg (Moody et al., 1981). After a single oral dose of 1,2-dichloroethane in corn oil at 770 mg/kg body weight in rats, dystrophy in the cytoplasm and hyperchromatosis in the nuclei of hepatocytes were observed. A decrease in protein synthesis and lysosomal enzyme activity was also reported. The same changes took place in renal nephrons (Boikova & Kravtsova, 1982). A single dose of 850 mg/kg in albino rats resulted in a decrease in RBC count, haematocrit, and other haematological changes (Larionov & Kokarotseva, 1976). Oral administration of 1,2-dichloroethane (615 mg/kg) to rabbits induced pronounced morphological changes in the liver in about 24 h (Nazikhi & Skrzhinsky, 1973). Effects on fibrinolytic activity in the blood of rabbits administered 1,2-dichloroethane at 1476 mg/kg have been reported by Kagramanov & Kazieva (1972). Electrocardiographic changes in albino rats associated with doses of 1, 1.5, and 2 mg/kg have been reported (Saitanov & Arsenieva, 1969).

7.1.2 Skin and eye irritation

When undiluted 1,2-dichloroethane was applied directly on the clipped skin of guinea-pigs for up to 12 h in occluded patch tests, no gross skin reactions were visible (Jakobson et al., 1982). Microscopic changes appeared 4 h after application, comprising karyopyknosis, perinuclear oedema, spongiosis, and junctional separation (Kronevi et al., 1981). In similar tests on rabbits, moderate erythema and oedema were observed, 24 h after application. Microscopy on the third day revealed necrosis and other lesions such as ulcerations and acanthosis. The severity of the changes was not indicated (Duprat et al., 1976).

Instillation of 0.1 ml of undiluted 1,2-dichloroethane into the conjunctival sac of the eye of rabbits generated reversible, mild irritation characterized by conjunctivitis and epithelial abrasion. Epithelial keratitis, described as being "in a state of repair", was observed microscopically, 7 days after application (Duprat et al., 1976). Reversible clouding of the cornea was observed in dogs within 10 h of subcutaneous administration of undiluted 1,2-dichloroethane at 0.9/kg body weight. The clouding continued up to 48 h, but the corneas appeared clear after 5 days. The histological changes, including necrosis of the corneal endothelium, partially denuded Descemet's membrane, formation of excess basement membrane, and swelling of the corneal stroma, were also observed in dogs, cats, and rabbits after ocular injection of 1.8 mg 1,2-dichloroethane (0.15 ml of a 1% solution) into the anterior chamber (Kuwabara et al., 1968).

7.2 Short-Term Exposures

7.2.1 Inhalation exposure
The effects of repeated exposure to 1,2-dichloroethane have been studied in mice, rats, guinea-pigs, rabbits, cats, dogs, and monkeys (Heppel et al., 1946; Spencer et al., 1951; Hofmann et al., 1971).

Heppel et al. (1946) exposed rats of the Wistar and Osborne-Mendel strains to 1,2-dichloroethane concentrations of 420, 730, 1540, or 3900 mg/m³ in air, 7 h daily, 5 days/week, for several weeks. The duration varied with each exposure level. No loss of weight and no deaths occurred in rats of either strain exposed to 420 mg/m³ for up to 4 months (74 exposures). Seven out of 12 Wistar rats exposed to 730 mg/m³ died within 15 weeks (after 1 - 73 exposures) and 8/12 similarly treated rats of the Osborne-Mendel strain died after 1 - 6 exposures. Nine out of 16 rats (strain unspecified) died within 12 weeks after 2 - 60 exposures to 1540 mg/m³; 20/26 (strain unspecified) died within 3 weeks after 3 - 15 exposures to 3900 mg/m³. Guinea-pigs were exposed to the same concentrations of 1,2-dichloroethane as the rats. Several deaths, which occurred in the lowest exposure group (420 mg/m³) and in controls, were attributed to an intercurrent disease. At higher dose levels, mortality was related to 1,2-dichloroethane exposure. Five out of 14 guinea-pigs died after 5 - 115 exposures to 730 mg/m³ within 23 weeks. Fourteen out of 20 guinea-pigs died after 8 - 65 exposures to 1,2-dichloroethane at 1540 mg/m³ within 13 weeks. All guinea-pigs exposed to 3900 mg/m³ had died by the 4th day of the study.

Rabbits were exposed to the three higher concentrations of 1,2-dichloroethane only. No deaths were observed when rabbits were exposed to 730 mg/m³ for 25 weeks. All 5 rabbits exposed to 1540 mg/m³ died, one after one exposure and the rest after 89 - 97 exposures within 19 weeks. Five out of 6 rabbits exposed to 3900 mg/m³ died after 2 - 43 exposures within 9 weeks.

A group of 19 mice survived for 4 weeks when exposed to 420 mg/m³, but 18/20 mice died within 10 days by the end of 7 exposures to 730 mg/m³. In other species, a group of 6 female dogs survived up to 35 weeks of exposure to 1540 mg/m³. Two out of 6 dogs exposed to 3900 mg/m³ died after 30 and 43 exposures, respectively. Two out of six cats exposed to 3900 mg/m³ died after 43 exposures. Cats were not exposed to lower concentrations. Two monkeys died after 2 and 32 exposures, respectively, to 3900 mg/m³, but 2 others exposed to 730 mg/m³ survived for 25 weeks.

Kidney and liver damage, consisting of fatty changes and necrosis in both organs, was found in animals that died from exposure to the highest dose level (3900 mg/m³). In addition, the rats showed pulmonary congestion and haemorrhage; one monkey that died after 32 exposures and one dog showed a focal myocarditis. Approximately half of the animals that died after exposure to 1540 mg/m³ showed similar histological changes in the liver and kidneys, but no such changes were observed in rats that died from exposure to lower levels. Hepatic fatty changes were observed in guinea-pigs exposed to 730 mg/m³. Histological examinations were not carried out on mice.

Spencer et al. (1951) exposed rats, guinea-pigs, monkeys,
and rabbits to 1,2-dichloroethane at concentrations of 1620, 810, or 405 mg/m³, 7 h per day, 5 days/week, for various lengths of time. In a group of 15 male and 15 female rats, exposed to the highest level, no animals survived for more than 8 weeks, and 60% mortality occurred in a second group exposed to the same regime after 2 or 3 exposures. Mortality was also high in a group of 8 male and 8 female guinea-pigs exposed to 1620 mg/m³. All males had died by the second week and all females by approximately the 5th week. Two male monkeys experienced rapid and severe intoxication. Both were killed when moribund after 10 - 12 exposures. On the other hand, 2 male and 1 female rabbits tolerated 33 weeks exposure with no evidence of adverse effects. No mortality was observed when groups of 15 male and 15 female rats and 8 male and 8 female guinea-pigs were exposed to 810 mg/m³ for about 30 weeks (151 exposures) or 36 weeks (180 exposures), respectively. Similarly, no clinical effects were observed in groups of 15 male and female rats, 8 male or female guinea-pigs, 2 male and 1 female rabbits, and 1 male and 1 female monkey exposed for approximately 30 - 36 weeks to 405 mg/m³.

Histological examination was carried out on animals exposed to the three dose levels. In both guinea-pigs and rats exposed to the highest dose level, liver changes consisting of cloudy swelling and fatty changes were observed. None of the other organs were affected. Similar but less marked changes were observed in the monkeys, while no adverse changes were found in the rabbits. In rats exposed to 810 mg/m³, there were no adverse changes in the liver or other organs, but reduced growth and some fatty changes were found in the liver of guinea-pigs. No adverse changes were found in animals exposed to the lowest dose level (405 mg/m³).

Hofmann et al. (1971) exposed cats, rabbits, guinea-pigs, and rats to 1,2-dichloroethane at 1980 mg/m³ or 405 mg/m³ for 6 h/day, 5 days/week, for up to 17 weeks. At the higher concentration, rats became dyspnoeic and guinea-pigs apathetic. Three out of 4 rabbits died after 10 - 17 exposures, and 9/10 guinea-pigs died after 4 - 14 exposures. Rats were more sensitive, dying after only 1 - 5 exposures. All cats survived 30 exposures. Histologically, rats showed pulmonary hyperaemia and oedema, fatty liver, and adrenal and myocardial necrosis. Cats and rabbits exhibited a heart lesion and guinea-pigs, fatty changes in the myocardium, liver, and adrenals and necrosis in the myocardium and liver. At the lower concentration (405 mg/m³), rats, guinea-pigs, rabbits, and cats exposed for 17 weeks did not show any clinical or histological changes.

Of the species studied, mice and rats appear to be more sensitive than other species to the adverse effects of 1,2-dichloroethane. The no-observed-adverse-effect level for short-term exposures (4 - 9 months) in rats studied in the 3 investigations is about 400 mg/m³.

Signs of central nervous system depression observed in the above studies were apathy in guinea-pigs at 1980 mg/m³ (Hofmann et al., 1971) and 3900 mg/m³ (Heppel et al., 1946), and coma in dogs and monkeys at 3900 mg/m³ (Heppel et al., 1946). When rats were exposed continuously for 3.5 months to 5 mg/m³, changes in EEG were observed (Dmitrieva & Kuleshova, 1971). However, the significance of these findings is not known.
7.2.2 Oral exposure

The liver appeared to be the principal target organ following oral exposure. Rats, treated by gavage with 1,2-dichloroethane in corn oil for 2 weeks, 5 times per week, at doses of 150 mg/kg body weight or less did not show any treatment-related abnormalities in organ or body weights, histology, clinical chemistry, or haematology (Van Esch et al., 1977; Reitz et al., 1982).

Rats were also exposed for 90 days, 5 times per week, to 0, 10, 30, or 90 mg/kg body weight (Van Esch et al., 1977). At the 2 highest exposure levels, a tendency to decreased weight gain was observed. At 90 mg/kg, rats of both sexes showed an increase in the relative weight of kidneys, but only the females on this dose showed increased relative weights of liver and brain compared with controls. Histology and clinical chemistry were normal. Some haematological parameters were altered, but not in a dose-related manner. In another study, after 5 doses of 300 mg 1,2-dichloroethane/kg body weight in 5 days, all 6 rats died, and their livers showed fatty degeneration with an increase in the triglycerides level (Van Esch et al., 1977).

Total fat and triglycerides were elevated in the livers of rats exposed to approximately 100 mg/kg body weight per day via the feed, which was administered twice daily, for 7 weeks (Alumot et al., 1976a).

No adverse effects related to liver and kidney function were observed at the lowest dose (10 mg/kg).

7.3 Long-Term Exposure

7.3.1 Inhalation exposure

Clinical chemical investigations were performed on Sprague Dawley rats exposed by inhalation to 1,2-dichloroethane at 0, 5, 40, 202, or 1012 mg/m³ for 7 h per day, 5 days/week (Spreafico et al., 1980). The highest exposure level was reduced to 607 mg/m³ after a few weeks because of high mortality. Animals of each sex were exposed, starting at 3 months of age, for 3, 6, or 18 months. In addition, animals starting at 14 months of age were exposed for 12 months. Groups of 8-10 animals of each sex were sacrificed at the specified time intervals and clinical chemistry tests performed. Changes in SGOT, SGPT, and c-glutamyl transpeptidase activities in the 12-month animals were not observed in the 18-month animals. Likewise, increases in serum-uric acid and blood urea-nitrogen levels in the 12-month animals were not observed in the 18-month animals. In addition, the 12-month animals, but not the 18-month animals, displayed decreases in serum-cholesterol. On the basis of the negative results obtained in the animals starting exposure at 3 months of age and sacrificed after 3, 6, or 18 months, the authors suggested a lack of significant toxicity, in spite of the biochemical changes found in the older 12-month animals.

Neurotoxic changes (conditioned reflexes) in albino rats have been associated with a 1,2-dichloroethane exposure of 50 mg/m³, 4 h/day, for 6 months (Borissova, 1957, 1960).

7.3.2 Oral exposure

In a controlled feeding schedule for 2 years, three groups
of 18 locally-bred rats of each sex were provided with feed fumigated with 1,2-dichloroethane. The doses of 1,2-dichloroethane administered were estimated to be 0, 11 - 17, or 23 - 35 mg 1,2-dichloroethane/kg body weight per day. No adverse effects were observed on growth, mortality rates, or serum composition. The mean survival period was 18 months or more (Alumot et al., 1976a).

7.4 Carcinogenicity

7.4.1 Inhalation exposure

Groups of 11-week-old Swiss mice and 12-week-old Sprague Dawley rats, comprising 90 animals of each sex, were exposed to 20, 40, 202, and 1012 mg 1,2-dichloroethane/m³ air (5, 10, 50, and 250 ppm) for 78 weeks, 7 h per day, 5 days per week, and observed for a lifetime. Purity was reported to be greater than 99%. The highest exposure was reduced to 607 mg/m³ (150 ppm) after a few weeks because of high mortality. Control groups contained 115 male mice, 134 female mice, or 180 rats of each sex. Percentage survival in male and female mice, 52 weeks after the beginning of treatment, was, respectively, 63 and 84% in the controls; 47 and 93% at 20 mg/m³; 66 and 80% at 40 mg/m³; 51 and 81% at 202 mg/m³; and 43 and 64% at 607 mg/m³. The last mouse died about 100 weeks after initiation of treatment. In male and female rats, survival at 52 weeks was, respectively, 67 and 73% in the controls; 75 and 85% at 20 mg/m³; 70 and 81% at 40 mg/m³; 70 and 84% at 202 mg/m³; and 67 and 79% at 607 mg/m³. Most rats had died by about 140 weeks after the start of treatment. No specific types of tumours or changes in the incidence of tumours were found in either species, with the exception of an increased incidence (not dose-related) of fibromas and fibroadenomas of the mammary glands of female rats at 20, 202, and 607 mg/m³. The average latency time for these tumours was 83 weeks in control rats and in rats exposed at 20 mg/m³, and 79 weeks at the 2 highest exposures. The authors ascribe the differences in the incidence of mammary tumours between the groups to the different survival rates in the groups (Maltoni et al., 1980).

7.4.2 Oral exposure

Groups of 50 Osborne-Mendel rats of each sex were exposed to average doses of 1,2-dichloroethane (technical grade with reported purity > 90%) in corn oil of 47 or 95 mg/kg body weight for 78 weeks (NCI, 1978). Treatment was usually given 5 times per week, and the animals were observed for another 15 - 32 weeks after the end of treatment. Control groups consisted of 20 matched controls of each sex treated with corn oil and 60 pooled control-treated rats of each sex. Eleven minor contaminants were detected in the test compound. The rats were housed in the same room as rats intubated with other halogenated hydrocarbons or carbon disulfide. Body weights were not affected by the exposures. A dose-related increase was found in mortality rate, which was 100%, 27 weeks after cessation of exposure to 95 mg/kg body weight. As shown in Table 9, male rats had a dose-related increased incidence of subcutaneous fibromas, and forestomach squamous cell carcinomas were observed. In treated females, the stomach showed hyperplastic lesions. The incidence of haemangiosarcomas (in various organs, mainly the spleen) was increased in a dose-related manner in both sexes, but the increase was statistically significant in
males only. In females, an increase was found in the incidence of adenocarcinomas of the mammary gland (NCI, 1978).

Subsequent analysis indicated a purity of about 98 - 99% (Hooper et al., 1980; Ward, 1980).

Table 9. Summary of main tumour types after oral administration of 1,2-dichlorethane

<table>
<thead>
<tr>
<th>Group</th>
<th>Maximum number of animals</th>
<th>Number of animals with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>examined</td>
<td>Forestomach squamous cell carcinomas</td>
</tr>
<tr>
<td>Rat (male)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled vehicle controls</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>Matched vehicle controls</td>
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</tr>
<tr>
<td>Low dose</td>
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<td>3</td>
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<tr>
<td>High dose</td>
<td>47</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(P &lt; 0.04)</td>
</tr>
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</table>

Rat (female)

<table>
<thead>
<tr>
<th>Group</th>
<th>Maximum number of animals</th>
<th>Number of animals with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>examined</td>
<td>Mammary gland fibroma</td>
</tr>
<tr>
<td>Pooled vehicle controls</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>Matched vehicle controls</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Low dose</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>High dose</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

Mice (male)

<table>
<thead>
<tr>
<th>Group</th>
<th>Maximum number of animals</th>
<th>Number of animals with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>examined</td>
<td>Hepatocellular carcinomas</td>
</tr>
<tr>
<td>Pooled vehicle controls</td>
<td>59</td>
<td>4</td>
</tr>
<tr>
<td>Matched vehicle controls</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Low dose</td>
<td>46</td>
<td>6</td>
</tr>
<tr>
<td>High dose</td>
<td>47</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(P &lt; 0.01)b</td>
</tr>
</tbody>
</table>

Mice (female)

<table>
<thead>
<tr>
<th>Group</th>
<th>Maximum number of animals</th>
<th>Number of animals with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>examined</td>
<td></td>
</tr>
<tr>
<td>Pooled vehicle controls</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Matched vehicle controls</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>Low dose</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>High dose</td>
<td>48</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(P &lt; 0.001)b</td>
</tr>
</tbody>
</table>

Adapted from: NCI (1978).

Statistical analyses shown are in comparison with the pooled matched controls in the same set of studies, B6C3F1 mice were exposed in a similar fashion to average doses of 0, 97, or 195 mg technical grade compound/kg body weight for males and 0, 149, or 299 mg/kg body weight for females. They were housed in the same room where several other hydrocarbons or other substances were
tested. After exposure, they were observed for another 12 – 13 weeks. In females, body weights were depressed at the highest doses from week 15 onwards, while the survival rate decreased in a dose-related manner. Mean survival exceeded 65 weeks in all groups. Many treated mice suffered from bronchopneumonia. As shown in Table 9, dose-related increased incidences of alveolar or bronchiolar adenomas were found in both sexes. In males, a dose-related increased incidence of hepatocellular carcinomas was observed. Female mice showed slight, dose-related increases in the incidence of squamous cell carcinomas of the forestomach, but this was not statistically significant. In male mice, hyperplastic changes were found at this site. The incidence of adenocarcinomas of the mammary gland was significantly increased in females at both doses (NCI, 1978).

7.4.3 Dermal exposure

Groups of 30 female Ha:ICR Swiss mice were treated with 42 or 126 mg 1,2-dichloroethane in acetone on the shaven dorsal skin, 3 times per week for 440 – 594 days. In a third group, each female received one application of 126 mg of the test compound followed 2 weeks later by phorbol myristate acetate, a promotor, in acetone 3 times per week for 428 – 576 days. There were 3 control groups, a positive control, one for the promotor, and one for no treatment. 1,2-Dichloroethane did not initiate skin tumours. There was an elevated incidence of lung papillomas at the highest dose compared with controls (Van Duuren et al., 1979).

7.5 Mutagenicity and Related End-Points

7.5.1 Mutations

Information in this section is summarized in Table 10.

7.5.1.1 Bacteria

Several investigators have observed a weak or no effect of 1,2-dichloroethane in Salmonella typhimurium TA1535 or TA 100 in spot tests or standard plate incorporation assays with or without rat liver S9 fraction or pure microsomes (Brem et al., 1974; McCann et al., 1975; King et al., 1979; Guengerich et al., 1980; Principe et al., 1981). A weak mutagenic effect was observed in 1,2-dichloroethane vapour-exposed S. typhimurium TA 1535 and TA 100, which did not increase further by the addition of a metabolic activation system (Barber et al., 1981). However, a stronger positive response was observed by others (Rannug et al., 1978; Rannug & Beije, 1979; Principe et al., 1981) in TA 1535 in the presence of rat liver metabolic activation system.

It has been established that this effect has been caused by cytosolic glutathione-S-transferases (Rannug et al., 1978; Guengerich et al., 1980; Reitz et al., 1982), and similar results have also been obtained in TA 100 (van Bladeren et al., 1981b). In vitro Salmonella tests using the bile of mice or rats exposed to 1,2-dichloroethane, probably containing active conjugates, have confirmed these results (Rannug & Beije, 1979).

No mutagenic effects were observed in forward mutation tests with Escherichia coli (King et al., 1979).

Table 10. Tests for gene mutations/chromosome/DNA damage and cell transformation by 1,2-dichloroethane
<table>
<thead>
<tr>
<th>Test description</th>
<th>System description</th>
<th>Activation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene mutations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 1530</td>
<td>A</td>
<td>+ (weak)</td>
</tr>
<tr>
<td></td>
<td>TA 1535 A</td>
<td>+ (weak)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1538 A</td>
<td>+ (weak)</td>
<td></td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 100</td>
<td>A</td>
<td>+ (weak)</td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 1535</td>
<td>P</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>TA 100 P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1537 P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1538 P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 98 P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 1535</td>
<td>P</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>TA 1537 A or P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1538 A or P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 98 A or P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 100 A or P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 1535</td>
<td>A or P</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>TA 100 A or P</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1538 A or P</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 98 A or P</td>
<td>-</td>
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<td>reverse mutation</td>
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<td>F</td>
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<tr>
<td></td>
<td>P</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 100</td>
<td>P</td>
<td>+</td>
</tr>
<tr>
<td>reverse mutation</td>
<td>bacteria S. typhimurium TA 1535</td>
<td>P</td>
<td>+</td>
</tr>
<tr>
<td>forward mutation</td>
<td>fungi S. coelicolor</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>A. nidulans</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td>sex-linked lethals</td>
<td>insect D. melanogaster</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>somatic cell mutation</td>
<td>insect D. melanogaster</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>forward mutation</td>
<td>Chinese hamster ovary cells in vitro</td>
<td>P</td>
<td>++</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>forward mutation</td>
<td>human lymphoblastoid cell line AHH-1 and TK6 in vitro</td>
<td>A</td>
<td>+</td>
</tr>
</tbody>
</table>
### 7.5.1.2 Fungi

Forward mutation tests conducted with *Streptomyces coelicolor* and *Aspergillus nidulans* were negative in plate incorporation assays and spot tests (Prinципе et al., 1981). In *A. nidulans*, 1,2-dichloroethane induced non-disjunction and haploidization (Crebelli et al., 1984). 1,2-Dichloroethane was found to be a weak inducer of mitotic crossing over in *Saccharomyces cerevisiae* (Simmon, 1980).

### 7.5.1.3 Insects

Sex-linked recessive lethal mutations were induced in *Drosophila melanogaster* by 1,2-dichloroethylene (Rapoport, 1960; Shakarnis, 1970; King et al., 1979). Non-dysjunction was observed inconsistently (Shakarnis, 1969, 1970), while the frequency of somatic mutations for eye pigmentation increased (Nylander et al., 1978).

### 7.5.1.4 Mammals/mammalian cells

<table>
<thead>
<tr>
<th>Test description</th>
<th>System description</th>
<th>Activation system (S9)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome/DNA damage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>micronucleus test mice (ip or gavage exposure)</td>
<td>NMRI/polychromatic erythrocytes</td>
<td>NA</td>
<td>-</td>
</tr>
<tr>
<td>micronucleus test mice (ip exposure)</td>
<td>CBA/polychromatic erythrocytes</td>
<td>NA</td>
<td>-</td>
</tr>
<tr>
<td>dominant lethal mice (ip exposure)</td>
<td>ICR Swiss/germ cells</td>
<td>NA</td>
<td>-</td>
</tr>
<tr>
<td>alkaline DNA unwinding mice</td>
<td>B6C3F1/liver in vivo/ in vitro</td>
<td>NA</td>
<td>+</td>
</tr>
<tr>
<td>alkaline DNA unwinding mice</td>
<td>B6C3F1/liver in vivo/ in vitro</td>
<td>NA</td>
<td>+</td>
</tr>
<tr>
<td>unscheduled DNA synthesis (exposure by addition in the medium) human lymphocytes</td>
<td>in vitro</td>
<td>NA</td>
<td>+</td>
</tr>
<tr>
<td>Cell transformation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cell transformation Syrian embryo cells</td>
<td>in vitro golden hamster</td>
<td>A</td>
<td>+[^c]</td>
</tr>
<tr>
<td>cell transformation mice BALB/c-3T3</td>
<td>in vitro</td>
<td>A</td>
<td>-</td>
</tr>
</tbody>
</table>

[^a]: Pure microsomes.
[^b]: Cytosol.
[^c]: Enhanced viral induced transformation.
NA = not applicable.
A spot test using mice provided weak evidence that 1,2-dichloroethane can induce somatic mutations (Gocke et al., 1983).

In Chinese hamster ovary cells, 1,2-dichloroethane induced mutations at the HGPRT-locus (Tan & Hsie, 1981; Zamora et al., 1983). Metabolic activation increased the mutation frequency in the presence of NADPH (Tan & Hsie, 1981). 1,2-Dichloroethane also induced a dose-related increase in the frequency of mutations at the HGPRT-locus in two human lymphoblastoid cell lines, AHH-1 and TK6. The mutation frequency in the AHH-1 cell line was 25 times that in the TK6 cell line. The difference in sensitivity was attributed to the difference in the levels of glutathione-S-transferase (EC 2.5.1.18) activity. The activity of this enzyme in the AHH-1 cell line was 5 times that in the TK6 cell line (Crespi et al., 1985).

7.5.2 Chromosome damage/DNA damage

In in vivo studies, no effects were observed in dominant lethal assays in 2 generations of ICR Swiss mice (Lane et al., 1982) and in the micronucleus test with CBA and NMRI mice (King et al., 1979; Jenssen & Ramel, 1980).

1,2-Dichloroethane was a weak inducer of unscheduled DNA synthesis in cultured human lymphocytes (Perocco & Prodi, 1981).

DNA alkylation in Salmonella by activated 1,2-dichloroethane was directly related to the mutation frequency, but absolute levels of DNA alkylation in Salmonella were considered low (Reitz et al., 1982).

1,2-Dichloroethane weakly inhibited growth of DNA polymerase deficient E. coli (Brem et al., 1974; Rosenkranz, 1977).

Administration of 1,2-dichloroethane to mice and rats resulted in covalent binding to macromolecules (Reitz et al., 1982; Arfellini et al., 1984; Inskeep et al., 1986). Absolute levels of DNA alkylation in rats, either by gavage or inhalation, were considered low (Reitz et al., 1982).

Hepatic DNA damage was demonstrated using the alkaline DNA unwinding assay in male B6C3F1 mice after a single intraperitoneal or oral dose of 1,2-dichloroethane that failed to induce toxic effects in the liver. It was also shown that, after one inhalation exposure, hepatic DNA damage only occurred at exposure levels that caused high mortality (Storer & Conolly, 1983; Storer et al., 1984).

7.5.3 Cell transformation

1,2-Dichloroethane did not transform BALB/c-3T3 mouse cells in a test conducted without any exogenous metabolic activating system (Tu et al., 1985). It enhanced transformation of Syrian hamster embryo cells by simian adenovirus (Hatch et al., 1983).

7.6 Reproduction and Teratogenicity

7.6.1 Inhalation exposure

It has been reported that 1,2-dichloroethane was found in the fetuses of rats after exposure to 600 mg/m³ for 5 h (Withey & Karpinski, 1985).
Female rats (strain unspecified) were exposed to 15 mg 1,2-dichloroethane/m³, for 4 h daily, 6 days/week, for 4 months prior to mating. During this period, the estrus cycle became longer than normal. The rats were then mated and exposure continued. No information on the effects on fertility was given, but the total embryonal mortality increased from approximately 11% in controls to 27% in treated dams, while pre-implantation losses were found to be 5 times greater in treated animals than in the controls. No fetal abnormalities were reported, with the exception of haematomas in the region of the head, neck, and anterior extremities (Vozovaya, 1977).

In a second study, 1,2-dichloroethane was administered to female albino rats at a concentration of 57 ± 10 mg/m³ in air, for 4 h daily, 6 days/week, for 6 and 9 months. When the rats were mated, a reduction in fertility was observed (6.5 fetuses per treated female versus 9.7 in controls). The weight of newborn rats was reduced (5.06 g versus 6.44 in unexposed females). Perinatal mortality was increased (Vozovaya, 1974).

1,2-Dichloroethane was detected in placental and fetal tissues after inhalation exposure to 1000 mg/m³ for 3 days (daily duration not stated). It was also found in the stomach of 12- to 14-day-old mice, when lactating females were exposed to an unspecified concentration of 1,2-dichloroethane by inhalation (Vozovaya, 1977).

While the above results indicate a possible adverse effect of 1,2-dichloroethane on reproduction, the following reproductive studies yielded negative results. Groups of 20 Sprague Dawley rats of each sex were exposed for 60 days prior to mating, for 6 h per day, and 5 days per week to 101, 304, or 607 mg 1,2-dichloroethane/m³ in air. After mating, they were exposed similarly, for another 116 days, but for 7 days per week. Females were not exposed between gestation day 21 and day 4 post partum. Control groups contained 30 rats each. Pups were removed and examined at 21 days of age, and the females were remated following the removal of the last litter. Each female produced 2 litters. The parents did not show any toxic effects and the fertility index and gestation period were normal. In the pups, no effects were found on sex ratio, survival indices, organ weights, or histology. A small decrease was noted in the number of pups in the first litters at 304 mg/m³ (Rao et al., 1980).

A teratogenicity study was further performed with groups of 16 - 30 female rats and 19 - 21 female rabbits (Rao et al., 1980). These groups were exposed through inhalation to 0, 405, or 1215 mg 1,2-dichloroethane/m³ air, for 7 h per day, from the 6th day of pregnancy onwards (rats up to the 15th day and rabbits up to the 18th day of gestation). Exposures at both levels were toxic for rabbit dams. The higher exposure level was severely toxic for the rat dams; only 1 of the few surviving females was pregnant, and all the implantation sites were resorbed. No adverse effects on reproduction were observed among rats exposed at 405 mg/m³ and rabbits exposed at 405 or 1215 mg/m³. The only gross change observed in rat fetuses was a decreased incidence of bilobed thoracic centra. There were no significant alterations in rabbit fetuses.

7.6.2 Oral exposure
Groups of 18 female rats that had received 0, 11 - 17, or 23 - 35 mg 1,2-dichloroethane/kg body weight per day via the feed, for up to 2 years, were mated with untreated males. The purity of the substance was not reported. No effects on reproduction were observed (Alumot et al., 1976a).

Lane et al. (1982) reported a 2-generation reproduction study on groups of 10 male and 30 female ICR Swiss mice receiving nominally 5, 15, or 50 mg 1,2-dichloroethane/kg body weight per day via the drinking-water, for up to 25 weeks. Control groups contained 20 male and 60 female mice. After 5 weeks of treatment, the mice were mated to produce F1A, F1B, and F1C litters. After weaning and 11 weeks of treatment, the F1B mice were mated to produce F2A and F2B litters. Remating always occurred 2 weeks after weaning. In the F1C and F2B matings, females were co-housed with untreated males for teratology screening. The parents did not show any toxic effects and fertility and gestation indexes were normal. There were no effects on survival, litter size, postnatal body weight, and gross pathology of pups. No congenital malformations were detected. In the F1C and F2B litters, no exposure-related reproductive effects were found. In the F2B litters, there was no increase in the incidence of fetal visceral or skeletal anomalies. F1C litters were not examined for skeletal anomalies.

7.7 Immunotoxicity

When rabbits were exposed for 7.5 - 8 months to 1,2-dichloroethane vapour of unspecified purity at a level of 100 mg/m³, for 3 h per day, 6 h per week, an 80% reduction in the production of antibodies against typhoid vaccine was observed. Concomitantly, there was a 2-fold increase in Forsman sheep erythrocyte antibodies (Shmuter, 1977).

Immunosuppression was also noted in a later oral study, in which groups of 32 male CD-1 mice were exposed to 3, 24, or 189 mg 1,2-dichloroethane/kg body weight (purity unknown) via the drinking-water for 90 days. In addition, groups of 10 male CD-1 mice were exposed, once a day, to 4.9 or 49 mg/kg body weight by water gavage for 14 days. Control groups comprised 48 mice in the 90-day study and 12 mice in the 14-day study. Apart from a 30% reduction in the leukocyte count after 14 days of exposure to 49 mg/kg body weight, no effects were found on other haematological parameters and relative organ weights. After the 90-day exposure, decreases in body weight and fluid consumption were noted. There was a tendency towards a reduction in immunoglobulin spleen antibody-forming cells and in the serum-antibody level after sheep erythrocyte immunization, while no effects were observed in the response to the B-cell mitogen lipopolysaccharide S. After the 14-day exposure, 25% and 40% suppression of antibody-forming cells were measured at 4.9 and 49 mg/kg body weight, respectively. After the 90-day exposure, no effects were seen on the cell-mediated immunity, assessed by measuring the delayed hypersensitivity response to sheep erythrocytes and the spleen cell response to the T-cell mitogen Concanavalin A. After the 14-day exposure, a slight suppression of the delayed hypersensitivity response was found, which was not dose-dependent (Munson et al., 1982).

8. EFFECTS ON MAN
Limited data are available on the effects on man of 1,2-dichloroethane. There are no adequate controlled studies, no recent occupational studies, and no mortality studies. However, case studies of accidental exposures have been reported.

### 8.1 Accidental Exposures

#### 8.1.1 Inhalation exposure

Many reports are concerned with mixed exposures. However, in this publication, only case studies are considered in which the exposure was reported to be to 1,2-dichloroethane alone. According to a review by NIOSH (1976), no data on exposure levels and duration of exposure were reported.

Inhalation of 1,2-dichloroethane vapour first afflicts the central nervous system. Symptoms include headache, dizziness, weakness, cyanosis, muscular spasms, hypotonia, vomiting, and unconsciousness. Death often follows. The respiratory tract can be irritated and inflamed with such symptoms as cough and rales over the chest. Cyanosis may occur either as the result of respiratory insufficiency due to depression of the central nervous system or by bronchial obstruction due to inflammation. Epigastric or visceral pains and diarrhoea have been observed. Autopsy reports frequently mention damage to the lungs, liver, and kidneys (Wirtschafter & Schwartz, 1939; Hadengue & Martin, 1953; Menschick, 1957; Troisi & Cavallazzi, 1961; Suveev & Babichenko, 1969). Changes in heart rhythm have been reported, which are probably secondary effects (section 8.1.2) (Suveev & Babichenko, 1969). Clinical findings include elevated serum-bilirubin levels and leukocytosis (Wirtschafter & Schwartz, 1939; Menschick, 1957) and elevations of blood-lactate, ammonia, ornithine carbamyl transferase, serum aspartate transaminase (EC 2.6.1.1), lactate dehydrogenase, and creatine phosphokinase (Nouchi et al., 1984).

#### 8.1.2 Oral exposure

The effects of acute oral exposure are very similar to those found after inhalation, but they are more pronounced. A summary of acute oral intoxications was prepared by US NIOSH in 1976. The lethal effects of 1,2-dichloroethane associated with oral exposure are presented in Table 11. Oral doses of 20 - 50 ml 1,2-dichloroethane have been identified as being lethal (IRPTC, 1984). Several major syndromes can be identified including central nervous system depression, gastroenteritis, and disorders of the liver and kidneys. Frequently-observed cardiovascular insufficiency and haemorrhagic diathesis may be related to changes in oxygenation and effects on the liver (Weiss, 1957; Morozov, 1958; Hinkel, 1965; Bogoyavlenski et al., 1968; Martin et al., 1968; Schönborn et al., 1970; Yodaiken & Babcock, 1973; Dorndorf et al., 1975; Andriukin, 1979).

<table>
<thead>
<tr>
<th>Amount ingested (g)</th>
<th>Findings</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>188 - 250</td>
<td>death of 4 males up to 35 h; internal haemorrhage at various sites; liver damage; symptoms at 3 - 4 h</td>
<td>Bry</td>
</tr>
<tr>
<td>87 - 125</td>
<td>death of 3 males after 5 - 8 h; internal</td>
<td>Kai</td>
</tr>
</tbody>
</table>
haemorrhage; symptoms immediate (unconsciousness, vomiting, dizziness)

103  death after 6 h; haemorrhagic lesions  Noe

75  death after 22 h; symptoms at 2 h (cyanosis, (cyanosis, vomiting, dilated pupils); brain haemorrhage, liver damage, nephrosis  Hue

63  death at 91 h; lack of eye reflex to light on 4th day; vomiting; rapid pulse  Roul

63  death in 3 - 4 h; liver damage  Sec

63  death at 17 h; cyanosis, diarrhoea; impaired blood coagulation  Sch

50  death at 24 h; haemorrhage at various sites; signs of cardiac damage  Mar

Table 11 (contd).

<table>
<thead>
<tr>
<th>Amount ingested (g)</th>
<th>Findingsb</th>
<th>Refc</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>death at 28 h; internal haemorrhage</td>
<td>Gar</td>
</tr>
<tr>
<td>37</td>
<td>death at 10 h; internal haemorrhage at various sites; adverse lung effects</td>
<td>Loc</td>
</tr>
<tr>
<td>25</td>
<td>death at 24 h; epigastric pain; slow pulse</td>
<td>Roul</td>
</tr>
<tr>
<td>25</td>
<td>death at 13 h; symptoms at 1 h (cyanosis, vomiting)</td>
<td>Flo</td>
</tr>
<tr>
<td>25</td>
<td>death within 12 h; symptoms not reported</td>
<td>Flo</td>
</tr>
<tr>
<td>19</td>
<td>death after 6 days; liver, kidney, renal damage; pulmonary oedema; hypoglycaemia; clotting time decreased; some haemorrhaging</td>
<td>Yod</td>
</tr>
<tr>
<td>10</td>
<td>death after 56 h; delirium; pulse deterioration</td>
<td>Bog</td>
</tr>
</tbody>
</table>

a  Studies in which doses could not be estimated have not been cited. The NIOSH (1976) for a description of these case reports.

b  Unless otherwise stated, death refers to single male individuals.

c  The reader is referred to NIOSH (1976) for a more complete description of symptoms of central nervous system depression commonly appear within 1 h, frequently with cyanosis, nausea, vomiting, diarrhoea, epigastric and abdominal pains, and irritation of the mucous membranes. Irreversible brain damage has been reported in one case, and brain damage has been found in several fatal cases (Rohmann et al., 1969; Dorndorf et al., 1975). In some of the cases, an interval relatively free of symptoms followed ingestion (Hinkel, 1965; Martin et al., 1968; Komarov et al., 1973; Dorndorf et al., 1975). In the next phase, decreasing consciousness and circulatory and respiratory failure may occur, often leading to death some hours to some days after exposure. During the intoxication, heart rhythm disturbances can lead to
cardiac arrest (Morozov, 1958; Martin et al., 1968; Yodaiken & Babcock, 1973; Andriukin, 1979). Autopsy reports have revealed damage to the mucosae of the gastrointestinal tract, liver, kidney, lung, heart, and brain. Livers can be enlarged. Liver and kidney epithelium can show fatty degeneration and necrosis. Renal insufficiency has been reported to follow development of hepatic insufficiency and has been known to progress to uremic coma (Natsyuk & Mudritsky, 1974). Lung oedema is frequently found. Hyperaemia and haemorrhagic lesions are found in some organs. According to some authors (Martin et al., 1968; Schönborn et al., 1970; Yodaiken & Babcock, 1973), it appeared that the blood coagulation time was increased because of a decrease in blood clotting factors and thrombocytes. These effects appear secondary to liver cell necrosis complicated further by intravascular coagulation. Biochemically, liver damage is illustrated by increased serum levels of bilirubin, transaminases, and lactate dehydrogenase (Martin et al., 1968; Yodaiken & Babcock, 1973; Dorndorf et al., 1975; Andriukin, 1979). Kidney damage is expressed by anuria or oliguria (Morozov, 1958; Bogoyavlenski et al., 1968; Yodaiken & Babcock, 1973) and albumin, leukocytes, and epithelium cells in the urine. Together with the histopathology, this points to acute necrosis of the kidney tubule, possibly as a result of the liver cell necrosis and the changes in circulation (Morozov, 1958; Hinkel, 1965; Yodaiken & Babcock, 1973). Haematological changes include decreases in the erythrocyte count and haemoglobin content (Morozov, 1958; Dorndorf et al., 1975).

8.1.3 Acute effects on eyes and skin

Dysfunction of the central nervous system, which could be caused by brain oedema, can lead to effects on the eyes such as dilation or constriction of the pupils and impairment of eye reflexes (Weiss, 1957; Troisi & Cavallazzi, 1961). Weiss (1957) reported a cloudy cornea in 2 cases of oral exposure; this has also been reported in dogs (section 7.1.2). Conjunctivitis was found in 2 out of 4 patients, who had been exposed to 1,2-dichloroethane vapour (Menschick, 1957). After intermittent immersion of the hands of 3 men in 1,2-dichloroethane for 4 h, severe dermatitis developed (Wirtschafter & Schwartz, 1939).

8.2 Occupational Exposure

Only 2 reports are available, and these date from before 1960. In the first study (Cetnarowicz, 1959), 16 male workers from an oil refinery, exposed for 2 - 8 months, were selected for close examination. A group of 6 workers was exposed to concentrations of between 40 and 150 mg 1,2-dichloroethane/m³ air, and a group of 10 workers was exposed to concentrations between 250 and 800 mg/m³. The workers were also exposed to benzene at levels between 10 and 25 mg/m³, which was considered not significant by the authors. A general reduction in body weight was observed. Complaints came mainly from the group with the higher exposure and included a burning sensation of the eyes, lachrymation, dizziness, lassitude, sleepiness, nausea, vomiting, constipation, poor appetite, epigastric pain, and weight loss. There was no control group, but symptoms reportedly disappeared when workers were removed from exposure; symptoms returned upon re-exposure. Most, but not all, abnormalities were found in the group with higher exposure and involved the liver (8 workers), central nervous system (3 workers), gastrointestinal tract (7 workers), and haematological parameters (1 - 7 workers). No lesions were found in the eye,
respiratory tract, lung, or heart.

The second study (Kozik, 1957), was conducted on workers employed in an aircraft factory using a gum dissolved in 1,2-dichloroethane. No data were given on the composition of the glue or on the employment status of the workers. Air concentrations of 1,2-dichloroethane varied considerably, the level being 5 mg/m³ or less during 70 - 75% of the working time, and 80 - 150 mg/m³ during 25 - 30% of the working time. The morbidity of the workers in this department during the whole period under study (1951-55) was increased for all disease categories in comparison with that in workers in the entire factory. A group of 83 workers was examined further, in the absence of controls. There were 19 workers with diseases of the liver and bile duct, 13 workers with neurotic conditions, 11 workers with autonomous dystonia, and 10 workers with hyperthyroidism and goitre.

These reports are difficult to evaluate, because no indication is given of the prevalence in unexposed workers of the symptoms and signs described in the case studies.

9. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

9.1 Evaluation of Human Health Risks

In spite of the high volume of production of 1,2-dichloroethane, there are no quantitative exposure-effect data on human beings. Frequently, 1,2-dichloroethane is not the only chemical involved in an exposure and thus, cause-effect relationships are difficult to derive. No epidemiological or mortality studies are available. There are only two old reports on small groups of occupationally-exposed men (section 8.2). These data indicate that repeated inhalation exposures in the range of approximately 40 - 800 mg/m³ may lead to central nervous system depression and gastrointestinal and liver abnormalities. As might be expected, such symptoms were more prevalent in individuals exposed to high levels. The only available data regarding oral exposure are those involving fatal intoxications (Table 11, section 8.1).

Because of the limitations of the human data base, it is necessary to rely on the available experimental animal data to derive a no-observed-adverse-effect level for human beings. This is possible because of the similarity in the spectrum of adverse effects in man and laboratory animals, which include central nervous system depression, liver and possibly kidney abnormalities, lung oedema, and cardiovascular disorders. The dose-response data from animal studies include a no-observed-adverse-effect level for the rat of about 400 mg 1,2-dichloroethane/m³ air (section 7.2.1), equivalent to an intake of about 35 mg/kg body weight per day (assuming inhalation of 42 litres over 7 h for a 500-g rat and 100% absorption). The highest registered air exposure level of the general population is 65 µg/m³ (Table 4, section 4.1.2). This level leads to a calculated intake of 1.3 mg per person per day (20 m³/day x 65 µg/m³). A comparable intake from drinking-water containing the highest level recorded (6 µg/litre) (Table 3, section 4.1.1) would amount to a daily intake of 12 µg (6 µg/litre litre/day). Thus, a combined air and water exposure, in the context of a worst-case scenario for the general population, when compared with the no-observed-adverse-effect level for animals, is lower by a factor of well over 1000. Consequently,
for the biological end-points considered so far, it can be concluded that 1,2-dichloroethane is unlikely to present a toxic hazard for the general population, under prevailing exposure conditions.

In an oral administration study, 1,2-dichloroethane produced a statistically-significant increase in squamous cell carcinoma of the forestomach, haemangiosarcoma, and mammary adenocarcinoma in rats, and mammary adenocarcinoma and hepatocellular carcinoma in mice (section 7.4.2). In one carcinogenicity study, inhalation exposure did not result in an increase in tumour incidence (section 7.4.1). The natural occurrence of forestomach squamous cell carcinomas in rats and haemangiosarcomas in laboratory rodents is unusual. Taking into consideration that cancer has been produced in two species of experimental animals and in several target organs, it can be concluded that 1,2-dichloroethane is carcinogenic for rats and mice, when administered by gavage.

In the absence of human data, and taking into account the fact that 1,2-dichloroethane produces a reactive intermediate that alkylates DNA, that it is positive in a number of in vitro mutagenicity tests, though weakly so (section 7.5), and that it results in the production of both rare and common tumours in rats and mice, it would be prudent to consider 1,2-dichloroethane as a possible human carcinogen. Therefore, 1,2-dichloroethane should be regarded, for practical purposes, as if it presented a carcinogenic risk for man. Thus, levels in the environment should be kept as low as feasible.

Since there are no human data, it is necessary to rely on the limited data available from experimental animal studies in evaluating reproduction hazards and teratogenicity. The weight of evidence (section 7.6) does not suggest that exposure to prevailing environmental levels would pose a human reproductive or teratogenic hazard.

9.2 Evaluation of Effects on the Environment

9.2.1 Air

Emissions of 1,2-dichloroethane into the air mainly occur in process industries. Other emissions occur during its use as a fumigant, solvent, and lead scavenger, and via evaporation from contaminated water and from waste disposal sites. Total emissions are estimated to amount to 0.2% of the production volume. Photochemical degradation via oxidation by hydroxyl radicals is the most important route of elimination from air. Rainout and adsorption on atmospheric particles are unlikely to be important processes of elimination. Photolysis is theoretically a possibility, but no evidence of this is available. The products of the photochemical degradation are carbon monoxide, carbon dioxide, hydrogen chloride, formyl chloride, and chloroacetylchloride. The two last compounds will degrade further. The process is rapid enough to prevent accumulation of the compound in the atmosphere (section 3.3).

9.2.2 Water

Emissions of 1,2-dichloroethane into water may amount to 0.1% of the production volume. Some of the emissions from EDC tars, which total about 0.5% of the production volume, will contaminate water. The main process of removal of 1,2-dichloro-
ethane from water is evaporation. Chemical degradation is not expected, nor is biodegradation fast enough to be of any significance (section 3.1). Bioconcentration in aquatic species is unlikely in view of the rather low octanol/water partition coefficient. This conclusion is supported by a low bioconcentration factor found experimentally (section 6.1.4).

The compound was only slightly toxic for aquatic species tested. A no-observed-adverse-effect concentration for Daphnia magna in a long-term test was 11 mg/litre (section 6.1.3). The lowest LC50 value (85 mg/litre) was found for the shrimp Crangon crangon (section 6.1.1). Average environmental levels of the compound in surface water are generally below 1 µg/litre, but, in heavily polluted surface water, average levels of 5.6 µg/litre have been measured with a maximum of 90 µg/litre (Table 3, section 4.1.1).

On the basis of the above data, it can be concluded that, except in case of accidents and inappropriate disposal, 1,2-dichloroethane does not pose a significant hazard for the aquatic environment. However, it should be noted that EDC tars are much more toxic than 1,2-dichloroethane (section 6.1.1).

9.2.3 Soil

Data are not sufficient to evaluate the effects of 1,2-dichloroethane in soil.

10. RECOMMENDATIONS FOR FURTHER STUDIES

1. DNA alkylation (adduct identification).
2. Studies on sub-chronic toxicity using various routes of exposure.
3. Assessment of the extent to which EDC tars contribute to contamination of groundwater by 1,2-dichloroethane.
4. Dose-response studies on sensitive, commercially important fish species (particularly studies relevant to EDC tar spills).

11. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

1,2-Dichloroethane was evaluated by IARC in 1979 (Volume 20 of the IARC Monographs). It was concluded that:

"There is sufficient evidence that 1,2-dichloroethane is carcinogenic in mice and rats. In the absence of adequate data in humans, it is reasonable, for practical purposes, to regard 1,2-dichloroethane as if it presented a carcinogenic risk to humans."

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See Also:

- **Toxicological Abbreviations**
- Dichloroethane, 1,2- (EHC 176, 1995, 2nd edition)
- Dichloroethane, 1,2- (FAO Nutrition Meetings Report Series 48a)
- Dichloroethane, 1,2- (WHO Food Additives Series 30)
- Dichloroethane, 1,2- (WHO Pesticide Residues Series 1)
- Dichloroethane, 1,2- (Pesticide residues in food: 1979 evaluations)
- Dichloroethane, 1,2- (CICADS 1, 1998)
- Dichloroethane, 1,2- (IARC Summary & Evaluation, Volume 71, 1999)